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Conference **Abstracts**

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Oral Presentations

1

A Comparison of Overall Obesity and Abdominal Adiposity in Predicting the Risk of Mortality Among US Adults

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Background: While numerous studies have examined the relation of overall obesity with mortality, few have included measures of abdominal adiposity, and none, to the best of our knowledge has included a nationally representative sample of US adults. **Methods:** We compared the prospective relation of BMI and measures of abdominal adiposity (i.e., waist circumference and waist-to-hip ratio) with the risk of total and cause-specific mortality in 5,799 men and 6,429 women in the third National Health and Nutrition Examination Survey cohort, aged 30–102 years at enrollment in 1988–1994. **Results:** During 12 years of follow-up, we documented 1,188 total deaths in men and 925 in women. In middle-aged adults (30–64 years), BMI exhibited a U-shaped relation with total mortality in men and a J-shaped association in women, while a positive association of waist-to-hip ratio with total mortality was observed in women (p_{trend}=0.003), but not in men (p_{trend}=0.2). Compared to BMI, abdominal adiposity was more strongly associated with the risk of death due to cardiovascular disease in middle-aged men and women. In older adults (65–102 years), BMI and waist circumference were each *inversely* associated with total mortality, largely attributed to death from respiratory disease in older men and cardiovascular disease in older women. **Conclusions:** The relation of adiposity with mortality appears to be modified by age, with abdominal adiposity providing a better health indicator of the risk for death from cardiovascular disease than BMI among middle-aged adults.

2

Effect of a School-Based Obesity Prevention Intervention on Body Mass Index and Nutrition in Inner-City, Multiethnic Preschool Children

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Background. Obesity continues to be a major public health problem and at increasingly younger ages. Efficacious early childhood health education programs to prevent the onset of obesity could be a useful strategy to prevent associated chronic disease onset. **Methods.** Eight subsidized childcare centers in Miami Dade County, FL were randomly assigned to either the intervention (N = 6) or attention control arm (N = 2). Center study eligibility criteria included: 1) > 30 2–5 year olds attending, 2) ethnically diverse, and 3) low-income families attending. Anthropometric, nutrition and physical activity data were collected at baseline, 3- and 6-month intervals and included waist circumference and body mass index (BMI), a modified version of the National Health and Nutrition Examination Survey (NHANES) and 24-hour dietary recalls to assess nutritional status. **Results.** The sample was 57% Hispanic and 21% black. Baseline to 6-month follow up analysis of changes in overall BMI percentiles showed (1) the percent who were normal weight at baseline (68.4%, N=212) increased to 73%, (N=137) at follow-up, (2) those at-risk for overweight (≥ 85th -<95th %ile for age) decreased from 16% (N=50) to 12% (N=23), and (3) those who were obese (≥ 95th %ile) decreased slightly from 15.5% to 14.9%. Baseline to 3-month/midpoint nutritional analysis showed that children in the intervention sites ate less junk food, more fresh fruits and vegetables, and drank less juice and more 1% milk compared to control sites. Specifically, (1) mean chip consumption decreased from daily to no consumption, (2) mean cookie consumption decreased 50%, (3) mean fresh fruit and vegetable consumption increased 25%, (4) juice consumption decreased 50%, and was replaced with a 20% increase in water consumption, and (5) 1% milk consumption increased 20%. In the control sites, cake and cookie consumption increased 35% and 75%, respectively, while mean fresh fruit and water consumption decreased. **Conclusions.** Designing health-education interventions to prevent childhood-onset obesity for the childcare setting may be an effective strategy to promote healthier eating habits and maintain healthy weight in this age group.

3

Prevalence of Left Ventricular Diastolic Dysfunction in Morbidly Obese Patients and Impact of Weight Loss Following Bariatric Surgery

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Obesity is an important risk factor for cardiovascular morbidity and mortality. Although obesity has been associated with left ventricular diastolic function (LVDD), there is paucity of data regarding the prevalence of LVDD among morbidly obese patients and the impact of weight loss following bariatric surgery is not well described. **Objective:** To determine the prevalence of LVDD in morbidly obese patients and the impact of bariatric-induced weight loss on LVDD. **Methods:** Sixty-height morbidly obese patients were recruited and 15 of them were evaluated at 6-month follow-up after bariatric surgery. Diastolic function was assessed with echocardiography including tissue Doppler assessment. **Results:** Among the 68 morbidly obese patients, 23 (34%) had normal left ventricular diastolic function, 22 (32%) had spontaneous LVDD and 23 (34%) had a pseudonormal pattern of ventricular filling. Therefore 66% (45 of 68) of our morbidly obese patients presented some degree of LVDD. Systolic function was normal in all subjects. Fifteen subjects had completed 6 months post surgery visit. Anthropometric data are presented below. Among the 15 patients, 3 had normal diastolic function, 5 (33%) had spontaneous LVDD and 7 (47%) a pseudonormal pattern of ventricular filling before surgery. At 6 months following surgery, 10 (67%) had normal diastolic function, 3 (20%) had spontaneous LVDD and 2 (13%) a pseudonormal pattern of ventricular filling. **Conclusion:** The presence of LVDD is high among morbidly obese patient and our preliminary data following bariatric surgery suggest an improvement and even a normalisation of LVDD in a significant proportion of patients.

N=15	Baseline	6 months post-op	P value
Weight (kg)	131,2 ± 20,9	95,1 ±14,1	<0,001
BMI (kg/m^2)	51,1 ± 6,4	37,3± 5,9	<0,001
Weight loss (kg)		36,1 ± 11,7	
% Initial weight loss (%)		27,2 ± 5,9	

4

Trends in Mortality Among Women and Men with and Without Diabetes in the Framingham Heart Study

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Background: Over the past several decades there has been a marked decline in all-cause mortality. A recent analysis of NHANES data, using self-reported diabetes (DM) status, suggested that women with DM have experienced an increase in mortality rates over time as compared to their male counterparts. Therefore, the objective of our study was to examine the change in all-cause mortality rates over time among women and men with DM relative to those without DM. **Methods:** Participants from the Framingham Heart Study, aged 45–64, who attended examinations during the "early" period (1950–1975) and the "late" period (1975–2001) were included in this analysis. Participants were considered to have DM if they had a casual glucose ≥200 mg/dL, fasting plasma glucose ≥126 mg/dL, or treatment. Cox proportional hazards models were used to calculate relative risks (RR) and 95% confidence intervals (CI). **Results:** A total of 839 deaths and 123,940 person-years of follow-up were included in the analysis (Table). Among women, the age-adjusted RR comparing DM to non-DM was 3.5 in the early period and 2.5 in the late period. The RR comparing the late to the early period was 0.6 for women without DM and 0.4 for women with DM. Similar results were observed for men (Table). The formal test for interaction between DM and sex was not significant (p=0.14 for the early period; p=0.34 for the late period). **Conclusion:** Among both women and men with and without DM, significant reductions in all-cause mortality have occurred over time. However, the mortality rates among individuals with DM still remain approximately 2-fold higher as compared to individuals without DM.

	Early Period (1950–1975)			Late Period (1975–2001)			
	# Deaths	# P-Y	Mortality Rate*	# Deaths	# P-Y	Mortality Rate*	RR** (95% CI)
WOMEN							
DM-	173	35,434	4.9	88	29,088	3.0	0.6 (0.4–0.8)
DM+	22	1,091	20.2	15	1,741	8.6	0.4 (0.2–0.8)
RR (95% CI)**			3.5 (2.2–5.5)			2.5 (1.4–4.3)	
MEN							
DM-	296	27,829	10.6	176	25,137	7.0	0.6 (0.5–0.7)
DM+	34	1,195	28.5	35	2,425	14.4	0.5 (0.3–0.8)
RR (95% CI)**			2.2 (1.6–3.2)			1.7 (1.2–2.5)	

* Mortality rate per 1000 P-Y ** Adjusted for age (years)

5

Associations of Skeletal Muscle Morphology with Serum Adiponectin in a Community-Based Sample

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Background: Adiponectin has been suggested to mediate skeletal muscle insulin resistance, but the potential relation between skeletal muscle morphology and circulating adiponectin has not been evaluated in a community-based sample. **Methods:** We measured serum adiponectin and obtained muscle biopsies from the vastus lateralis muscle in 505 men aged 70, participants of the community-based Uppsala Longitudinal Study of Adult Men (ULSAM). Insulin sensitivity (insulin-mediated glucose disposal) was measured with the euglycemic insulin clamp technique. Capillary density and muscle fiber composition were determined with the use of computerized image analysis and related to serum adiponectin (dependent variable) using linear regression models. **Results:** Capillary density (β, 0.43 per 1-standard deviation (SD); P=0.022) and proportion of type I muscle fibers (slow oxidative, used for e.g. long distance running; β, 0.48 per 1-SD; P=0.010) were positively associated with serum adiponectin, whereas proportion of type IIb fibers (fast-twitch glycolytic, used for e.g. sprinting) were inversely associated (β, -0.52 per 1-SD; P=0.005). The mean adiponectin concentrations were 10.6, 9.7, and 8.7 mg/L when type I, type IIa (fast oxidative-glycolytic, used for e.g. middle distance running), and type IIb fibers was the major fiber type, respectively (P for trend=0.001).

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When adding body mass index and leisure time physical activity to the models, capillary density was no longer associated with adiponectin (P=0.29), whereas major fiber type still was a strong determinant of adiponectin concentrations (P=0.004). Additional adjustment for glucose disposal rate (insulin sensitivity) weakened the association of major fiber type with serum adiponectin (mean adiponectin concentration, 10.6, 9.9, and 9.3 mg/L; P for trend=0.027). **Conclusions:** In our large community-based sample, examined with muscle biopsies and a gold standard insulin sensitivity technique, circulating adiponectin concentrations were higher with increasing skeletal muscle capillary density and in individuals with higher proportion of muscle fibers of slower type. These associations were partly accounted for by insulin sensitivity, indicating a common pathophysiological pathway.

6

RANTES/CCL5 Gene Polymorphisms, Serum Concentrations, and Incident Type 2 Diabetes: Results from the MONICA/KORA Augsburg Case-Cohort Study, 1984–2002

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Background: RANTES (regulated on activation, normal T-cell expressed and secreted)/CCL5, a chemokine which is expressed by adipocytes, has been hypothesized to be involved in leukocyte infiltration of adipose tissue in obesity. The aim of this study was to analyze whether RANTES may be involved in the pathogenesis of type 2 diabetes by investigating the triangular relationship between CCL5 gene polymorphisms, RANTES serum levels and the risk for type 2 diabetes mellitus (T2DM) in the population-based MONICA/KORA case-cohort study. Methods: RANTES serum concentrations (ELISA, R&D Systems) were determined in 502 individuals with incident T2DM and 1,632 individuals without T2DM during follow-up (mean follow-up time 10.1±4.9 years). Six single nucleotide polymorphisms (SNPs) were genotyped within the CCL5 gene (promoter: rs2107538 [-403G>A], rs2280788 [-28C>G]; intronic: rs2280789, rs4796120, rs3817655; 3'-flanking region: rs1065341). Results: Minor alleles of rs2280788, rs2280789, rs4796120 and rs3817655were associated with lower serum levels (P additive between 1.2x10 -9 and 3.1x10 -8). When compared with the lowest RANTES quartile, higher RANTES concentrations were not associated with significantly increased risk to develop type 2 diabetes during follow-up. Finally, no association was found between six CCL5 SNPs or CCL5 haplotypes and incident T2DM neither in crude nor in the fully-adjusted models. Conclusion: Although several CCL5 minor alleles were strongly related to decreased RANTES levels, neither CCL5 genotypes nor RANTES concentrations were associated with the risk for T2DM.

7

Non-High-Density-Lipoprotein Cholesterol and Cardiovascular Risk Factors Among Adolescents with and Without Impaired Fasting Glucose

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To evaluate the impact of IFG on the association of non-HDL cholesterol (equal to total cholesterol - HDL cholesterol) with CV risk factors among adolescents, we pooled 2,758 adolescents (1,424 males and 1,334 females) aged 12 - 19 years from three data sets of the National Health and Nutrition Examination Survey (NHANES 1999, 2001, and 2003), who had no self-reported history of physician diagnosed diabetes and fasted overnight (>8 hrs) and had no missing information of plasma glucose and lipids profile for this analysis. IFG was defined as fasting glucose level >100 mg/dL. Age-specific cut-off points were used for CV metabolic risk factors including higher levels of triglycerides (TG), waist circumference (WC), blood pressure (BP), and lower level of HDL cholesterol. The clustered metabolic CV risk was defined as any two of the four CV metabolic risk factors and obesity was defined as BMI-z score >0.85. In general, the level of non-HDL cholesterol was positively associated ($p<.05$) with BMI, girth measurements, systolic BP, and all lipids protein cholesterol except for HDL cholesterol, which had a negative association. Approximately 10.2% of adolescents had IFG, but their non-HDL cholesterol levels were much higher than those adolescents without IFG (121.4 vs. 110.1 mg/dL, $p<.05$). Using multiple regression model to adjusted for age, gender, race, family income, smoking status, physical activity, BMI, and LDL cholesterol, we observed that the level of fasting glucose was significantly associated with the level of non-HDL cholesterol (regression coefficient 0.12, $p<.01$). If high non-HDL cholesterol was defined as the gender-specific levels higher than the 3nd quartile of non-HDL cholesterol, then those with IFG and high non-HDL cholesterol had 7-fold higher odds of being with the clustered metabolic CV risk and approximately 4-fold higher odds of being obese compared to those without IFG and a low level of non-HDL cholesterol ($p<.001$). Those results suggest that the non-HDL cholesterol level is an important indictor in monitoring CV risk among adolescents with IFG.

8

A National Survey of the Effectiveness of the KID-FIT Program in Altering Children's Fitness and Knowledge About Health-Related Behavior and Nutrition

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Purpose: The present study was conducted to examine the physical fitness and health knowledge benefits for Kindergarten age children participating in KID-FIT, a preschool physical education program. **Background/Significance:** Although children's fitness levels continue to decline and childhood obesity is on the rise, few programs have been identified as interventions that work to address the above concerns **Methods:** This pre-post study recruited 824 Kindergarten and Grade 1 public school children. Fitness level was determined by a 5-part P.E. assessment recording measures of strength, flexibility, endurance, balance and sports skills. Health knowledge was measured by a 28-item questionnaire using illustrations for identification and recall, and a series of 3 drawings done by each child of their internal organs, and healthy and harmful behavior that also allowed for an examination of their cognitive development. All of the children were given the pre-test at the beginning of the school year, but only the Kindergarten students were exposed to the KID-Fit program and tested again at the end of the school year. The data was analyzed first with ANOVA and then Tukey's tests as appropriate. **Results:** A significant improvement in physical fitness and in objective health related knowledge was found in Kindergarten children by the end of the study. These improvements placed them at a level significantly above the Grade 1 controls. The KID-FIT program did not affect the children's cognitive development which showed age appropriate progression during the study. **Conclusions:** The KID-FIT program appears to be an effective intervention for helping small children learn healthy lifestyle habits while increasing their physical fitness abilities. Whether these improvements persist, and any other health benefits occur in the children exposed to the KID-FIT program will require further study. For more details, contact Michele Silence: michele@kid-fit.com

PHYSICAL FITNESS LEVEL

	Kindergarten Pre	Kindergarten Post	Grade 1 Post
No. of Students	241	240	340
Mean	69.98	80.43	70.12
Standard Error	1.14	.954	1.042

Fitness significantly improved

9

Determinants of Older, Urban African Americans' Neighborhood Walking

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Physical inactivity is a risk factor for cardiovascular disease, and is higher in ethnic and racial minorities, older adults, and lower SES groups. Walking is the most common type of physical activity (PA) chosen by older adults. It is unclear how characteristics of the neighborhood environment influence walking in older, African American urban adults. Purpose: To identify characteristics of the neighborhood environment which encourage or discourage walking in older, urban African American adults. Methods: A convenience sample of African Americans aged 60 years and older was recruited from a Midwestern urban senior center. Data were collected using focus groups and Photovoice to help identify neighborhood environmental walking determinants. For Photovoice, participants took pictures of the characteristics in their neighborhood that promoted or inhibited walking. The pictures were used to facilitate focus group discussions. Focus group data collection continued until saturation of responses was reached. Experts evaluated the responses and themes to assure content validity. Results: Twenty-one participants (2 male & 19 female; 9 walkers & 12 non-walkers), aged 61 to 85 years (mean = 70.7) were enrolled. The themes of environmental determinants of neighborhood walking that emerged included: pleasant objects to observe while walking such as greenery, wildlife, parks, and water; presence of others in the immediate vicinity; safety from crime; weather; presence of a track or trail and places to rest, eat, or use the bathroom; adequate lighting; loose dogs; vacant lots; abandoned buildings; obstacles in the walking path; and sidewalk maintenance. Walkers reported using strategies to overcome barriers such as walking early in the day, walking with a partner, and combining walking with stops such as restaurants. Conclusions: Several important determinants for walking and strategies for managing barriers emerged for this sample. This study begins to examine strategies to overcome environmental barriers that can be used to increase walking. Further research is needed to identify which environmental characteristics are most salient and determine the effective strategies used by older, urban African American adults to walk in their neighborhoods.

10

Sedentary Activity Is Independently Associated with Endothelial Dysfunction

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Introduction: Individual sedentary activities such as television viewing are associated with increased cardiovascular risk. However, there is limited literature regarding the role of total sedentary activity and specific sedentary activity in cardiovascular risk or the physiological mechanisms through which this risk occurs. The effect of physical activity on cardiovascular risk has been researched and reported; however, sedentary activity is not simply the inverse

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of physical activity. Therefore, studies of the association between total and specific sedentary activities and cardiovascular risk factors are needed to assess the independent effects of sedentary activity on cardiovascular risk. **Hypothesis:** Increased sedentary activities are associated with markers of cardiovascular risk. **Methods:** Using the validated Seated Activity Scale, a nine item questionnaire that we developed to determine total and specific time spent in sedentary activities, a group of 73 participants were assessed for sedentary behaviors. Postischemic flow mediated vasodilation, lipids, HOMA, QUICKI, WHR, BP, and Framingham risk scores were also determined. Regression analysis was used to determine correlations between these cardiovascular risk factors and total sedentary activity. **Results:** The Seated Activity Scale had a test-retest reliability of r=0.68 (p<0.0001) and a correlation with patient-recorded activity logs of r=0.66 (p<0.0001). Total sedentary activity was positively correlated with BMI (r=0.24; p=0.04), Framingham risk score (r=0.26; p=0.03), and minimum forearm vascular resistance (r=0.28; p=0.02), and negatively correlated with the ratio of postischemic to baseline forearm blood flow (r=-0.26; 0.03). No other correlations were significant. **Conclusions:** Sedentary activity is associated with impaired endothelial function and greater BMI. This may identify some of the physiological mechanisms through which sedentary behaviors increase cardiovascular risk.

11

Patterns of Physical Activity Among Overweight and Obese Adults

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Little is known about patterns of physical activity in overweight and obese adults, although these are groups at high risk for chronic disease and premature mortality and can clearly benefit from regular physical activity participation. This study describes daily and weekly patterns of minutes spent in moderate to vigorous physical activity (MVPA) and in 10-minute MVPA bouts using an objective measure of physical activity, accelerometry, in a large sample of overweight and obese individuals. Overweight (body mass index [BMI] 25 - 29.9 kg/m2) and obese (BMI > 30.0 kg/m2) participants (n=1648; 67% female, 43% African American) undergoing screening procedures for the multi-center Weight Loss Maintenance trial wore RT3 accelerometers for at least three weekdays and one weekend day. Time in moderate, vigorous, and MVPA was determined overall, by weekend versus weekday, and by time-of-day (morning, afternoon, evening). Minutes of MVPA that occurred during at least a 10-minute bout of sustained MVPA also was assessed. Results show that participants engaged in 15.8 ± 22.5 daily minutes of MVPA. Among those engaging in sustained 10-minutes bouts of MVPA, the mean number of MVPA minutes per bout was 33.3 ± 26.2 minutes. Daily minutes of MVPA was significantly greater for those less than 50 years of age, male, non-African American, and overweight compared with those older, female, African American, and obese. MVPA was more likely to occur on weekends compared with weekdays (16.0 ± 25.9 vs 15.8 ± 20.9 minutes; p = 0.003) and in the mornings compared with afternoons and evenings (8.3 ± 15.3 vs 7.6 ± 13.8 vs 3.1 ± 8.3 minutes, respectively; p < 0.0003). Approximately 25% of study participants met national physical activity guidelines for health. Only 2% met guidelines for weight maintenance. These results demonstrate that there are demographic and weight status differences in physical activity even when measured using accelerometry. Weekend mornings may be an opportune time segment to promote additional minutes to meet national recommendations.

12

Dietary Patterns Predict Subsequent Coronary Heart Disease Risk in Postmenopausal Women: The Women's Health Initiative Observational Cohort Study

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Background: Evidence suggests that dietary patterns predispose to the development of coronary heart disease (CHD). The relationship between dietary patterns and CHD risk was assessed in postmenopausal women participating in the Women's Health Initiative Observational Study (WHI-OS). Methods: Case-control study, matching criteria were age, date of enrollment, race/ethnicity and absence of CHD at baseline. A total of 2448 women with complete dietary data were studied, 1224 cases with centrally confirmed CHD, fatal or non-fatal MI, and 1224 controls free of CHD or MI, angina, CABG/PTCA, CHF, stroke or peripheral vascular disease. Baseline data for 43 nutrient/food intakes from the WHI Food Frequency Questionnaire were analyzed. Subjects were clustered into groups based on constructed principal components analysis using K-mean method. CHD risk was compared across the groups based on odds ratios using conditional logistic regression. Results: The first five principal components accounted for >60% of the variance in the 43 nutrient/food group intakes of the cases and controls. Three major eating patterns (groups) were formed driven mainly by the value of the first principal component, a weighted sum of the 43 nutrient/food intakes. Using cluster 2 (n=1122) as the reference group, the odds ratio of CHD for clusters 1 (n=674) and 3 (n=652) were 1.27 and 0.76, respectively (p <0.01). Comparisons of the average intakes and risk of CHD among the three dietary patterns are shown in the table. Conclusion: In this case-control study of free-living postmenopausal women participating in the WHI-OS, distinct dietary patterns reported at baseline were associated with subsequent CHD risk. The pattern associated with lowest risk (group 3) was characterized by a diet rich in vegetables, fruits and fish, and is consistent with current dietary recommendations for CHD prevention.

DIETARY PATTERNS AND SUBSEQUENT CHD RISK

Food or Nutrient	Group 1 (n=674)	Group 2 (n=1122)	Group 3 (n=652)
CHD (Odds Ratio)	1.27	1 (reference)	0.76
Energy (kcal)	1756	1614	1343
Total Fat (g/1000 kcal)	45.7	33.4	23.7
Total Fiber (g/1000 kcal)	7.8	10.3	14.8
Vegetable Protein (g/1000 kcal)	10.7	12.5	15.9
Red Meat (Servings/1000 kcal)	0.6	0.4	0.2
Fish: dark fish or tuna (servings/1000 kcal)	0.06	0.07	0.11
Deep Yellow/Green Vegetables (servings/1000 kcal)	1.0	1.3	2.1
Deep Yellow/Orange, Citrus and Blue-Red Fruits (servings/1000 kcal)	0.7	1.0	1.4
Folate Equivalents (ug/1000 kcal)	256	315	393
Total Carotenoids (ug/1000 kcal)	5204	6664	10979
Dietary Calcium (mg/1000 kcal)	419	545	627
Dietary Vitamin D (ug/1000 kcal)	2.4	2.9	3.3
Dietary Vitamin K (ug/1000 kcal)	51	54	89
DHA (22:6n-3)(g/1000 kcal)	0.04	0.05	0.07

13

Linoleate-Rich Diet Preserves Mitochondrial Respiratory Capacity and Systolic Function in the Failing Heart: Role of Cardiolipin

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Cardiac mitochondrial respiratory dysfunction may contribute to the pathogenesis of heart failure (HF). Cardiolipin (CL) is a dimeric mitochondrial phospholipid that is essential for optimal mitochondrial energy metabolism. In the healthy human and rat heart, ~77–80% of CL species contain four linoleate acyl chains (L_4CL), which are important for its support of mitochondrial respiratory function. Cardiac L_4CL levels decrease in humans and animal models of HF, which may contribute to the mitochondrial dysfunction and metabolic stress observed in the failing heart. Recent work in our laboratory has shown that dietary supplementation with linoleate (high-linoleic safflower oil, 10% w/w; HLSO) restores cardiac L_4CL and prolongs life in aged spontaneously hypertensive heart failure (SHHF) rats. In the present study, we examined the effects of HLSO feeding on cardiac CL, mitochondrial respiratory capacity, and left ventricular (LV) function when administered during compensated LV hypertrophy (5–15 mo of age; LVH) and decompensated HF (21–22 mo of age; DCM) in SHHF rats. In rats fed a standard chow diet, cardiac L_4CL levels decreased from near normal levels in LVH (74% of total CL species) to 54% of total CL in DCM ($P < 0.001$). HLSO increased L_4CL in both LVH (to 83% of total CL) and DCM (to 65% of total), and increased mRNA expression of L_4CL biosynthesis enzymes, indicating that linoleate may increase L_4CL levels by incorporating directly into CL and/or by upregulating biosynthesis. State III mitochondrial respiration rate (mitoVO_2) decreased 38% from LVH to DCM, and was 70% restored by HLSO administration in the DCM period ($P < 0.01$). Interestingly, HLSO had no effect on mitoVO_2 during the LVH period, suggesting that increasing L_4CL to above normal levels does not augment respiratory capacity. LV fractional shortening decreased 27% during the LVH period and 23% during DCM in rats fed the standard diet. HLSO significantly preserved LV function during both phases, and correlated closely with L_4CL levels ($r = 0.59$; $P < 0.05$). In summary, a HLSO-supplemented diet preserves mitoVO_2 and LV systolic function in decompensated HF, which may result from a restoration of cardiac L_4CL. The HLSO diet also appears to preserve LV function in LVH by mitoVO_2-independent mechanisms.

14

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15

A Priori-Defined Dietary Patterns and Markers of Cardiovascular Disease Risk in the Multi-Ethnic Study of Atherosclerosis

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Objective: We determined the cross-sectional associations between two unique a priori-defined dietary patterns and traditional and novel cardiovascular disease (CVD) risk factors. **Methods**: At the baseline exam, diet (by food frequency questionnaire), markers of inflammation and subclinical atherosclerosis, and other traditional CVD risk factors were measured in 5,089 men and women, 45–84 years of age without clinical CVD or diabetes from the Multi-Ethnic Study of Atherosclerosis (MESA). We defined a Comprehensive Healthy Dietary Pattern by summing quartile ranks of 36 narrowly-defined food groups (21 rated favorably and 15 rated unfavorably with quartile ranks reversed). We also defined a Simplified Healthy Dietary Pattern composed of 3 favorable (whole grains, fruit, nuts/seeds) and 3 unfavorable food groups (added fats/oils, processed meats, fried potatoes) using similar scoring techniques. We further calculated the difference between the Comprehensive and Simplified scores. **Results**: Chinese scored higher, and Blacks lower, than Whites or Hispanics on the Comprehensive Healthy Dietary Pattern. After adjustment for demographic and lifestyle characteristics, the Comprehensive pattern was associated with lower levels of inflammatory markers (c-reactive protein, interleukin-6, homocysteine, fibrinogen, $p<0.001$–0.046), urinary albumin:creatinine ratio ($p=0.004$), common carotid intima-media thickness (IMT; $p=0.005$), triglycerides ($p=0.005$), insulin ($p<0.001$), and measures of adiposity ($p<0.001$). The magnitudes of most associations with these outcomes were similar between the comprehensive and simplified dietary patterns, but some unique information remained in the difference between scores. The Comprehensive Healthy Dietary Pattern contributed significantly beyond the Simplified Healthy Dietary Pattern with respect to IL-6, HDL-C, and insulin ($p<0.001$). Neither dietary pattern was associated with blood pressure, coronary artery calcium, internal carotid IMT, or ankle:brachial index. No race/ethnicity or sex interaction was seen with dietary patterns. **Conclusions**: While many food groups likely contribute to associations with CVD risk markers, much of the information in MESA was contributed by only 6 food groups.

16

Medium Chain Triglyceride Consumption Leads to Improved Weight Loss Relative to Olive Oil Without Adversely Affecting Cardiovascular Disease Risk Factors

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Medium chain triglycerides (MCT) have been shown to enhance energy expenditure and potentially lead to better weight control than fats rich in long chain triglycerides. However, concerns regarding their cardiovascular health effects have blunted enthusiasm for their inclusion in weight loss diets. The objective of this study was to compare the effects of weight loss diets supplemented with MCT oil or olive oil for 16 weeks on body composition and cardiovascular disease risk factors. A total of 31 overweight men and women completed the study (age [X $\pm$ SEM] 37.0 $\pm$ 1.4 y; body mass index 29.8 $\pm$ 0.4 kg/m^2). Subjects underwent weekly group weight loss counseling with a dietitian to reduce energy intakes to 1500 kcal/d for women or 1800 kcal/d for men. The weight loss diet recommended the adoption of a low energy density diet and healthy eating. All subjects consumed 10 g of oil/d in muffins and an additional 8 g/d (women) or 14 g/d (men) in the form of liquid oil. As a result, subjects consumed approximately 12% of their weight loss energy prescription in the form of study oil. Body weight and waist circumference were measured weekly. Body composition was assessed by dual energy X-ray absorptiometry (DXA) and computed tomography (CT) at 0 and 16 weeks and fasting lipids, insulin, and glucose were measured at 0, 8, and 16 weeks. Subjects in the MCT group lost more weight than those in the olive oil group (-3.77 $\pm$ 0.54% versus -1.73 $\pm$ 0.56%, $P = 0.011$) and had a reduction in % fat mass (-1.46 $\pm$ 0.44, $P = 0.0045$). There was no difference between groups in change in waist circumference or body composition sub-compartments assessed by DXA and CT. There was no time by diet interaction on any of the metabolic parameters studied after controlling for body weight but there was a significant effect of time on glucose ($P = 0.0177$) and total cholesterol ($P = 0.0386$) concentrations, and on diastolic blood pressure ($P = 0.0413$). Our results show that MCT, when consumed as part of a weight loss diet, can enhance the degree of weight loss achieved and can do so without adversely affecting cardiovascular disease risk. MCT oil can therefore be safely advocated as an adjunct for weight loss in dietary management of overweight and obesity.

17

The Paradox of Low Triglycerides and High CVD Risk in Blacks: Steps Toward a Resolution Through Nutritional Interventions, Apo C-III and ApoE

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Blacks have lower plasma triglycerides (TG) than whites, yet have a higher incidence of CVD. In the general population, low TG indicates a lower concentration of highly atherogenic VLDL and LDL containing apolipoprotein C-III, which predicts CVD more strongly than TG. ApoC-III impairs clearance from plasma of VLDL and LDL, and has direct pro-inflammatory, pro-atherogenic effects on vascular cells. We compared types of VLDL and LDL in blacks and whites (N~50 each) during self-selected dietary intake and after 6 weeks of controlled intake of three healthy DASH-based diets rich in either carbohydrate (CARB), unsaturated fat (UNSAT), or protein (PROT) in the OMNI-HEART trial. Compared with whites, blacks had lower TG not only during their own diet (mean 117 vs 145 mg/dl, $p=0.04$) but during each of the controlled diets (10–16% lower). The study diets reduced TG in whites more than blacks bringing whites closer to the low means of blacks. Blacks had lower apoC-III concentrations in total plasma (25%, $p=0.01$) and in VLDL and LDL (43% and 22%, both $p<0.01$) on their own diet and on the controlled diets (CARB 30% and 25%, UNSAT 44% and 31%, PROT 29% and 19%, all $p<0.05$). For the same level of plasma TG, blacks compared to whites had lower apoC-III concentrations. These findings were confirmed in multiple variable analysis controlling for age, gender, BMI, HOMA index of insulin resistance, and recruitment center. In contrast, Blacks had higher apolipoprotein E levels than whites. ApoE accelerates the clearance of VLDL from plasma. In summary, differences in dietary intake do not explain low TG and apoC-III in blacks compared to whites. Low apoC-III and high apoE favors rapid clearance of TG-rich lipoproteins from plasma and may be a mechanism for low TG in blacks. This should be protective against CVD. However, the fact that blacks suffer a higher incidence of CVD despite a more favorable lipoprotein profile indicates either hyper-responsiveness to these lipid risk factors or that other nonlipid factors playing a stronger role.

18

Effect of Different Doses of Physical Activity on Quality of Life in Overweight, Sedentary, Postmenopausal Women

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Objective: To examine changes in measures of health-related quality of life (QOL) in 430 women who participated in 6 months of supervised exercise training at three different exercise doses versus a no exercise control group. **Method and Results:** Overweight and obese, sedentary women [mean age (SD): 57.4 (6.5) y] were randomly assigned to one of three exercise groups: 4 kcal/kg/wk (n= 147), 8 kcal/kg/wk (n= 96), or 12 kcal/kg/wk (n= 95) or a no-exercise control group (n= 92). QOL was measured at baseline and following the 6 month intervention using the Medical Outcomes Study Short-Form 36 Health Status Survey (a self-administered 36-item questionnaire). In a multivariable analysis adjusted for baseline score, ethnicity, age, education, smoking, antidepressant use and history of depression, all three exercise groups had significant ($p<0.05$) improvements in social functioning compared to the control group. The 4- and 12- kcal/kg/wk group had significant improvements in 3 additional dimensions including general health, vitality, and mental health. Only the 12-kcal/kg/wk group also had improvements in physical functioning, role limitations due to physical problems and role limitations due to emotional problems. No group reported a change in bodily pain. **Conclusion:** In this population of women, our data show a positive association between 6 months of exercise and QOL. This association was strongest among the group receiving the highest dose of exercise, which was 150% of the NIH Consensus Development Panel recommended physical activity dose.

19

Blood-Based Gene Expression Signatures Distinguish Exercise Training Regimens

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Purpose: Peripheral blood gene expression patterns or "signatures" have been used to distinguish and predict complex disease states such as kidney disease and atherosclerosis. It is unknown whether blood-based gene expression patterns can also distinguish 'lifestyle traits'. The purpose of this pilot study was to explore if distinct gene expression signatures are detectable for a) pre- vs. post-exercise status and b) mode of exercise in peripheral blood messenger ribonucleic acid (mRNA). Methods: Following informed consent, we collected fasting peripheral blood samples via venipuncture from a subset of 20 subjects participating in the Studies of a Targeted Risk Reduction Intervention through Defined Exercise II (STRRIDE II), a randomized controlled clinical trial of a six-month structured exercise program. Subjects were randomized to aerobic training (AT), resistance training (RT), or both AT and RT. Blood was collected at true baseline (pre) and at the end of training (post), using PaxGene RNA tubes. RNA was extracted using the Versagene RNA Purification Kit (Gentra Systems Inc.) and globin reduced with the GLOBINclear (Ambion) protocol. Affymetrix GeneChip one-cycle in vitro transcript labeling protocol produced cRNA probes. The probes were hybridized to the Affymetrix U133 2.0 Plus Human microarray chip. Data were imported into RMA, background-corrected, log2 transformed and median normalized. Gene signature scores represent a numeric composite of the magnitude/direction of change for the expression signal intensities of the 49 most influential genes.Findings: Gene signatures were composed of the top 49 genes unique to each group. Heat map and scatter plot data show distinct gene expression signatures for a) pre- and post-exercise regimen, and b) for the type of exercise in which they participated (AT, RT, or both).Discussion: This pilot study provided evidence for 1) clinically-obtained peripheral blood detection of unique gene expression signatures for mode of exercise, 2) candidate genes that may be important in exercise physiology and training, and 3) the future ability to "control for" exercise in future genetic studies using expression signatures. Our next step is validation of these gene signatures with future samples from STRRIDE II.

20

Oral Health, Inflammatory Markers, and Lifestyle Factors in a Diverse Population Eligible for the Primary Prevention of Cardiovascular Disease

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Background: Epidemiologic data have documented an association between oral health and cardiovascular disease (CVD) and between inflammation and CVD, but the interrelation among

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these factors is not fully understood. The purpose of this study was to characterize associations between lifestyle factors, inflammatory markers, and oral health status in a diverse population eligible for the primary prevention of CVD. **Methods:** Participants in the NHLBI **F**amily **I**ntervention **T**rial for **Heart** Health (**F.I.T. Heart**) (n=501; mean age 48 ± 13.5y; 36% non-white; 66% female) completed assessment of 1) oral health and demographics by standardized questionnaires, 2) high sensitivity c-reactive protein (hsCRP), and lipoprotein-associated phospholipase A_2 (Lp-PLA_2) by venous blood analyzed using validated methods, 3) traditional CVD risk factors assessed by standardized methods, and 4) dietary intake evaluated by Gladys Block food frequency questionnaire. Elevated hsCRP was defined as hsCRP ≥ 3mg/L vs <3mg/L and elevated Lp-PLA_2 defined as highest quartile vs lower three. Diagnosed periodontal disease, periodontal treatment or dentures and risk factors was correlated with CVD risk factors and inflammatory markers using chi square statistics. Logistic regression was used to adjust for confounding. **Results:** Univariate associations between oral health and inflammatory markers are in Table 1 with potential confounders. Factors significantly associated with periodontal disease were age (OR=2.1; 95% CI=1.1–4.0) and non-white race (OR=.5; 95% CI=.3-.8). Periodontal disease was a significant predictor of elevated Lp-PLA_2 however the relationship did not persist in multivariate models controlling for age, sex, non-white race, and education. **Conclusion:** Our data support inflammation as a common link between periodontal disease and CVD risk in an ethnically diverse population, and suggests that screening for periodontal disease may identify individuals at risk for CVD.

TABLE 1: ASSOCIATIONS BETWEEN INFLAMMATORY MARKERS AND ORAL HEALTH OR LIFESTYLE FACTORS

	hsCRP (≥ 3mg/L vs. <3mg/L) OR (95% CI)[1]	Lp-PLA_2 (≥ 217ug/L vs. < 217ug/L)
Oral Health Status:		
Ever diagnosed with periodontal disease	1.2 (.7–2.0)	**1.7 (1.0–2.9)**
Ever treated for periodontal disease	1.2 (.7–2.1)	1.5 (.9–2.6)
Wears partial or compete removable dentures	1.0 (.4–2.1)	1.0 (.5–2.1)
Lifestyle Factors:		
Waist circumference (>40inches (male); >35 inches (female))	**4.1 (2.6–6.4)**	1.2 (.76–1.7)
BMI ≥ 25 mg/dL	**3.8 (2.1–6.6)**	1.3 (.9–2.1)
BMI ≥ 30 mg/dL	**5.1 (3.2–8.1)**	1.3 (.8–1.9)
Saturated fat ≥ 10% of calories/day	1.2 (.8–1.9)	**1.7 (1.1–2.6)**
Dietary cholesterol ≥ 200 mg/day	1.2 (.8–1.9)	1.1 (.8–1.7)
Dietary fiber < 20g/day	1.4 (.9–2.2)	.9 (.6–1.4)
Omega-3 fatty acids < 1g/day	1.2 (.7–2.0)	.7 (.4–1.2)
Exercise < 4 days per week for 30 minutes	**2.7 (1.2–5.7)**	**.6 (.3-.98)**
Current Smoker	.7 (.3–1.6)	.9 (.5–1.8)
Demographics:		
Male	**.5 (.3-.85)**	**1.5 (1.0–2.3)**
Age ≥ 65 years	1.3 (.7–2.5)	1.0 (.5–1.8)
Non-White Race	**2.0 (1.3–3.1)**	**.4 (.2-.6)**
≤ High School Education	1.5 (.9–2.5)	.8 (.5–1.4)

(1) Values > 10mg/L excluded

21

Variants in the Transcription Factor 7-like 2 Gene Region Are Associated with Incident Kidney Disease and Markers of Kidney Function in the Atherosclerosis Risk in Communities Study, the Framingham Heart Study Offspring Cohort, and the Heredity and Phenotype Intervention (HAPI) Heart Study

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Based on evidence from rare Mendelian syndromes, clinical observations, and linkage studies, we hypothesized that pleiotropic genetic variants may increase susceptibility to both diabetes mellitus (DM) and kidney disease. The objective of our study was to investigate the association of known DM-associated variants in the *TCF7L2* gene and incident chronic kidney disease (CKD) and levels of kidney function markers in a population-based setting. **Methods:** Participants of the ARIC Study (n = 11061 self-identified white and n = 4014 black), FHS (n = 2468, white) and HAPI (n = 861, white) were genotyped at 5 (ARIC) and 2 (FHS) common *TCF7L2* variants. Association between each variant and kidney traits was analyzed using an additive genetic model adjusting for DM and fasting glucose, among others, as well as stratified on DM, and accounting for relatedness within FHS and HAPI. **Results:** The DM-conferring risk alleles at rs7903146 and rs7901695, among others, were significantly associated with incident CKD in white and black ARIC participants. The adjusted hazard ratio was 1.17 (95% CI 1.04–1.32), p=0.008 (whites), and 1.20 (1.03–1.41), p=0.023 (blacks) per rs7903146 T allele, and 1.19 (1.06–1.34), p=0.002 (whites), and 1.27 (1.09–1.48), p=0.002 (blacks) per rs7901695 C allele. The associations remained significant even after accounting for incident DM during follow-up, but were not observed with continuous measures of kidney function. Results were confirmed in the FHS: the T allele at rs7903146 was significantly associated with lower estimated glomerular filtration rate (eGFR, p=0.01) and higher serum cystatin C (p=0.004) in adjusted analyses; rs7901695 was not typed. Using data on 66 SNPs in the *TCF7L2* region (Affymetrix 500K chip) from HAPI participants, the C allele at rs7901695 (r2 = 0.8 with rs7903146 in CEU, rs7903146 not typed) was significantly associated with lower eGFR in adjusted analyses. In addition, several variants upstream and downstream of *TCF7L2* also showed significant association (p <0.003). No variant in ARIC or FHS was associated with albuminuria. **Conclusion:** Variants in the *TCF7L2* region are reproducibly associated with reduced kidney function and incident CKD above and beyond their association with DM in several population-based settings.

22

Joint Effects of Sodium and Potassium Intake on Subsequent Cardiovascular Disease: The Trials of Hypertension Prevention Follow-up Study

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Background Previous studies of dose-response effects of usual sodium and potassium intake on later cardiovascular disease (CVD) have largely relied on sub-optimal measures of intake. **Methods** Two randomized trials of sodium reduction and other interventions collected 24-hour urinary excretions over 18 months in 1987–1990 (TOHP I) and 36 months in 1990–1995 (TOHP II) among pre-hypertensive adults aged 30–54. Among those not assigned to an active sodium reduction intervention, we assessed the relation of an average of 3 to 7 measures of sodium and potassium excretion and the sodium-potassium ratio with subsequent CVD (myocardial infarction, stroke, coronary revascularization, or CVD mortality) through 10–15 years of post-trial follow-up. **Results** Among 2,974 participants, follow-up information was obtained on 2,275 (76.5%), with 193 CVD events. After adjustment for baseline variables and lifestyle changes, there was a non-significant trend in CVD risk over gender-specific quartiles of sodium (rate ratio (RR) from lowest to highest = 1.00, 0.99, 1.16, 1.20, p-trend=0.38), and potassium (RR=1.00, 0.94, 0.91, 0.64, p-trend=0.08) excretion, but a significant trend over quartiles of the sodium-potassium ratio (RR=1.00, 0.84, 1.18, and 1.50, p-trend=0.04). In models containing both measures simultaneously, linear effects were RR=1.42 (95% confidence interval (CI) =0.99–2.04) per 100 mmol/d of sodium excretion (p=0.05) and RR=0.67 (95%CI=0.41–1.10) per 50 mmol/d of potassium excretion (p=0.12). A model containing the sodium-potassium ratio (RR=1.24 per unit, 95%CI=1.05–1.46, p=0.01) had the lowest Bayes information criterion (best fit). **Conclusion** A higher sodium/potassium ratio is associated with increased risk of later CVD, and more strongly than sodium or potassium alone.

23

Clinical and Subclinical Cardiovascular Disease and Kidney Function Decline in the Elderly

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Background: Chronic kidney disease is common in persons with cardiovascular disease (CVD). However, the effects of clinical and subclinical CVD on kidney function decline are not well understood. **Methods**: This study included 4,380 subjects from the Cardiovascular Health Study, a longitudinal, community-based cohort of persons aged ≥ 65 from 4 U.S. communities. Cystatin C was measured at baseline, year 3, and year 7; eligible subjects had at least two measures. Cystatin C-based estimated glomerular filtration rate ($eGFR_{cys}$) was estimated using the equation GFR = 76.7 * (cystatin C)-1.18. Rapid kidney function decline was defined as an annual $eGFR_{cys}$ loss >3 mL/min/1.73m^2. Predictors of rapid kidney decline included prevalent and subclinical measures of CVD. **Results**: 1,083 (25%) persons had rapid kidney function decline during follow-up. Prevalent coronary heart disease (CHD), heart failure (CHF), and stroke were independent predictors of rapid kidney decline after adjustment for demographic, CVD risk factors, and inflammation. Among persons without prevalent disease, the subclinical disease measures low ankle arm index (AAI) and high internal carotid intima medial thickness (IMT) had independent associations with rapid kidney function decline (Table). **Conclusion**: Clinical and subclinical measures of CVD have independent associations with kidney disease progression in the elderly.

TABLE: PREDICTORS OF RAPID KIDNEY FUNCTION DECLINE

	Adjusted Odds Ratio*
Clinical CVD	
CHD	1.61 (1.33, 1.95); p<0.001
CHF	2.32 (1.83, 2.93); p<0.001
Stroke	1.47 (1.13, 1.92); p=0.005
Subclinical CVD	
AAI >0.9	1.56 (1.18, 2.07); p=0.002
Carotid IMT ≥1.82	1.30 (1.05, 1.60); p=0.02

* Adjusted for demographics, CVD risk factors, inflammation, and baseline kidney function

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24

Myocardial Glucose and Lactate Metabolism During Rest and Atrial Pacing in Humans

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There is minimal in vivo data in humans evaluating myocardial substrate utilization during increased heart work. This study was performed to determine myocardial glucose and lactate metabolism during rest and increased heart work induced by atrial pacing in healthy humans. We studied 6 healthy men and women (age=52.2+/-3.2 yr; BMI=22.7+/-1.0 kg/m2, VO2max=32.8+/-1.5 ml/kg/min, ejection fraction=68+/-3%, left ventricular mass 132.2+/-11.9 g). After 3 days of dietary control, coronary sinus, femoral artery and vein, and peripheral venous catheters were placed using standard techniques. Subjects received a primed continuous infusion of [3,3,3]2H lactate and [6,6]2H glucose throughout the study. Arterial and coronary sinus blood sampling and measurements of coronary sinus blood flow were made during rest and atrial pacing at approximately 110 bpm. Myocardial MVO2 increased ($p<0.05$) from 33.89+/-5.9 ml/min at rest to 85.12+/-14.9 ml/min during atrial pacing. Myocardial RQ was not different from rest (0.82+/-0.01) to atrial pacing (0.79+/-0.05). Net glucose uptake increased ($p<0.05$) from rest (21.4+/-6.4 mg/min) to atrial pacing (44.8+/-8.4 mg/min) with unchanged myocardial fractional extraction (11.0+/-3.0% at rest and 10.0+/-3.2% during atrial pacing). Isotopically measured lactate uptake also increased from rest (0.11+/-0.02 mmol/min) to atrial pacing (0.28+/-0.03 mmol/min, p=0.002) with no significant differences in myocardial fractional extraction (64.5+/-3.2 % at rest, and 65.4+/-4.5 % during atrial pacing). The myocardium also released lactate throughout the experiment, which increased significantly from rest and atrial pacing (0.04+/-0.01 mmol/min at rest, and 0.11+/-0.03 during atrial pacing, p=0.02). These data suggest: 1) in the absence of ischemia the myocardium is constantly releasing lactate at rest which increases during atrial pacing, and 2) when arterial substrate delivery is unchanged, increased myocardial work is accomplished with similar proportions of glucose and lactate utilization in healthy humans in vivo.

25

Detrimental Effects of the Atkins Diet on Myocardial Metabolism and Function During Ischemia

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Ischemic cardiac muscle utilizes primarily carbohydrates for energy production rather than its normal dependence on lipids. With the increased popularity of the high fat, high protein and low carbohydrate diets (Atkins Diet), the reduced carbohydrate availability could be contraindicated during a myocardial ischemic episode. This study investigated the effects of an Atkins Diet in a canine model and compared the cardiac response to a normal dietary group. Twelve animals were maintained on a control diet (Group I) and 12 animals on an Atkins Diet (Group II). After 6 weeks, anesthetized animals were surgically prepared to measure the myocardial uptake of glucose (Glu), free fatty acids (FFA), lactate (Lac), pyruvate, oxygen and hemodynamic parameters (end systolic elastance (EES), LV pressure, HR and dp/dt) while increasing the heart rate (50%, 25 minutes) before and after β-blockade (propranolol, 0.3 mg/Kg, 15 min). In Group I, pacing before β-blockade caused an increase in FFA (25%) and Lac (125%) uptake, and no change in Glu. Fifteen minutes after β-blockade, FFA uptake was reduced from 3.65 to 1.71 μEq/min/100g (LV weight) and was unchanged during pacing. Lac uptake increased 1.15 to 2.27 mg/min/100g following β-blockade and from 1.25 to 5.15 mg/min/100g during pacing. In Group II, FFA uptake was elevated and remained during pacing while both Glu and Lac were significantly reduced. Following β-blockade, Lac, Glu and FFA uptakes were markedly reduced following β-blockade and pacing. Hemodynamically in Group II, EES was significantly elevated during pacing before β-blockade, but after, there was a marked reduction in EES and during pacing, there was little functional activity. In conclusion, increasing cardiac work (pacing) elevated FFA and/or carbohydrate uptake before β-blockade in Groups I and II. After propranolol (which decreases myocardial FFA uptake with an increased carbohydrate utilization and RQ's near 1.0), pacing plus the Atkins Diet reduced carbohydrate availability concomitant with a decreased FFA uptake. The resulting deterioration of myocardial functional activity was predictable and was supported by the present experiments. Therefore, the Atkins Diet with cardiac ischemia or extreme exercise would be contraindicated.

26

Peripheral Blood Metabolic Signatures Are Markers of Coronary Artery Disease and Myocardial Infarction

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"Unbiased" metabolomic profiling has been used to predict the presence of coronary artery disease (CAD), but the non-quantitative, non-targeted nature of such an approach reduces clinical utility. We hypothesized that targeted, quantitative metabolomic profiling could accurately identify patients with CAD and myocardial infarction (MI). To this end, we performed metabolomic profiling on frozen, fasting plasma collected from patients undergoing cardiac catheterization, using gas chromatography/mass spectrometry (MS) with internal spiked standards for targeted quantitative measurement of ~60 metabolites (free fatty acids, acylcarnitines, amino acids). Clinical chemistry was used to measure lipids, glucose, ketones, CRP. In the initial "training" cohort, 74 individuals with very early-onset CAD and 74 sex- and race-matched controls without cardiovascular disease were profiled. Given collinearity of metabolites in related pathways, principal components analysis (PCA) was used for data reduction. Generalized linear models were used to test for differences in components between cases and controls. PCA identified 13 factors with metabolites clustering in known biological pathways. Of these, three factors were associated with CAD and/or MI. These results were then validated in a second cohort of 109 individuals with early-onset CAD and 109 sex- and race-matched controls. The most strongly associated factor consisted of glutamate and C3, C4:Ci4 and C5 acylcarnitine (p-values 0.01 - <0.0001 for association with CAD and MI). A second factor was composed of acylcarnitines (C18-OH:C16-DC, C18:1-DC, C20-OH:C18-DC, p-values 0.05–0.0004 for association with CAD and MI), and a third factor consisting of branched chain amino acids (valine and leucine/isoleucine), methionine, phenylalanine, tyrosine, and C5 acylcarnitine was primarily associated with MI. Hence, we have observed that components of a simple metabolomic panel, in particular glutamate and branched chain amino acids and their byproducts, strongly differentiate patients with CAD and MI. These results implicate branched chain amino acid catabolism in cardiovascular disease pathogenesis, and could have significant clinical implications for prediction and diagnosis.

27

Metabolic Profiling of Cultured Muscle Cells from Lean and Extremely Obese Subjects

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Primary human cultured skeletal muscle cells express metabolic characteristics that approximate the in vivo phenotype of the donor subject, particularly in extremely obese and type 2 diabetic subjects. Metabolic profiling or "metabolomics" describes the identification and quantification of numerous small molecular-weight compounds in biological fluid samples. To date, the ability of metabolomics to predict nutritional responsiveness and chronic disease states is challenged by the variability and complexity of biological model. As such, primary cultured muscle cells are an ideal model system to identify a "clean" metabolite signature of obesity apart from confounding systemic influences. Experimental Design: Total cellular metabolites will be extracted from cultured myotubes from lean (BMI $<$ 20 kg/m3, n=8) and extremely obese (BMI $>$ 45 kg/m3, n=8) women using cold methanol. One-dimensional nuclear overhauser effect spectroscopy (NOESY) spectra will be acquired from these samples using an automated NMR Case sample changer on a 600 MHz Bruker Ultrashield spectrometer. Processed spectra will be imported into Chenomx software version 4.6 for quantification. For metabolomics data, all concentration measurements will be exported into SIMCA-P for multivariate analysis towards identifying a unique metabolic signature of obesity in muscle. Results and Perspectives: Cell extracts were analyzed by 1H-NMR spectroscopy and 46 known compounds were detected. Multivariate analysis by orthogonal partial least squares discriminant analysis (OPLS-DA), a projection method for class separation was then used to establish models of each treatment. Models were able to predict class separation between diets with $>$90% accuracy. Variable importance plot revealed the most important metabolites in this discrimination to include: lysine, glycine, citrate, leucine, suberate and acetate. These metabolites are all involved in energy metabolism and may be representative of the perturbations taking place with obesity. Metabolomic profiling will give us a more complete understanding of the metabolic dysfunction in muscle with obesity and potentially identify novel biochemical markers, which could be used as diagnostic benchmarks of disease progression.

28

Sleep Disordered Breathing Is Associated with Impairment of Cardiac Autonomic Control in Children

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Studies in adult population have demonstrated significant adverse cardiovascular effects of sleep-disordered breathing (SDB). However, such effects have not been systematically investigated in children. We examined the cross-sectional association between SDB and cardiac autonomic control in a population-based sample of 616 K-5 school-aged children randomly selected from Harrisburg, PA metropolitan area. SDB was measured as the hourly average Apnea Hyponea Index (AHI) over one night of sleep in our sleep research laboratory. Cardiac autonomic control was measured by heart rate variability (HRV) analysis of the beat-to-beat RR interval data collected during the one night AHI data collection. The mean (SD) age of participants was 9.12 (20.2) months, with 47% females. The average AHI (SD) was 0.79 (1.03) / hour during the entire sleep, with 73.1% had AHI $<$ 1 / hour (No SDB group), 25.8% had 1–5 AHI / hour (mild SDB group), and 1.1% had $\geq$ 5 AHI / hour (Moderate SDB group). As shown in the table below, after adjusting for age, sex, body mass index, percentage of REM sleep, snore status, and sleep efficiency, individuals with moderate SDB, as compared to either persons without SDB or with mild SDB, had significantly impaired cardiac autonomic control measured by lower values of High Frequency Power (HF) and Root Mean Square of Successive Differences (RMSSD), and higher value of Low Frequency Power (LF) to HF ratio. Conclusions: In this healthy population-based sample of K-5 school-aged children, moderate SDB as measured by AHI $\geq$ 5 / hour is already associated with impaired cardiac autonomic control. If confirmed by other studies, this association may contribute to increased risk of acute cardiac event in persons with SDB, even before they reach the traditional "high risk age."

TABLE1. MULTIVARIABLE ADJUSTED MEANS (SE) OF HRV INDICES CALCULATED FROM OVERNIGHT EKG, ACCORDING TO SDB CATEGORIES

	Adjusted Mean and Standard Error of HRV Indices					
SDB	HF (ms^2)	LF (ms^2)	LF/HF	SDNN (ms)	RMSSD (ms)	HR (bpm)
No - AHI $<$ 1 (N=450)	6.68 (0.04)	6.55 (0.03)	0.99 (0.02)	92.89 (1.25)	72.49 (1.55)	77 (0.4)
Mild - AHI 1 - 5 (N=159)	6.85 (0.07)	6.67 (0.05)	0.91 (0.04)	99.11 (2.17)	78.70 (2.68)	76 (0.6)
Moderate - AHI $\geq$ 5 (N=7)	6.06 (0.32)#	6.46 (0.25)	1.64 (0.20)#	88.07 (10.45)	52.07 (12.91)#	77 (3.0)

# $p<0.05$ comparing the mean HRV indices with No SDB group.

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29

Maternal Obesity, Offspring Birth Weight, and Offspring Body Mass at Age 17: The Jerusalem Perinatal Study

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BACKGROUND: Maternal obesity (MO) alters the intrauterine environment and is associated with their offspring's birth weight (BW) and obesity later in life. We examined the association between MO and offspring body mass index (BMI), measured at age 17, and whether this association is mediated through offspring's BW. METHODS: The Jerusalem Perinatal Study (JPS) collected extensive prenatal, perinatal and postnatal data on all 17,003 births during 1974–1976. Measurements of BMI at age 17 were obtained from military draft records for 11,729 individuals. The analyses were restricted to full-term offspring (gestational age >36 weeks) without congenital malformations. Linear and logistic regression was used to examine the association between MO and offspring BM (age 17). Multivariate models included MO and BW, after controlling for maternal age, gestational age, weight-gain during pregnancy and maternal smoking. RESULTS: A linear model indicated a significant positive association between MO and offspring's BMI at age 17. Compared to the offspring of mothers with a pre-pregnancy BMI of <25, the offspring BMI at age 17 increased by a mean of 1.37, 1.91, and 2.66 kg/m-squared for offspring of mothers in pre-pregnancy BMI groups of 25–26, 27–29, and >30 respectively. Offspring BW also was positively associated with BMI at age 17 in a linear model. However, the association of MO with an increase in BMI at age 17 was altered only slightly, when offspring BW was included in the model. In a multivariate linear model, both MO and BW were associated with BMI at age 17; however, the coefficient for BW was reduced from b= 0.0004; p≤0.0001 (in the univariate model) to 0.0002; p=0.01 (in the multivariate model). In addition to MO and BW, weight-gain during pregnancy, maternal smoking, and maternal age were significantly associated with offspring BMI at age 17. Sex specific analyses yielded similar results. CONCLUSIONS: These findings suggest an association between MO and offspring BMI at age 17; and, the association is not mediated through an effect on BW adjusted for gestational age. Differences in MO may confound, at least to some extent, the association between BW and BMI at age 17. These findings warrant replication in other birth cohorts.

30

Prediction of Acute Coronary Syndrome by Fatty Acid Profile

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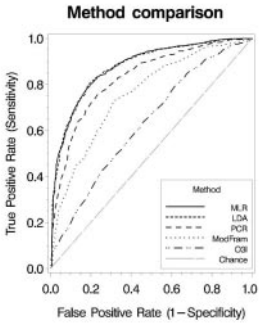
Background: Red blood cell omega-3 fatty acids (n-3 FA) levels (the omega-3 index, O3I) are inversely associated with risk for developing acute coronary syndromes (ACS). **Purpose**: We sought to determine whether RBC FA *profiles* (rather than individual FAs) would have stronger associations with ACS. **Methods**: A dataset containing 768 ACS cases prospectively paired with controls on age, sex, and race, was split into 4 subsets to develop receiver operator characteristic (ROC) curves based on 1) total FA profiles (using 3 analytical approaches [multiple logistic regression (MLR), linear discriminant analysis (LDA), principal components regression (PCR)], 2) the O3I, and 3) a modified Framingham score. The mean performance of each was assessed for sensitivity/specificity (s/s), positive likelihood ratios (PLR), area under the ROC curve (c-statistic), and calibration (goodness-of-fit). **Results**: Based on the c-statistic, all 3 analyses using the total FA profile (MLR, LDA and PCR) performed better than either the O3I or the modified Framingham risk score (Figure). The overall performance of the MLR was the best of the 3. The MLR yielded a c-statistic of 0.88, a PLR of 4.7, and s/s of 76%/84%. Values for the modified Framingham score were c=0.76, PLR=2.3, and s/s=71%/70%; and for the O3I, c=0.63, PLR=1.4 and s/s=64%/54%. The Hosmer-Lemeshow goodness-of-fit was robust with the PCR and O3I methods, acceptable for the MLR and modified Framingham and unacceptable for the LDA. **Conclusion**: FA profiles alone discriminated ACS cases from controls better than the modified Framingham score or the O3I. The use of FA patterns to assess risk in prospective studies should be explored.



31

Incidence and Risk Factors for Stroke in American Indians: The Strong Heart Study

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Background There are few published data on the incidence of fatal and non-fatal stroke in American Indians. The aims of this observational study were: to determine the incidence of stroke in American Indians and to assess risk factors for incident stroke in this population. **Methods and results** This report is based on 4549 participants aged 45–74 at enrollment in the Strong Heart Study, the largest longitudinal, population-based study of cardiovascular disease and its risk factors in a diverse group of American Indians. At baseline examination in 1989–1992, 42 participants (923/100,000) had prevalent stroke. As of December 2004, 306 (6.8%) of 4507 participants without prior stroke suffered a first stroke at a mean age of 66.5 years. The incidence was 679/100, 000 person-years, adjusted to the age and gender distribution of the U.S. adult population in 1990. Non-hemorrhagic cerebral infarction occurred in 85.7% (221 of 258) of participants; 14.3% (37 of 258) suffered hemorrhagic stroke. Overall age-adjusted 30-day case-fatality from first stroke was 18% (56 of 306), with a one-year case-fatality of 32% (95 of 295). Age (hazard ratio (HR) = 1.07, 95% confidence interval (CI): 1.05, 1.09), diastolic blood pressure (HR = 1.02, 95% CI: 1.01, 1.04), fasting glucose (HR = 1.004, 95% CI: 1.002, 1.005), $HbA1_C$ (HR = 1.2, 95% CI: 1.1, 1.2), current smoking (HR = 2.4, 95% CI: 1.7, 3.4), past smoking (HR = 1.6, 95% CI: 1.1, 2.3), macro-albuminuria (HR = 3.3, 95% CI: 2.3, 4.8), micro-albuminuria (HR = 1.7, 95% CI: 1.3, 2.4), hypertension (HR = 2.2, 95% CI: 1.2, 3.2), pre-hypertension (HR = 1.8, 95% CI: 1.2, 2.6) and diabetes (HR = 2.1, 95% CI: 1.4, 3) were independent predictors of incident stroke. Risk factors were similar for cerebral infarction or hemorrhagic stroke. **Conclusions** Compared to U.S. white and black populations, American Indians have higher incidence of stroke and younger age of first stroke. The case-fatality rate for first stroke is also higher in American Indians than in the U.S. white or black population with the same age range. Our findings suggest that blood pressure, glucose control and smoking avoidance are especially important for stroke prevention in this population.

32

Associations of Pentraxin 3 with Cardiovascular Disease Risk Factors, Events, and All-Cause Death: Results from the Cardiovascular Health Study

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Background: Pentraxin 3 (PTX3) is a marker of vascular inflammation. However, little is known about PTX3 associations with cardiovascular disease (CVD) risk factors, events and all cause death. *Methods:* We examined these associations in 1,583 men and women from the Cardiovascular Health Study. Participants were ≥65 years and free of clinical CVD at baseline. Non-exclusive case groups were incident angina (n=476), myocardial infarction (MI; n=237), stroke (n=310), CVD death (n=282) and all cause death (n=772). 535 participants had no events. We used Cox proportional hazards models to determine hazard ratios (HRs) and 95% confidence intervals (95% CIs). *Results:* PTX3 distribution was skewed in these older adults. The geometric mean was 1.82 ng/ml (standard deviation 1.89); range of 0.25–23.05 ng/ml. PTX3 was positively associated with age (p<0.001), fasting glucose (p=0.02) and insulin (p=0.03) and another pentraxin, C-reactive protein (CRP; p<0.001). PTX3 was not associated with lipids, blood pressure or obesity (all p>0.10). Mean (standard deviation) PTX3 was higher in those with subclinical CVD (1.90 ± 1.89 ng/ml) than those without (1.71 ± 1.88 ng/ml; p=0.001). In Cox models adjusted for age, sex and ethnicity, a standard deviation increase in PTX3 was associated with CVD death (HR 1.11; 95% CI 1.02–1.21) and all cause death (1.08; 1.02–1.15), but not angina (1.09; 0.98–1.20), MI (0.96; 0.81–1.12) or stroke (1.06; 0.95–1.18). Adjusting for CRP and CVD risk factors (obesity, diabetes, smoking, dyslipidemia and hypertension) had no significant effect on associations. *Conclusions:* In a population-based sample of older adults free of prevalent CVD, PTX3 was associated with CVD death and all cause death independently of CRP and CVD risk factors. PTX3 likely reflects different aspects of inflammation than CRP and may provide insight into the role of vascular health in aging and chronic diseases of aging that lead to death.

33

The Effects of Macronutrient Intake on Insulin Resistance: Findings from the Optimal Macro-Nutrient Intake Trial to Prevent Heart Disease

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Improvement of insulin resistance through weight loss is well known. The independent effects of macronutrient intake without weight loss on insulin resistance remain unclear. OMNI-Heart was a randomized, cross-over feeding study with 164 healthy adults. Participants underwent

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three 6-week feeding periods: one rich in carbohydrates (CARB), one rich in monounsaturated fat (MUFA), and one rich in protein (PROT), while maintaining body weight. Fasting blood samples were obtained at baseline (while participants ate their own diet) and at the end of each feeding period. Insulin resistance was calculated based on the homeostasis model of assessment (HOMA-IR), which was log-transformed. Three pair-wise comparisons using paired t-tests were conducted to test the effects of each diet on HOMA-IR, insulin and glucose. At baseline, mean age, body mass index (BMI), and geometric means of fasting glucose, insulin, and HOMA-IR were 54 years, 30.3 kg/m^2, 5.10 mmol/L, 7.9 μIU/mL, and 1.79, respectively. HOMA-IR decreased after all feeding periods, perhaps because each of the 3 diets was healthy in comparison to baseline diet; however, the difference was only significant for MUFA (-11% from baseline, p=0.01). Across diets, the MUFA diet tended to reduce HOMA-IR more than either CARB or PROT diets (Table). Among non-obese (BMI<30 kg/m^2) participants, mean HOMA-IR on MUFA was 1.11 vs 1.26 on CARB (12% reduction, p=0.009) and 1.24 on PROT (11% reduction, p=0.08); however, a diet-obesity interaction test was non-significant (p=0.10). Similar results were obtained for insulin levels. None of the diets affected glucose levels. In conclusion, a healthy diet rich in MUFA may have small beneficial effects in reducing insulin resistance even without weight loss.

DIFFERENCES IN LOG HOMA-IR BY MACRONUTRIENT CONTENT IN OMNI-HEART, N=160

	Differences from Baseline (by paired t-tests)		
Log HOMA-IR	CARB	MUFA	PROT
Mean difference	-0.05	**-0.11**	-0.06
p-value	0.20	**0.01**	0.20
Between Diet Differences*:			
Log HOMA-IR	MUFA-CARB	MUFA-PROT	CARB-PROT
Mean difference	-0.06	-0.05	0.01
p-value	0.10	0.25	0.78

*Difference represents MUFA minus CARB, MUFA minus PROT, CARB minus PROT

34

Strategies for Sustaining Weight Loss: Findings from the Weight Loss Maintenance Trial

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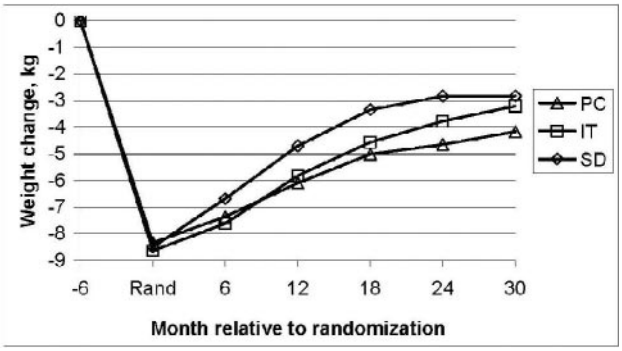
Behavioral interventions achieve short-term weight (wt) loss, but re-gain is common. The NHLBI-sponsored Weight Loss Maintenance trial (WLM) tested strategies to maintain wt loss in overweight/obese (BMI 25–45 kg/m^2) adults with hypertension and/or dyslipidemia. In Phase I, participants received a 6 month behavioral wt loss intervention; those who lost $\geq$ 4 kg were eligible for a 30-mo maintenance phase (Phase II). Of 1,685 in Phase I, 1032 (61%) were randomized in Phase II to: 1) monthly Personal Contact (PC) by telephone (9/yr) and in-person (3/yr); 2) Interactive Technology (IT) with unlimited access to an intervention website; or 3) a Self-Directed (SD) comparison group. Phase II participants were 38% African American, 63% female, with mean age 56 yrs (range 28–83). PC participants completed an average of 90% of monthly contacts; IT participants logged onto the website an average of once a week. Final Phase II wt was measured in 93%. All groups regained, but mean final wt in each group was lower than it was prior to Phase I. The figure suggests that both PC and IT diverged from SD through 18 months. At 30 months, weight regain in PC participants was significantly less than in SD (mean difference = -1.47 (se 0.45) kg, p = 0.001) but there was no difference between SD and IT (mean difference = -0.29 (se 0.44) kg, p = 0.51). At 30 months, 39% of SD, 41% of IT, and 45% of PC were still maintaining wt loss of at least 4 kg. WLM is the largest, most diverse, and longest trial testing strategies to sustain wt loss. A large proportion maintained clinically significant wt loss. The PC intervention, developed as a practical strategy that could be widely disseminated, significantly improved wt loss maintenance.



35

Marginally Increased Waist Circumference Predicts Hypertension Prevalence Among Normal and Overweight Adults: The REGARDS Study

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Background: For persons who are overweight or mildly obese, elevated waist circumference, defined as >88 cm for women and >102 cm for men, independently predicts obesity-related risk factors and morbidity. The cardiovascular risks of marginally increased waist circumference, 80–88 cm for women and 94–102 cm for men, have not been well examined. We hypothesized an association of marginally increased waist circumference with prevalent hypertension, independent of body mass index, and assessed this association in a national sample of community-dwelling US adults. ***Methods and Results:*** We measured hypertension prevalence (systolic blood pressure (BP) >140 mm Hg, or diastolic BP >90 mm Hg, or self-reported current treatment for hypertension) at study baseline among 21,351 participants with normal (18.5–24.9), overweight (25–29.9) and obese class I (30–34.9) body mass index from the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a population-based cohort of black and white participants aged $\geq$45 years. Hypertension was present in 45% of those with normal body mass index (n=6104), 56% of those overweight (n=9519), and 67% with class I obesity (n=5728). After adjustment for age, race, sex, region, tobacco use, glomerular filtration rate, alcohol use, income, education and physical activity, marginally increased waist circumference was independently associated with hypertension prevalence within normal and overweight body mass index groups(Table). For all body mass index groups, elevated waist circumference was significantly associated with prevalent hypertension. ***Conclusions:*** Marginally increased waist circumference is independently associated with hypertension prevalence in normal weight or overweight persons. Further classification of accepted definitions of elevated waist circumference may be needed to accurately assess cardiovascular risk in normal and overweight individuals.

TABLE: ADJUSTED ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR HYPERTENSION PREVALENCE BY WAIST CIRCUMFERENCE CATEGORY STRATIFIED BY BODY MASS INDEX GROUP

	OR (95% CI) for Hypertension Prevalence		
	Body Mass Index Group		
Waist Circumference	Normal (18.5–24.9)	Overweight (25–29.9)	Obese Class I (30–34.9)
Normal Waist Circumference (<80 cm for women and <94 cm for men)	1.00	1.00	1.00
Marginally Increased Waist Circumference (80–88 cm for women and 94–102 cm for men)	1.58(1.36, 1.85)	1.31 (1.16, 1.47)	1.05 (0.74, 1.49)
Elevated Waist Circumference (>88 cm for women and >102 cm for men)	2.13 (1.64, 2.76)	1.55 (1.36, 1.75)	1.48 (1.07, 2.05)

36

Fetuin-A and Risk of Incident Diabetes Mellitus in Elderly Persons: The Health Aging and Body Composition (Health ABC) Study

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Background: Fetuin-A is a hepatic secretory protein that binds the insulin receptor in muscle and fat and inhibits insulin action, *in vitro*. Prior cross-sectional studies demonstrated that higher fetuin-A levels were associated with insulin resistance in humans, however the longitudinal association of fetuin-A with incident diabetes is unknown. *Methods:* The Health Aging and Body Composition study enrolled 3,075 well-functioning black and white persons aged 70 to 79 years. This case-cohort study included 406 randomly selected participants without prevalent diabetes at baseline, and all participants who developed incident diabetes during 6-years of follow-up. Fetuin-A was measured by ELISA among baseline sera. Modified Cox regression analyses evaluated the association of fetuin-A with incident diabetes. *Results:* Incident diabetes developed in 135 participants (10.1 cases per 1,000 person-years) over 6-years. Participants with fetuin-A levels within the highest tertile (> 0.97 g/L) experienced more than two-fold risk of incident diabetes (adjusted HR 2.18; 95% CI 1.17 - 4.06; P = 0.02), compared to those within the lowest third of the cohort ($\leq$ 0.76 g/L) in models adjusted for age, gender, race, physical activity, systolic and diastolic blood pressure, fasting glucose, waist circumference, HDL cholesterol, triglycerides, and CRP levels. *Conclusions:* Among well functioning older persons, serum fetuin-A is a novel and independent risk factor for incident diabetes.

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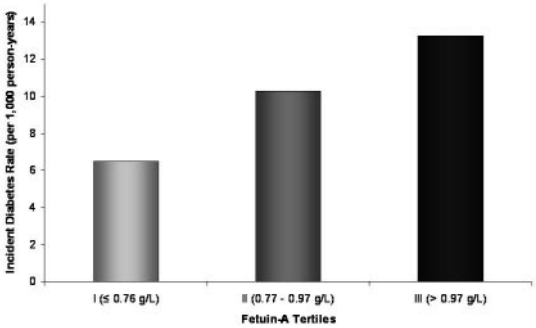

37

Lifestyle Interventions Reduce Estimated Framingham Risk: Results from the PREMIER Trial

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Most trials of lifestyle modification test the effects of interventions on cardiovascular risk factors. In the PREMIER trial, two comprehensive lifestyle interventions lowered blood pressure over 6 months. We used data from PREMIER to test the effects of these interventions on estimated 10-year coronary heart disease risk using the Framingham risk equation (Framingham risk). Eight hundred ten healthy adults with pre- or stage I hypertension, not on anti-hypertensive medication, were randomized to one of 3 intervention groups: 1) an "advice only" group, 2) a lifestyle intervention (EST) which focused on "established" recommendations for BP control (weight loss, sodium reduction, physical activity, and alcohol intake), or 3) a lifestyle intervention (EST+DASH) which combined established lifestyle recommendations with the DASH diet. We used linear regression to estimate and compare the differences in the logarithm of Framingham risk at 6 months and baseline post-randomization for the 3 groups. Of participants with complete data, 61% (445/730) were female, 33% (243/730) were black, 60% (439/730) had a total cholesterol ≥ 200 mg/dl, and 4.8% (35/730) were current smokers. Mean age was 50.3 years, mean systolic/diastolic blood pressure was 134.8/84.7 mmHg, and median baseline Framingham risk was 7.1%. The ratio of 6-month to baseline Framingham risk was 0.96 (95% CI: 0.90 to 1.02) in 'advice only', 0.87 (95% CI: 0.82–0.92) in EST, and 0.87 (95% CI: 0.82 to 0.92) in EST+DASH. Compared to advice alone, EST and EST+DASH reduced estimated Framingham risk by 10% (P=0.001) and 9% (P=0.001). These reductions in estimated coronary heart disease risk are substantial and, if achieved, should have important public health benefits.

38

Shared Genetic and Environmental Factors Do Not Confound the Association Between Adherence to the Mediterranean Diet and Oxidative Stress

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OBJECTIVES: The cardio-protective property of the Mediterranean diet (MedD) has been attributed to its antioxidant capacity, but direct investigation of this mechanism is limited. We examined the association between the MedD and an established plasma marker of oxidative stress, the ratio of reduced to oxidized glutathione (GSH/GSSG), controlling for shared genetic and environmental factors. METHODS: We administered the Willet Food Frequency Questionnaire to 297 middle-aged men (171 monozygotic [MZ] and 126 dizygotic [DZ] twins), drawn from the Vietnam Era Twin Registry. We derived a score measuring adherence to the MedD according to a published algorithm. Plasma GSH and GSSG concentrations were measured with high-performance liquid chromatography and used to calculate the GSH/GSSG ratio. The higher the ratio, the lower the oxidative stress. Mixed-effect regression analysis examined the association between MedD score and the log-transformed GSH/GSSG ratio. Models were adjusted for total energy intake, other nutritional factors, coronary heart disease (CHD) risk factors, and medication use. Effects were partitioned into between- and within-twin pair differences in oxidative stress based on MedD adherence. When examining within-pair effects, twins are matched for demographic, familial and other environmental influences while growing up. MZ pairs are 100% matched for genetic factors, and DZ pairs share on average 50% of their genes. RESULTS: Adherence to the MedD was positively associated with the GSH/GSSG ratio (P=0.02) after adjusting for total energy intake, other nutritional factors, CHD risk factors and medication use. The association persisted within twin pairs (P = 0.007). A one-unit within-pair absolute difference in the MedD score was associated with a 10% (95% CI, 2.7 to 18.0) higher GSH/GSSG ratio comparing a twin with a higher score to his co-twin with a lower score. Results were similar in MZ and DZ twins, suggesting little genetic confounding on this association. CONCLUSIONS: The association between the MedD and plasma oxidative stress is robust, and is not confounded by genetic or shared environmental factors. Decreased oxidative stress is a possible mechanism linking the MedD to reduced CHD risk.

39

Normal Weight Obesity: A Risk Factor for Cardiometabolic Dysregulations

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Objective: We hypothesized that a significant proportion of subjects despite having a normal body mass index (BMI) could have a high body fat content (defined as normal weight obesity, NWO) and consequently they could be at higher risk for cardiometabolic disturbances when compared to normal weight subjects with normal body fat content. **Methods:** A cross-sectional study of 2,127 subjects with a normal BMI (18.5–24.9 kg/m^2) who had body composition assessment by bioelectrical impedance, fasting morning laboratory measurements and full assessment of anthropometric variables and cardiovascular risk factors from the Third National Health and Nutrition Examination Survey. We defined NWO as a normal BMI with high body fat % (>20% in men and >30% in women), and compared several cardiometabolic parameters, including metabolic syndrome (ATP-III criteria) and traditional cardiovascular risk factors with subjects with a normal BMI and no excess in body fat (≤20% in men and ≤30% in women). **Results:** Women comprised 51% of the sample and 61 % of subjects with a normal BMI were NWO. When compared to subjects with a normal BMI and no excess in body fat, NWO subjects were older (44 ± 17 vs. 39 ± 16, p<0.0001) and Hispanics were the race with the highest rates of NWO (72%). After controlling for age, sex and race, NWO subjects had significantly higher rates of several cardiometabolic parameteres (Table). Conclusions: NWO subjects had several cardiometabolic disturbances, including an altered lipid profile, high leptin and higher rates of metabolic syndrome. In addition, NWO appears to be highly prevalent, constituting more that half of the patients with a normal weight as defined by the BMI.

Variable	Normal Weight (N=806)	Normal Weight Obese (N=1,321)	Age, sex and race adjusted p-value
METABOLIC SYNDROME	Number (%)	Number (%)	
Waist circumference (M>102, W>88cm)	7 (0.87)	133 (10.0)	<0.0001
Triglycerides or lipid treatment (>150mg/dl)	88 (11.0)	268 (20.5)	<0.0001
High density lipoprotein (M<40, W<50mg/dl)	183 (22.9)	343 (26.2)	0.08
Blood pressure/treatment for such (>130/85mmHg)	226 (29.5)	493 (38.8)	0.31
Fasting plasma glucose or diabetic (>100mg/dl)	131 (16.2)	351 (26.6)	0.004
Metabolic syndrome definition (ATP-III)	40 (5.3)	171 (13.6)	0.0002
CARDIOVASCULAR RISK FACTORS			
Dyslipidemia	273 (33.9)	556 (42.0)	0.004
Hypertension	153 (20.2)	351 (27.7)	0.39
Diabetes	16 (2.0)	58 (4.4)	0.28
Ever smokers	421 (52.2)	683 (51.7)	0.65
OTHER CARDIOBIOMARKERS			
Elevated ApoB/apoAI ratio (M>0.88, W>0.73)	212 (27.2)	511 (40.2)	<0.0001
Elevated CRP (M>0.50, W>0.55mg/dl)	69 (8.7)	159 (12.2)	0.16
Elevated Leptin (M>3.9, W>12.5 ng/ml)	53 (7.1)	433 (25.6)	<0.0001

40

Effects of Macronutrient Intake on Self-Reported Appetite and Fasting Hormones (Leptin, Obestatin, and Ghrelin): Results from the Omni-Heart Trial

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Background: The effects of macronutrients on appetite are controversial. Understanding how appetite varies with exposure to diets having different macronutrient composition could inform recommendations for weight maintenance. Leptin and obestatin may enhance satiety whereas ghrelin may increase hunger. **Objectives:** 1) To compare the effects of 3 diets, each rich in a different macronutrient, on select hormones and self-reported appetite measured by visual analog scales (VAS). 2) To estimate associations between hormones and self-reported appetite. **Methods:** Omni-Heart was a randomized, three period, cross-over feeding study (n=164) comparing the effects of 3 healthy diets [termed PROT, CARB, UNSAT]. The macronutrient profile (%kcal carbohydrate, fat, protein) of the 3 diets were for PROT (48%, 27%, **25%)** , CARB (**58%**, 27%,15%), and UNSAT (48**%**, **37**%,15%). All food and drink were provided for each isocaloric 6-week intervention diet separated by washout periods. VAS was administered before and after the main meal of the day for five days during week 3. Hormones were measured from week 6 fasting plasma. Associations between hormones and VAS ratings were estimated by partial Spearman correlations adjusted for diet, period, and site. **Results:** Pre-meal hunger was lower and post-meal satiety was higher on the PROT diet compared to the other two diets, as reflected by lower summary VAS (Table). Leptin was modestly correlated with summary VAS (r=-0.2, p<0.0001), but obestatin and ghrelin were not associated with self-reported appetite. **Conclusions:** A healthy diet rich in protein reduces appetite compared to diets rich in carbohydrate and fat. The effects of the diets on appetite hormones were complex and, in some cases, the opposite of expected.

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Appetite Measure	PROT Mean (95% CI)	CARB Mean (95% CI)	UNSAT Mean (95% CI)	CARB VS PROT p-value[1]	UNSAT VS PROT p-value[1]	CARB VS UNSAT p-value[1]
Hormones						
Leptin, ng/ml[2]	10.0 (8.2, 11.0)	11.0 (9.0,12.2)	10.0 (8.2,12.2)	0.002	0.42	0.05
Obestatin, pg/ml	114.7 (108.5,120.9)	123.0 (115.0,130.9)	122.1 (115.8,128.4)	0.02	0.004	0.80
Ghrelin, pg/ml	826.0 (768.7,883.4)	837.1 (781.8,892.5)	834.4 (779.1,889.7)	0.42	0.48	0.83
VAS Summary[3]						
Pre-meal	77.8 (69.1, 86.5)	88.9 (81.4, 96.5)	88.7 (80.8, 96.6)	0.004	0.004	0.94
Post-meal	-55.3 (-60.6,-50.0)	-48.0 (-54.2, -41.8)	-48.8 (-54.1, -41.5)	0.006	0.006	0.94

[1]Generalized estimating equations (exchangeable correlation) accounting for site and period. [2]Geometric mean. [3] VAS Summary rating:=hunger + prospective consumption - fullness. Range for each of the 3 ratings was 0 to 100mm.

41

FTO Gene Variants and Obesity: Longitudinal, Genome-Wide Association–Based, and Functional Analyses

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CONTEXT: *FTO* gene variant was recently associated with obesity. However, little is known the longitudinal pattern of the association and potential function of *FTO* gene. DESIGN, SETTING, AND PARTICIPANTS: We genotyped FTO variants in 2,287 men and 3,520 women from two prospective cohorts: the Health Professionals' Follow-up study and Nurses' Health Study. We also analyzed the associations of 605 genotyped and imputed SNPs near *FTO* gene from a genome-wide association (GWA, Illumina HumanHap500k) study in 2,268 women. In addition, we investigate the expression of FTO gene in tissues with high metabolic capacities. RESULTS: SNP rs9939609 was significantly associated with higher BMI at early adulthood in both men (age 21, P=0.0007) and women (age 18, P<0.0001), with a 0.29 and 0.37 kg/m^2 difference per allele A, respectively. Using the longitudinal measurements, we found each allele A was associated with 0.25 (P=0.03) and 0.59 kg/m^2 (P<0.0001) higher BMI, as well as 1.21-(P=0.007) and 1.19-fold (P=0.0008) greater obesity risk in men and women respectively. AA homozygotes were associated with 1.18- to 2.04-fold and 1.32- to 1.71-fold higher obesity risk than TT genotype across different age groups in men and women respectively, with a trend toward decreasing effects at older age especially in men. rs9939609 was significantly associated with greater diabetes risk (P=0.019) and lower plasma adiponectin (P=0.02) in women. Adjustment for BMI significantly attenuated these associations. Our GWA based analyses indicate a clustering of significant associations in FTO genes. We found that *FTO* gene was widely expressed in various tissues in mice and human. In white adipose tissue from db/db mice, *FTO* expression decreased by ~50% compared with the wild types. *FTO* expression was significantly induced by inflammatory stimulants. CONCLUSIONS: Common variants in *FTO* gene were associated with obesity risk and the association declined with advancing age. Our data indicate *FTO* may regulate adiposity metabolism.

42

ABCG1 SNPs, Diabetes, and Variation in Lipid Levels in the Multi-Ethnic Study of Atherosclerosis

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ABCG1 is a member of the ATP-binding cassette (ABC) transporter family that mediates cholesterol efflux to HDL. ABCG1 expression in the db/db mouse is regulated by chronic glucose, and decreased ABCG1 function increases foam cell formation and risk of atherosclerosis. We hypothesize that SNPs in the ABCG1 gene are associated with features of HDL metabolism in humans, and these SNPs will explain some of the variation in lipid metabolism and subclinical atherosclerosis risk in participants in the MESA who are free from clinical cardiovascular disease. A total of 2,847 MESA participants from four ethnic groups (Caucasians, n=712; African-Americans, n=712; Hispanic Americans, n=705; Chinese-Americans, n=718) were genotyped for 40 tagging SNPs in ABCG1. Risk factor data were collected at MESA clinics using standardized methods. Blood samples were obtained after an 8 hour fast (lipid profiles); lipid size determinations were measured by NMR. Linear regression methods were used to evaluate associations between phenotypes and ABCG1 SNPs and haplotypes after adjustment for covariates. P-values were determined by permutation tests of association at each SNP. The strongest associations with ABCG1 SNPs were observed with HDL levels, medium HDL particles, and VLDL size (P < 0.01). Patterns of association in ABCG1 introns 1 and 2 with HDL phenotypes (HDL level, HDL particles, large HDL, medium HDL, and HDL size) were observed. ABCG1 SNP rs6586298 (intron 2) was associated with HDL level (P=0.007), large HDL (P=0.008), and HDL particles (P=0.06). Those with ABCG1 rs6586298 C/C genotype had higher HDL, larger HDL, and more HDL particles than those with either the G/C or G/G genotypes, independent of other risk factors. Two adjacent SNPs (rs3787995 and rs225406) contained in associated haplotypes were observed all ethnic groups. Stratification by diabetes status suggested the ABCG1 effect was primarily observed in those with diabetes. These data support the role of variation in ABCG1 contributing to variation in HDL concentration and particle size distribution, and may identify an important region of the gene for risk contributing to cardiovascular disease.

43

Variation in 10 Sodium-Handling and Related Genes, Diuretic Use, and the Risk of Incident, Nonfatal Myocardial Infarction, and Stroke in Pharmacologically Treated Hypertensive Patients

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Diuretics are, on average, highly effective, but individual response varies. Interindividual variability may be attributable to genetic factors. We used a population-based case-control study of drug-treated hypertensives to replicate a previously reported interaction between diuretic use and the *ADD1* Gly460Trp variant on the combined outcome of incident, nonfatal myocardial infarction (MI) and ischemic stroke. The secondary aim was hypothesis-generating: to identify novel interactions between diuretic use and a total of 51 variants in sodium-handling and related genes including *ADD1*, *SCNN1A*, *SCNN1B*, *SCNN1G*, *CLCNKB*, *SLC12A1*, *SLC12A3*, *HSD11B2*, *GNB3*, and *CYP11B2* on MI and stroke risk. Tag-single nucleotide polymorphisms (SNPs) were identified for *ADD1*, *SLC12A1*, *SLC12A3*, *GNB3*, and *CLCNKB*; known SNPs of interest were selected for the other genes. The replication sample consisted of 405 MI and stroke cases and 989 controls identified between 1999 and 2002. The hypothesis-generating sample consisted of 514 MI cases, 215 stroke cases and 1731 controls identified between 1995 and 2002. We used synergy indices (SI) - the ratio of the SNP-outcome odds ratios in strata of diuretic use - to describe interactions. In the original analysis, there was a significant interaction between the 460Trp allele and diuretic use on MI and stroke risk [SI = 0.45, 95% CI = 0.26 to 0.79]. In the replication sample, the SI was more modest; the confidence interval included values compatible with no interaction [SI = 0.76, 95% CI = 0.47 to 1.24]. When data were combined, the association was significant [0.62, 95% CI = 0.43 to 0.89]. In hypothesis-generating analyses, the interaction most significantly associated with MI risk was between a *GNB3* SNP and diuretic use (p=0.008). The interaction most significantly associated with stroke risk was between a *SLC12A1* SNP and diuretic use (p=0.004). Corrected p-values derived from a parametric bootstrap test were not significant (p=0.305 and p=0.151, respectively). These results suggest strong interactions are unlikely. Larger studies would be needed to reliably estimate any small to moderate interactions. The Gly460Trp replication results are compatible with our earlier findings, although they did not achieve statistical significance.

44

Potential Reductions in Coronary Heart Disease Mortality by Treating More Patients in the United States

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Background: Between 1980 and 2000, the age-adjusted mortality rate from coronary heart disease (CHD) in the United States fell by 45% among adults aged 25–84 years, resulting in approximately 341,745 fewer deaths in 2000. We estimated that evidence-based medical and surgical treatments in 2000 accounted for almost half this reduction. However, in 2000, overall, only about 30% - 60% of eligible patients received appropriate treatments. Meanwhile, the Public Health Action Plan to prevent Heart Disease and Stroke has prioritised the need to maximise effective treatments. We therefore examined the potentially achievable coronary mortality reduction through increased treatment levels. **Methods:** We use the previously validated IMPACT CHD mortality model; this integrates data on CHD patient numbers, specific medical and surgical treatments uptake level, and treatment effectiveness. We estimated the number of deaths prevented or postponed for the year 2000 (baseline) and for an alternative scenario: increasing treatment uptake to reach 60% of eligible patients. Sensitivity analyses were then performed. **Results:** In 2000, medical and surgical treatment levels in the USA were generally modest; only 30% - 60% of eligible patients received appropriate therapies. These treatments together resulted in approximately 171,700 fewer deaths. Treating 60% of eligible patients would have achieved approximately 301,700 fewer deaths *(minimum estimate 118,300; maximum estimate 635,000),* 130,000 better than in 2000*:* 33% coming from increases in heart failure therapies, 31% from secondary prevention therapies, 19% from acute coronary syndrome treatments, 15% from the primary prevention with statins, and 1% from a 60% increase in the number of revascularisation procedures. These findings remained stable in the sensitivity analysis. **Conclusions:** Increasing the proportion of eligible CHD patients receiving appropriate treatments could have achieved approximately 300,000 fewer deaths in 2000, more than doubling the benefit actually achieved from therapies. Future national strategies should therefore maximise the delivery of appropriate therapies to all eligible CHD patients, and prioritise therapies for secondary prevention and heart failure.

45

Pharmacist-Led Group Medical Visits for Cardiovascular Risk Reduction in Diabetes

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Simultaneous control of multiple cardiovascular risk factors in diabetes mellitus (DM) is labor intensive and difficult to accomplish in traditional care settings. We tested the feasibility and efficacy of a pharmacist-led Multi-disciplinary Education and Diabetes Intervention for Cardiac

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risk reduction (MEDIC) program that targets hypertension, hyperglycemia, dyslipidemia and tobacco use, delivered as group medical visits for patients with DM. We conducted a randomized controlled trial of MEDIC vs. usual care in DM with a hemoglobin A1c between 7–9% within 6 months at the Providence VA medical center. A clinical pharmacist comprehensively intervened on the behavioral and pharmacotherapy aspects of DM and cardiovascular risk over 4 weekly sessions. Educators in nursing, physical therapy and nutrition provided subject-specific education in this multidisciplinary model. We then compared the reduction in cardiovascular risk burden as estimated by the ratio of the United Kingdom Prospective Diabetes Study (UKPDS) risk score at 4 months to baseline between MEDIC and usual care. MEDIC patients were younger than usual care 62.3±10.4 vs. 65.4±10.2 years. After an average of 3.7 ± 0.6 weekly MEDIC visits, patients in the intervention arm had higher improvement of cardiovascular risk factors as compared to usual care (Table). The UKPDS risk score decreased by 15% for MEDIC and increased by 3% for usual care (ratio 4 months/baseline = 0.85±0.29 vs. 1.03±0.21, p=0.004). Pharmacist-led group medical visits are feasible and effective for improving cardiac risk factors in DM. Our results demonstrate a potentially less costly, yet effective collaborative approach to manage DM and associated cardiac risk.

RISK FACTORS BEFORE AND AFTER THE MEDIC INTERVENTIONS

	MEDIC group			Usual Care		
	n=58			n = 51		
Parameters	Baseline	4 Months	Average Change	Baseline	4 Months	Average Change
SBP (mmHg ± SD)	131.1 ± 18.8	124.3 ± 15.3	-6.8± 21.0*	137.2 ± 17.5	135.4 ±16.9	-1.8 ± 19.6
DBP (mmHg ± SD)	74.8 ± 10.6	68.3 ± 10.9	-6.5 ± 10.0 *	74.2 ± 9.8	75.2 ± 10.4	1.0 ± 11.0 †
Cholesterol / HDL ratio	4.6 ± 1.6	4.2 ± 1.3	-0.5 ±1.5	4.3 ± 1.4	4.4 ± 1.1	0.1 ± 1.0 †
LDL (mg/dL± SD)	93.6 ± 32.8	82.8 ± 24.3	-12.2 ± 31.4 **	93.2 ± 33.0	85.2 ± 27.0	-7.8 ± 27.2
Active Smokers (%)	18.4	19.3	0.9	6.42	6.42	0
A1C (% ± SD)	8.1 ± 1.6	7.3 ± 1.1	0.9 ± 1.6 **	7.9 ± 1.1	7.7 ± 1.2	0.2 ± 0.9 †
BMI (Kg/M^2)	33.9 ± 6.4	33.7 ± 6.3	-0.2 ± 1.3	31.7 ± 7.1	31.7 ± 7.3	0.03 ± 1.0

* P < 0.01 from baseline ** P <0.05 from baseline † P <0.05 Change MEDIC group vs. Usual care

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Poster Presentations

P1

Determinants of Blood Cell Omega-3 Fatty Acid Content

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Introduction: Low red blood cell eicosapentaenoic acid (EPA) plus docosahexaenoic acid (DHA) content (the omega-3 index) has been proposed as a cardiovascular death risk factor. However, the factors that determine the omega-3 index are not well described. **Hypothesis:** We hypothesized that EPA+DHA intake, from fish and/or capsules, would be the primary determinant of the omega-3 index. **Methods:** We collected demographic, dietary, and clinical information and measured the omega-3 index in 704 outpatients in Kansas City. The use of fish oil capsules and the frequency of tuna/other non-fried fish intake were used as the EPA+DHA intake predictor variables. A multivariable log-normal regression model was constructed to explore associations between demographic characteristics, clinical factors, and EPA+DHA intake, with the omega-3 index. **Results:** The subjects were 67% male, age 62 ± 12, BMI 28 ± 6 kg/m^2. Frequency of fish oil consumption was 34%, smoking (13%), and diabetes (16%). Factors significantly associated with the omega-3 index in decreasing order were: EPA+DHA supplement use, fish consumption frequency (positive), serum triglyceride level (negative), age, history of high cholesterol (positive), and smoking (negative). Gender, BMI, HDL, LDL, and diabetes were not significantly related to the omega-3 index. A regression model containing these significant factors explained 59% of the variation in the omega-3 index, with capsules/fish intake together accounting for 47%. The omega-3 index increased by 13% ($p<$ 0.0001) for each serving level increase in fish intake (<1 serving/month; 1–3 servings/month; one serving/week; and ≥ 2 servings/week), and EPA+DHA supplementation correlated with a 58% increase ($p<$ 0.0001) in the omega-3 index regardless of background fish intake (p=0.25; test for interaction). A 100 mg/dL decrease in serum triglycerides was associated with a 15% higher (p<0.0001) omega-3 index. For women, being estrogen sufficient was not associated with the omega-3 index (p=0.09). **Conclusions**: In conclusion, the intake of EPA+DHA-rich foods and supplements were the principal determinants of the omega-3 index, but they explained only about half of the variability in this marker. Genetic/metabolic factors may affect the omega-3 index.

P2

Inflammation, Hemostasis, and the Risk of Chronic Kidney Disease in the Atherosclerosis Risk in Communities Study

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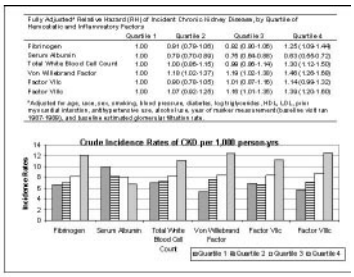
BACKGROUND: Cardiovascular disease (CVD) and chronic kidney disease (CKD) share common antecedents. Markers of inflammation and hemostasis predict CVD, but their relationship with CKD risk is unknown. **METHODS:** Glomerular filtration rate (GFR) was calculated from serum creatinine, using the abbreviated Modification of Diet in Renal Disease equation, in 14,854 participants of the Atherosclerosis Risk in Communities (ARIC) Study with a baseline estimated GFR > 60mL/min/1.73m^2. Incident CKD was defined as the earliest of 1) a decline in estimated GFR below 60 mL/min/1.73m^2 at one of two follow-up visits (3 and 9 years after baseline), **or** 2) a hospitalization discharge or death coded for CKD over 18 years of follow-up. Multivariable Cox proportional hazards regression was used to estimate relative hazards of CKD associated with quartiles of inflammatory and hemostatic factors measured at baseline. **RESULTS:** A total of 1,787 cases of CKD developed (incidence rate = 8.37/1,000 person-years). After adjustment, CKD incidence was greater with higher quartiles of fibrinogen, white blood cell count, von Willebrand Factor, and Factor VIIc. A strong inverse association was found between serum albumin and incident CKD. No independent association was found between quartiles of Factor VIIIc and CKD. Associations were similar after stratification for race, gender, diabetes, and prevalent myocardial infarction. **CONCLUSIONS:** Elevated markers of inflammation and hemostasis are associated with a greater risk of incident CKD. These findings suggest that inflammation and hemostasis are important pathways in the development of kidney disease, independent of traditional CVD risk factors.



P3

Incremental Value of Carotid Intima-Media Thickness Lesion Complex Measurement in Management of Cardiovascular Disease Risk Factors

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Early detection of cardiovascular disease is a challenge in a routine clinical care setting. Many cases are at risk but few show signs or symptoms. We studied he impact of routine Carotid Intima Media Thickness (CIMT) and Plaque assessment. Application of a fully automated web-embedded analysis software (ZoeXp) to measure CIMT and detect plaque formation was used. The hypothesis being that the CIMT/Plaque findings could assist the patient management in the asymptomatic patient at risk. All cases were seen during 5 sequential weekdays in a routine clinical care setting in a suburban clinic. Cases were not to have any sign or symptom of cardiovascular disease and were not known with cardiovascular disease, Cases were analyzed for major risk factors and CIMT /Plaque formation. . . A total of 556 patients (301 women and 255 men) were studied. All underwent a standardized procedure using a 7.5–10 MHZ linear array probe. Lesions were automatically assessed, once identified.Images were sent and received using the internet to assess the extent and severity of disease as measured by a carotid IMT thickness measurement as well as the presence (size) or absence of plaque formation. Patients were analyzed using the standardized PCI nomograms. The quintiles that were used indicated an A (pc<50%) a B (pc 50–90 %) a C (pc 90–125 %) D (pc125%-200%) and E (above pc: 200%) pc=percentile Major cardiovascular risks were assessed: The results were : Conclusion: In a clinical setting, CIMT analysis and plaque assessment are early detection tools in cardiovascular disease, superior to individual risk factor assessment alone and allow in asymptomatic patients a customized risk factor management approach

cases	Elevated LDL	Low HDL	hypertension	diabetes	smoking	BMI	Category
137	40	3	14	0	3	14	A
206	58	39	30	7	15	20	B
105	59	49	41	15	21	40	C
82	60	50	40	42	26	56	D
13	62	56	84	53	31	69	E

percentage of studied population in category

P4

Metabolic Syndrome and Cancer Mortality in Men

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Objective: Although most of the components of the metabolic syndrome (MetS) have individually been linked in some way to the development of cancer, epidemiological studies linking the MetS to cancer are scarce. We explored the potential relationship between the presence of clinically defined MetS and number of MetS components and any death from cancer and site-specific cancer death in a large cohort of men enrolled in the Aerobics Center Longitudinal Study (ACLS). **Methods**: Participants were 33,230 men (mean±SD age 44.9±10.0 yr) who were free of known cancer at baseline and who had a preventive medical examination at the Cooper Clinic, Dallas, TX between 1977 and 2003. MetS components and other risk factors were collected at baseline and the presence of MetS was defined as having three or more of the following components: abdominal obesity, fasting hypertriglyceridemia, low HDL cholesterol, high blood pressure, or high fasting glucose with NCEP ATP-III criteria. Mortality follow-up was through December 31, 2003 using the National Death Index. Cox regression models were used to examine associations. **Results**: There were 685 cancer deaths (157 lung cancer, 57 colorectal cancer, and 34 prostate cancer) during an average of 14 yrs of follow-up. Baseline MetS (≥3 components vs. 0 components) had a positive association with age-adjusted cancer mortality (hazard ratio [HR], 1.56; 95% confidence interval [95% CI], 1.34–1.82); this association remained significant after multivariate adjustment (HR, 1.49; 95% CI, 1.27–1.74). There was a dose-response association between cancer mortality and the number of MetS components present at baseline (P for trend <0.001). Each of the individual MetS components was positively associated with cancer deaths (P <0.05 for each). The presence of MetS was also positively associated with death from lung and colorectal cancer. Risk associated with MetS was particularly increased for individuals that were over 60 yrs of age, overweight and obese, or current smoker. **Conclusions**: MetS was a risk factor for cancer mortality and for some site-specific cancer (lung and colorectum) in men. The prevention or control of abnormalities associated with the syndrome may lead to a reduction in the premature cancer death.

P5

An Elevation of White Blood Cells Is Associated with Metabolic Syndrome in Black and White Children and Adults: The Bogalusa Heart Study

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Introduction - White blood cell (WBC) count, an important marker of systemic inflammation, is associated with cardiovascular disease and risk factors. This study assessed the hypothesis that elevated WBC is related to metabolic syndrome components in children and adults. **Methods** - The study cohorts for cross-sectional analyses consisted of 939 white children (49.4% male) and 771 black children (51.1% male) aged 4–14 years, and 1002 white adults (39.7% male) and 406 black adults (37.2% male) aged 19–38 years enrolled in the Bogalusa

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Heart Study. Race-, sex- and age-specific quartiles of body mass index, mean arterial pressure, high-density lipoprotein cholesterol (bottom quartile), triglycerides and homeostasis model assessment of insulin resistance derived from fasting glucose and insulin were used to define metabolic syndrome in children and adults. **Results -** White versus black subjects had significantly higher WBC in both children (6852/μL vs 5974/μL, $p<0.001$) and adults (6572/μL vs 6086/μL, $p<0.001$). Females showed significantly higher lymphocytes and neutrophiles, but lower monocytes than males in children and adults for both races. Current smoking was associated with elevated WBC in black ($p<0.001$) and white ($p<0.001$) adults. Mean values of WBC increased with the number (0, 1, 2 and 3 or more) of metabolic syndrome risk variables in black ($p=0.025$), white ($p=0.012$) and total sample ($p=0.002$) of children. Furthermore, the mean values of smoking-adjusted WBC increased with the number of metabolic syndrome risk variables in black ($p=0.685$), white ($p<0.001$) and total sample ($p<0.001$) of adults. With respect to WBC differential counts, similar increasing trends in lymphocytes, monocytes and neutrophiles were noted in children ($p=0.019$, $p=0.028$ and $p=0.019$, respectively) and adults ($p<0.001$, $p=0.032$ and $p<0.001$, respectively). **Conclusions** - The results from this study show that the WBC count is associated with metabolic syndrome starting from childhood. The findings suggest that WBC levels are related to cardiovascular disease, at least partially, through mechanistic link between increased systemic inflammation and metabolic syndrome components.

P6

The Effects of Obesity, Self-Reported Physical Activity, and Cardiorespiratory Fitness on Metabolic Profiles in the NHANES 1999–2002

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Background: This study was designed to elucidate the effects of self-reported physical activity and cardiorespiratory fitness, as well as obesity, on the components of the metabolic syndrome (MS). **Methods:** A total of 950 Caucasian subjects aged between 19 and 49 from the National Health and Nutritional Survey (NHANES) 1999 to 2002 was included into this study, and the metabolic profiles were retrieved from NHANES database. Cardiorespiratory fitness (VO_2 max) was predicted from a submaximal exercise stress test. Self-reported physical activity was measured by metabolic equivalent score transformed from a questionnaire. A structural equation model (SEM) was constructed to validate the relationship between cardiorespiratory fitness, self-reported physical activity, and the components in MS. **Results:** The model showed that obesity was positively linked to hypertension ($B = 0.50$, $p < 0.001$) and C-reactive protein (CRP; $B = 0.15$, $p<0.05$), which in turn led to insulin resistance ($B = 0.44$, $p<0.05$). Increased cardiorespiratory fitness was negatively associated with CRP ($\Gamma=-0.23$, $p < 0.01$), but not correlated to hypertension after adjustment of potential confounding factors. No significant association was found between self-reported physical activity and the components of MS. **Conclusion:** Obesity has contributed to the development of other components of MS. Improved cardiorespiratory fitness might lead to clinical and biochemical improvement in MS by reducing the proinflammatory state. Self-reported physical activity is not useful in predicting the changes in metabolic profiles.

P7

Alcohol Intake and 19-Year Mortality in Diabetic Men: NIPPON DATA80

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Backgrounds: Although moderate alcohol intake in diabetic Caucasian is associated with a reduction in coronary heart disease mortality, no study in Japanese with diabetes has examined the association between alcohol intake and mortality outcomes. **Methods:** We analyzed the relationship between alcohol intake and all-cause and cause-specific mortality using the database from NIPPON DATA80. At baseline in 1980, data on history, lifestyle and physical examinations were collected on study participants aged 30 years and over from randomly selected areas in Japan. After excluding participants with co-morbidities, we followed 4,018 male participants (3,614 non-diabetics, 195 with impaired glucose tolerance and 209 diabetic) for 19 years. **Results:** During the 19 years of follow-up, there were 990 deaths; 328 were from cardiovascular disease, and 157 from all heart diseases. With the never-drinking category serving as a reference, the Cox multivariate adjusted hazard ratios for non-daily and daily drinkers for cardiovascular mortality were 0.43 (95% confidence intervals: 0.19–0.95) and 0.45 (0.25–0.80) , respectively, and 0.33 (0.12–0.91) and 0.31 (0.15–0.67) for all-heart disease mortality in the combined impaired glucose tolerance and diabetic Japanese men. In the normal Japanese men, the hazard ratios for non-daily and daily drinkers for cardiovascular mortality were 0.55 (0.37–0.81) and 0.85 (0.63–1.15), respectively, and 0.41 (0.23–0.79) and 0.65 (0.42–1.10) for all-heart disease mortality. **Conclusions:** Alcohol drinking in men with glucose intolerance was associated with a significant reduction in cardiovascular and all-heart disease mortality as seen in the general population in Japan.

P8

Increased Lipid Peroxidation, Inflammation, and Reduced Antioxidant Potential of Treated Hypertensive Patients in the Presence of Metabolic Syndrome

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Objective Both hypertension and metabolic syndrome (MetS) have been associated with increased risks for coronary heart disease. In the present study, we investigated whether the presence of MetS would aggravate the features of inflammation and antioxidant potential in treated hypertensive patients. **Subjects and Methods** MetS was defined as three or more of the following abnormalities according to NCEP ATP III definition modified by WHO Western Pacific Region obesity criteria: (1) waist circumference $\geq$90 cm in men, $\geq$80 cm in women; (2) hypertriglyceridemia, $\geq$150 mg/dL (3) low HDL-cholesterol, $<$40 mg/dL in men and $<$50 mg/dL in women; (4) hypertension (systolic blood pressure $\geq$130 mmHg or diastolic pressure $\geq$85 mmHg) or on anti-hypertensive medication; (5) high fasting glucose, $\geq$110 mg/dL or under treatment for diabetes. Subjects were all treated hypertensive patients ($n=124$) and three groups were classified by the components of MetS: a reference group of treated hypertensive subjects: group A ($n=37$), with one additional MetS criterion; group B ($n=40$), with more than two additional MetS criterion; group C ($n=47$). Blood lipids, apolipoproteins, C-reactive protein (CRP), conjugated dienes of LDL (CD), total radical trapping antioxidant potential (TRAP) and cytokines such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and intercellular adhesion molecule-1 (ICAM-1) were measured. **Results** Age, BMI and gender distribution were not different among three groups. ANOVA analysis showed that as the number of components of MetS were increased, the levels of TRAP ($p<0.01$) were significantly decreased and the levels of CD ($p<0.05$) and IL-6 ($p<0.005$) were significantly increased. When comparing between hypertension only (group A) and hypertension with MetS (group C) using independent t-test, TRAP ($p<0.01$) was significantly lower and CD ($p<0.05$), IL-6 ($p<0.001$), TNF-α ($p<0.05$) were significantly higher in the hypertensive patients with MetS than in hypertensive patients. **Conclusions** Our results showed that the profiles of inflammation and antioxidant potential resulted in more unfavorable patterns in treated hypertensive patients in the presence of MetS, suggesting the importance of therapeutic lifestyle changes to modify the features of MetS.

P9

Withdrawn

P10

Circulating Metabolic Intermediates Are Markers of Insulin Resistance in a Population at Risk for Coronary Heart Disease

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Background: The incidence of type 2 diabetes is increasing at alarming rates. Our objective was to determine if measurement of metabolic intermediates with a targeted mass-spectrometry based platform might provide insight into the pathogenesis of insulin resistance, a harbinger and essential component of type 2 diabetes. **Methods and Results:** This investigation was performed in 73 sedentary, middle-aged, dyslipidemic individuals enrolled in

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an exercise training intervention (STRRIDE). Insulin sensitivity (IS_I) was derived from glucose and insulin measurements obtained during a frequently sampled intravenous glucose tolerance test. Fasting plasma was used to measure concentrations of 74 circulating amino acids, acylcarnitines, free fatty acids, and conventional metabolites. Subjects also underwent anthropometric measurements, skeletal muscle biopsies, and cardio-respiratory exercise treadmill testing. Principal components analysis (PCA) followed by backward stepwise linear regression was used to explore relationships between metabolic intermediates and IS_I. Using PCA, the 74 metabolic intermediates clustered into 18 retained components. Of these 18 components, medium- and long-chain acylcarnitines, fatty acids, and amino acids clustered into three distinct factors. When the 18 factors were evaluated in the context of a previously established model for IS_I containing gender, lean body mass, cardio-respiratory fitness, LDL particle size, skeletal muscle fiber area, and waist circumference, we found that two factors improved the explanation of variance in IS_I from 71% to 81%. These included a factor containing fatty acids and one comprised of large neutral amino acids. Both factors were independently and inversely related to IS_I. Alone, the factor comprised of large neutral amino acids was inversely related to and accounted for 19% of the variance in IS_I. **Conclusions:** In addition to previously identified risks for insulin resistance, elevated concentrations of large, neutral amino acids independently associate with insulin resistance. Efforts are underway to determine if these metabolic intermediates might be altered in the context of a physical activity intervention that improves insulin resistance.

P11

Vascular Function Measured by Fingertip Thermal Reactivity Is Impaired in Patients with Insulin Resistance

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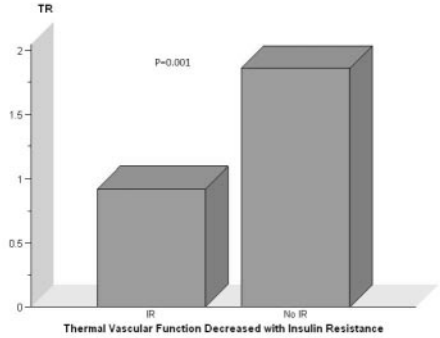
Background: Endothelial dysfunction precedes atherosclerotic disease and is associated with insulin resistance, metabolic syndrome, and diabetes. Digital Thermal Monitoring (DTM) of vascular reactivity is a new test of vascular function that has been shown to correlate with Framingham Risk Score, sub-clinical coronary artery disease measured by coronary calcium score, and angiographically defined coronary artery disease. Present study tests whether DTM of vascular reactivity is impaired with insulin resistance (IR) defined as plasma triglyceride/high-density lipoprotein cholesterol ratio >3.5. **Methods:** 128 subjects (mean age 57 ± 11years, 65% male), without CHD, diabetes and NCEP metabolic syndrome were studied. Each underwent DTM during and after 5 minutes supra-systolic arm cuff inflation. Post-cuff deflation temperature rebound (TR), was studied as indices of vascular reactivity. **Results:** TR was lower in subjects without IR compared to IR (figure). After adjustment for age, gender and conventional risk factors using logistic regression analysis , the odds of lower tertile vs. upper 2 tertile of TR was 1.3 (95% CI 1.05–1.60, p0.002) for IR compared to without IR. **Conclusion:** Vascular dysfunction measured by DTM is associated with insulin resistance.



P12

Alteration in Peripheral Lymphocyte Gene Expression by Fenofibrate Treatment in GOLDN Study

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Fenofibrate is widely used for the management of hyperlipidemia. Its pharmacologically active metabolite, fenofibric acid activates peroxisome proliferator-activated receptor-α (PPAR-α) and results in increased triglyceride (TG) clearance and reduced TG synthesis. PPAR-α-independent action of fenofibrate due to cross-talk with other PPAR family members has also been reported. The mechanisms underlying these effects are not currently well documented. Gene expression analyses in animal studies have revealed that the action of fenofibrate involves proliferation induction and apoptosis suppression. In the current study, we selected 19 participants with hypertriglyceridemia (baseline plasma TG levels >150 mg/dL) from the Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study, and compared the gene expression profile in peripheral blood cells before and after treatment with 3-week open-label fenofibrate (160 mg/d). RNA was extracted using Trizol immediately after blood collection. Gene expression profiling was performed on Affymetrix™ U133Plus2.0 platform (Affymetrix, CA) and data analysis was performed by GeneNews (GeneNews Corp., Toronto, Canada). 20 paired and 5 unpaired samples that passed quality control were used for gene expression analysis. Paired t-test was used for comparison of mRNA levels in samples obtained before and after fenofibrate treatment. Using all 25,801 genes filtered by expression signal, 91 genes showed significant change after treatment ($P<0.05$). Analysis using either all samples or 8 unclustered samples consistently revealed the two genes that showed the greatest changes in expression were B cell lymphoma-6 (BCL6) and SPEN. SPEN is involved in the Ras-MAPK pathway, which may be regulated through the activation of PPAR-α, while BCL6 may be involved in the PPAR-ä signaling pathway and/or play a role in PPAR-ä regulation in peripheral lymphocytes. These findings may have therapeutic and/or pharmacogenetic implications and may also explain the anti-inflammation effect of fenofibrate. More studies are required to understand the significance of these findings and confirmatory studies are needed to demonstrate that fenofibrate administration consistently and reproducibly activate BCL6 and SPEN.

P13

Lipoprotein (a) Is a Strong Significant Independent Predictor of Severe Coronary Artery Disease Among Indian Population

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Background: Indian population is witnessing an epidemic of coronary artery disease (CAD), whereas its incidence is going down in the developed countries. Reasons underlying this fact are not well understood. Most of the current recommendations for primary and secondary prevention and lipid management are based on research done in the Western hemispehere. We evaluated lipoprotein 'a' [Lp(a)] and lipid tetrad index among Indian patients with CAD. **Methods:** 213 patients undergoing invasive coronary angiography (ICA) to rule out CAD were included and their lipid profile and Lp(a) levels were measured. Lipid tetrad index is derived by multiplying the three lipids directly associated with CAD and dividing the product by HDL, which is inversely associated with CAD [total cholesterol x triglycerides x Lp(a)/HDL]. **Results:** There were 94 females and the average age was 52. Patients with CAD had significantly higher Lp(a) 41 ± 7.8 vs. 14.4 ± 9.69, $p<0.0001$. We found that of the 96 patients with high Lp(a) (≥ 30 mg %), 91 (94.8%) had significant CAD on diagnostic ICA as compared to 61 (52%) patients with Lp(a) <30 ($p<0.0001$). The lipid tetrad index was significantly higher in those with coronary artery disease as compared to those with normal coronaries, 28240.2 ± 8668.9 vs. 9101.80 ± 7277, $p=0.001$. Patients with Lp(a) ≥ 30 were 7 times more likely to have triple vessel disease (43.7% vs. 6%, $p<0.0001$). On multiple regression analysis with other lipid parameters Lp(a) was the only significant independent predictor of significant CAD ($p=0.005$). **Conclusions:** Lipoprotein 'a' is a strong independent predictor of CAD in the Indian population. We suggest that Indian population may need different set of targets for prevention and treatment.

P14

Influence of Insulin, Leptin, and Adiponectin on Blood Pressure in a Population-Based Sample of Youth

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Background. The mechanisms underlying the association between body fat and BP are still imperfectly understood but may involve hyperinsulinemia and/or insulin resistance as well as fat-derived adipokines, leptin and adiponectin. However, clinical studies assessing these factors showed inconsistent results in both, adults and youth. **Methods**. BP was measured with an ocillometric device (Dinamap) in 655 boys and 667 girls aged 9, 13 and 16 years who participated in a province-wide survey conducted in 1999 in Quebec, Canada. Linear regression assessed the association between BP and questionnaire data, physical measurements, fasting plasma insulin, leptin and adiponectin. **Results**. Strong positive associations between BMI, insulin and leptin Z scores, and systolic and diastolic BP were found univariately in both sexes (all $p < 0.002$). Adiponectin Z score was negatively associated with systolic BP in girls only ($p = 0.039$). In multivariate analysis only BMI and insulin Z scores remained significantly associated with systolic BP: for each 1SD increase in insulin Z score, mean systolic BP increased by 1.3 and 1.8 mm Hg in boys and girls, respectively while for each 1 SD increase in BMI Z score, mean systolic BP increased by 4.2 and 2.5 in boys and girls, respectively. Diastolic BP was independently associated with insulin Z score only: for each 1SD increase in insulin Z score, mean diastolic BP increased by 1.0 and 1.1 mm Hg in boys and girls, respectively. The same analyses repeated with HOMA-IR as the surrogate measure of insulin resistance gave similar results. **Conclusion**. Insulin resistance as indirectly measured by fasting insulin is an important determinant of systolic and diastolic BP in children and adolescents in both sexes. Although animal studies support a role for leptin and adiponectin in controlling BP, they were not independently associated with BP in our population.

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P15

Inflammatory Profile in Subject with Hypertriglyceridemia Managed by Fenofibrate, a PPARα Agonist

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Hypertriglyceridemia (HTG) and the associated atherogenic lipoprotein profile of low HDL cholesterol and elevated small LDL are risk factors for cardiovascular diseases. Fenofibrate (FEN), a PPARα agonist is commonly used as therapy to treat a constellation of lipid abnormalities, particularly when Statin treatment does not fully control HTG and low HDL. HTG is also a feature of the metabolic syndrome. Individuals with this syndrome are frequently obese, displaying glucose intolerance, hyperinsulinemia, insulin resistance (IR) with concomitant elevation of TG and low HDL. Obesity and IR are also inflammatory conditions, associated with abnormal peripheral adipokine and cytokine levels. While FEN has been demonstrated to be an effective agent to decrease TG levels, it is not known whether FEN reduces IR and confers an improved inflammatory profile in treated subjects. This study has as its aim to determine the response of TNFα soluble receptor 1 (TNFα SR1) and 2 (TNFα SR2), surrogates for blood TNFα, as well as C-reactive protein (CRP) in 52 subjects with HTG on FEN therapy (8 weeks of 145mg daily). Results are presented as mean $\pm$ SEM. Subjects were all Hispanics, age (39.6 $\pm$ 1.4 yr), gender (M:27, F:25) and BMI (30.4 $\pm$ 0.6 kg/m^2) respectively. We observed a significant decrease in TG (252 $\pm$ 25 vs 140 $\pm$ 9 mg/dl, p$<$.001), cholesterol (194 $\pm$ 5 vs 173 $\pm$ 4 mg/dl, p$<$.002), FFA (497 $\pm$ 23 vs 421 $\pm$ 25 μmol/l, p$<$.05) as well as glucose (101 $\pm$ 2 vs 96 $\pm$2 mg/dl, p$<$.02). CRP trended down (0.63 $\pm$ 0.37 vs 0.46 $\pm$ 0.42 μg/ml, p=.064). However, there were no changes observed in insulin (12.2 $\pm$ 1.0 vs 12.4 $\pm$ 1.0 μU/ml), TNFα SR1 (1.63 $\pm$ 0.05 vs 1.75 $\pm$ 0.05 ng/ml) or TNFα SR2 (6.55 $\pm$ 0.21 vs 6.88 $\pm$ 0.20 ng/ml). In summary, management of HTG with FEN effectively decreases TG, cholesterol, FFA and glucose, but did not improve fasting insulin concentration and $HOMA_{IR}$ (3.1 $\pm$ 0.3 vs 3.0 $\pm$ 0.3 μU•mM/ml). FEN appeared to have a favorable effect on CRP but not on the TNFα related inflammatory pathway. These data confirm that activation of PPARα with FEN favorably regulated the genes of FFA transport and oxidation. This in turn improved hepatic insulin resistance and lowered the blood glucose concentration. By contrast, FEN did not change the whole body insulin resistance and the TNFα related inflammatory marker levels.

P16

Association Between Aerobic Training–Induced Changes in Heart Rate Variability and Insulin

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Back Ground: Epidemiology studies have found low heart rate variability (HRV) to be associated with increased risk for diabetes. There are few studies directly examining the association between change in HRV and changes in measures of glucose utilization. Objective: To examine the association between changes in HRV and changes in insulin using the combined data from a large exercise dose response study (The DREW Study). Method and Results: The study population consisted of overweight and obese, sedentary post-menopausal women [57.6 (6.3) y] who were randomly assigned to one of three exercise groups: 4, 8, or 12 kcal/kg/wk or a no-exercise control group. This analysis was limited to women (n=332) with baseline and follow-up fasting insulin and measures of HRV. For brevity we only present the data for the HRV index rMSSD, a measure of parasympathetic tone. It is worth noting that the other HRV indices that quantify parasympathetic tone had similar results. Baseline insulin was 74.5 (63.5) mmol/L and rMSSD was 23.1 (20.7) ms. At follow-up, change in rMSSD was correlated (Spearman) with change in insulin (r = -.21, p = 0.0002). Examined categorically to minimize the effect of outliers, the association was even more striking. The mean (SE) change in insulin across quartiles of change in rMSSD were: Q1 (least improvement) = 8.5 (3.2), Q2 = -3.3 (3.2), Q3 = -5.6 (3.2) and Q4 = -9.7 (3.3). These changes in insulin were adjusted for age, ethnicity, change in fitness, BMI, and randomization group. All groups were significantly different from Q1 with a highly significant p-trend (p$<$0.0001) for change in insulin across change in rMSSD quartiles. Conclusion: In this population of women, exercise associated changes in HRV are highly correlated with change in insulin (inversely). The mechanisms responsible for this association warrant further investigation.

P17

Meta-Analytic Multivariate Engineered Model of Preventable Coronary Heart Disease Risk

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Objective: While several existing heart disease risk models (Framingham, QRISK, SCORE) provide excellent tools for identifying those at risk, the risk factors utilized are not always directly tied to modifiable dietary and lifestyle factors or appropriate pharmaceuticals. Therefore, a new model was engineered to summarize the direct connection between these factors and the risk of heart disease. This should improve patient communication and motivation. **Method**: Starting with a heart disease risk model that we had previously developed based on the Framingham model, our initial model included basic nonmodifiable risk factors (age, gender, prior heart disease, family history, and diabetes) and 3 modifiable risk factors: body mass index, smoking, and exercise level. We then surveyed the literature and summarized the age-gender adjusted risks of the following dietary factors: fruits and vegetables, red meat, alcohol, whole grains, and fish. We also found published meta-analytic results for antihypertensive and antihypercholesterolemic drugs and for aspirin. A risk model was constructed adjusting for colinearity between the risk factors using a propriety tool, Synthesis Analysis™. Dietary variables were imputed to the NHANES 1999–2000 cohort for this modeling effort. A minimized risk was also calculated based on commonly accepted salutary dietary, lifestyle and pharmaceutical recommendations. **Results**: The original risk factor odds ratios were recapitulated demonstrating the success of the colinearity adjustment. Fidelity to the Framingham model was demonstrated. When applied to the NHANES cohort, 62% (2607 of 4188) of heart disease risk among Americans could be reduced by optimizing these risk factors. A 15 fold range of age-adjusted risk existed between the lowest and highest quintiles of the cohort stratified by calculated risk. **Conclusion**: While not intended to assess heart disease risk based on known physiological biomarkers, this more consumer friendly model identifies a person's preventable risk with an accurate evidence-based model that ties risk directly to modifiable activities of daily life.

P18

Withdrawn

P19

Effects of Low-Carbohydrate and Low-Fat Diets on Inflammation and Endothelial Function

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Background The cardiovascular effects of weight loss through low-carbohydrate (LoCarb) diets compared to low-fat diets (LoFat) is uncertain. Objective To determine the effects of LoCarb and LoFat weight loss diets on inflammation and endothelial function. Methods Obese adults with T2DM (HbA1c ranges 6–11%) were randomized to a LoCarb diet (n=14) initiated with $<$20 grams of carbohydrate daily or an energy matched LoFat (n=13) diet (25% of calories from fat). Changes in weight and HbA1c were measured at 6 months. Measures of glucose, inflammation (high sensitivity C-reactive protein, hsCRP) and endothelial function (reactive hyperemic peripheral arterial tonometry, RHPAT) were obtained fasting and 3 hours after a 500 calorie LoCarb or LoFat mixed meal. Mann-Whitney U compared fasting and postprandial changes in CRP and RHPAT between diet arms. Results At baseline, participants had a mean ($\pm$SD) weight of 217$\pm$42 lbs., HbA1c of 7.2$\pm$1.4,%; glucose of 143$\pm$41, CRP=3.96$\pm$4.35mg/dl and RHPAT= 2.3$\pm$.87, with no significant between group differences. Both dietary arms achieved weight loss and reduction in fasting hsCRP. Postprandial glucose change differed between dietary arms as seen in the Table. Conclusions Our findings suggest that using either a low-fat or a low-carbohydrate approach to weight loss may improve inflammation in T2DM. While the postprandial glucose increased following a low-fat meal test, neither meal resulted in postprandial changes in inflammation or endothelial function. Weight loss and dietary composition may have independent effects on indices of CVD risk.

SIX MONTH CHANGES IN GLUCOSE, CRP, AND RHPAT

	LoCarb	LoFat	p*
Δ Weight (lbs)	-10.3**	-12.2**	.68
Δ HbA1c%	-.75**	-.45	.59
Δ fasting glucose (mg/dl)	+6	-25	.21
Δ fasting CRP (mg/L)	-1.66**	-1.94	.83
Δ fasting RHPAT	-.21	-.08	.93
Δ postprandial glucose (mg/dl)	-9.5	+71	.04
Δ postprandial CRP (mg/L)	+.13	+.02	.35
Δ postprandial RHPAT	-.13	+.30	.23

*p value represents between dietary arm differences **p$<$.05 for within group change from baseline to 6 months

P20

Association Between Dietary Patterns, Cardiovascular Risk Factors, and C-Reactive Protein in a Large, Healthy Italian Population: Results from the Moli-sani Study

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Background: Dietary habits may influence cardiovascular disease (CVD) risk modulating CVD risk factors and markers of inflammation. **Aim:** To evaluate the association of dietary patterns with CVD risk factors and C-Reactive Protein (CRP). **Methods:** The *Moli-sani* Project is an on-going cohort study of men and women aged $\geq$ 35, randomly recruited from the general population of Southern Italy. Until July 2007, 10994 subjects have been enrolled. After the exclusion of subjects with a history of CVD, diabetes, hypertension or hyperlipidemia, we analyzed 5120 subjects (mean age 50$\pm$10; 49% males). A validated food frequency questionnaire was used. Dietary patterns were generated through a principal factor analysis based on 51 food groups. High sensitivity CRP levels were measured by immunoturbidimetric method (IL, Milan, Italy). **Results:** We identified 3 dietary patterns, accounting for 66% of the total variance. The first pattern was characterized by higher intake of pasta, tomato sauce, red meat, animal fats and alcohol, the second by higher intake of olive oil, vegetables and legumes and the third by higher intake of eggs, sugar, cakes and dairy products. In multivariate analyses adjusted for age, sex, total energy intake, social status, smoking and physical activity, increasing quintiles of the first pattern were associated with higher values of waist to hip ratio, body mass index (BMI), triglycerides (TG), blood glucose, CRP (p$<$0.0001), LDL, total

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cholesterol and diastolic blood pressure ($p<0.01$) and with lower values of HDL ($p=0.006$). The second pattern was associated with an increase BMI ($p=0.006$) and a decrease TG ($p=0.034$). The third pattern was associated with an increase CRP ($p<0.0001$). After further adjustment for BMI and TG, the first and the third patterns still remained associated with an increase of CRP ($p<0.0001$). The CRP values ranged from 1.1 to 1.4 mg/L across increasing quintiles of pattern 1 or 3. The prevalence of subjects with CRP>3 mg/L ranged from 16% to 21% across increasing quintiles of pattern 1. **Conclusions:** In a large healthy Italian population, two dietary patterns characterized by mostly unhealthy foods were associated with higher levels of known cardiovascular risk factors and CRP, whereas a "prudent-healthy" pattern was not.

P21

Moderate Consumption of Dark Chocolate Is Associated with Low Plasma Levels of C-Reactive Protein in a Large, Healthy Italian Population: Results from the Moli-sani Study

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Background: Flavonoids are associated with reduced inflammatory reactions. Dark chocolate (DC) contains high concentrations of flavonoids, and may have anti-inflammatory properties. **Aim:** To evaluate the association of DC intake with C-Reactive Protein (CRP) levels. **Methods:** The Moli-sani Project is an on-going cohort study of men and women aged ≥35, randomly recruited from a Southern Italy general population. Until July 2007, 10,994 subjects have been enrolled**.** Among 5,008 subjects apparently free of any chronic disease 1,365 subjects who declared they did not eat any chocolate during the past year (mean age 53±12; 51% males) and 853 subjects who did eat chocolate but only in the form of DC (50±10; 55% males) were selected. High sensitivity-CRP plasma levels were measured by an immunoturbidimetric method (IL, Milan, Italy). The EPIC Food Frequency questionnaire was used to determine nutritional intake. Differences in CRP distribution were estimated by binomial Poisson regression. **Results:** DC consumers were younger, had a higher social status and a lower physical activity than non-consumers ($p<.0001$). They consumed less cereals, meat and alcoholic beverages ($p<.0001$), more nuts and seeds, fish, sweet confectionary, sweet beverages, coffee and tea ($p<.05$) and had a higher intake of total energy ($p<.0001$), and of all micro and macro-nutrients with the exception of total carbohydrates and total dietary fiber. After adjustment for age, sex, social status, physical activity, systolic blood pressure, BMI, waist to hip ratio, food groups and total energy intake, DC consumption was inversely associated with CRP ($p=.034$). When adjusted for nutrient intake, analyses showed similar results ($p=.019$). CRP mean values were 1.28 (1.22–1.34) and 1.17 (1.10–1.24) mg/L, in non consumers and in DC consumers, respectively. The prevalence of non-consumer subjects with CRP>3 mg/L was 19% while it was 14% in DC consumers. A U-shaped relationship between DC consumption and CRP was observed: consumers with a low intake of DC (up to 6.7 g/day) had CRP levels lower than non consumers or high consumers. **Conclusions:** Our findings suggest that moderate daily DC consumption may reduce inflammation (as shown by reduced CRP levels) thus contributing to cardiovascular health.

P22

Americans' Awareness, Knowledge and Behaviors Regarding Fats: 2006–2007

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Introduction: In recent years, epidemiologic and clinical studies, public and regulatory policy activity, and media coverage have focused on issues related to *trans* fat. To help raise awareness and understanding of *trans* fats and other fats, the American Heart Association (AHA) launched the "Face the Fats" national consumer education campaign in April 2007. The AHA commissioned a quantitative tracking study to measure changes in consumer awareness, perceptions and behavior related to fats and oils and their perceived impact on heart disease between 2006 and 2007. **Methods:** The study was conducted by Cogent Research. Data were collected during March 2006 and May 2007. At both time points, the survey included a representative sample of the American population aged 18–65 (n=1,000). The sampling plan for the study was designed based on the 2000 U.S. Census. The margin of error was +/- 3.10 percentage points. **Results:** Awareness of *trans* fats increased from 84% in 2006 to 92% in 2007 ($P<0.05$). The 2007 level was similar to awareness of saturated fats (93%). Perceptions that certain fats and oils increase the risk of heart disease increased for *trans* fats (63% to 73%), saturated fats (73% to 77%), and partially-hydrogenated oils (49% to 56%) ($P<0.05$). Knowledge of food sources of fats remains low. On an unaided basis, 21% could name three food sources of *trans* fats in 2007, up from 17% in 2006 ($P<0.05$). Similar knowledge of saturated fat food sources remained unchanged at 30% in 2007. Significantly more Americans in 2007 report behavioral changes related to *trans* fat information, for example, buying food products because they show "zero *trans* fat" on labels or packages (32% in 2006 vs. 37% in 2007; $P<0.05$). **Conclusion:** During the period of time between 2006 and 2007, consumer awareness about *trans* fats increased and reached levels similar to saturated fats. The increased awareness is associated with improved self-reported behaviors in grocery shopping. Nonetheless, overall knowledge, especially regarding food sources of saturated and *trans* fats, remains relatively low. The positive change in consumer awareness is likely attributable to the wide range of messages available to them, including the "Face the Fats" national consumer education campaign.

P23

Cardiac Apoptosis and Cardiac Hypertrophy in Obese Rats

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Background. The purpose of this study was to evaluate the cardiac apoptotic and hypertrophic pathways in obese Zucker rats. ***Methods.*** Sixteen obese Zucker rats were studied at 5–6 months of age and sixteen age-matched lean Zucker rats served as control. The heart weight index, myocardial architecture, key components of Fas receptor-dependent, mitochondrial-dependent apoptotic pathway and hypertrophic pathway in the excised left ventricle from rats were measured by weight scales, Hematoxylin-eosin staining, Western blotting, RT-PCR, TUNEL assay and Masson trichrome staining. ***Results.*** The body weight, whole heart weight, left ventricular weight, the ratios of whole heart weight to tibia length, % TUNEL-positive cardiac myocytes, and % cardiac fibrosis were significantly increased in the obese group. Cardiomyocyte disarray and increased cardiac interstitial space were observed in obese rats. The protein levels of Fas ligand, Fas death receptors, and Fas-associated Death Domain (FADD) were all significantly increased in obese group. Pro-apoptotic Bcl2 family members, BNIP3 and Bad levels, were significantly increased in obese rat hearts as well as anti-apoptotic Bcl2 family member, Bcl2 level, was significantly decreased. Cytosolic cytochrome *c* indicating cytochrome *c* release from mitochondria was significantly increased in obese rat heart. In addition, pro-caspase-8, pro-caspase-9 and pro-caspase-3 were significantly decreased whereas activated caspase-8, caspase-9 and activated caspase-3 were significantly increased in obese rat hearts, compared with lean rat heart, imply pro-forms of caspase-9 and caspase-3 were cleaved into active-forms caspase-9 and caspase-3. The cardiac hypertrophy markers, atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), tumor necrosis factor-alpha (TNFα) and eccentric hypertrophic markers interleukin (IL)-6-MEK5-ERK5 were significantly increased in obese rat heart. ***Conclusions.*** The cardiac Fas and mitochondrial-dependent apoptotic pathways and cardiac hypertrophic markers were more activated in obese Zucker rat, which may provide one of possible apoptotic and hypertrophic mechanism for developing heart abnormalities in obesity.

P24

An Alternative Technique for Blood Pressure Measurement in Morbid Obesity

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Background: Obesity and hypertension are closely associated. Medical professionals do not always have all the appropriate equipment on hand to properly measure blood pressure (BP) in the morbidly obese i.e. the use of a larger cuff bladders may be inadequate. The hypothesis of the study was that a non-invasive technique of BP measurement on the forearm with an appropriate cuff bladder will be comparable, to intra-arterial radial artery BP measurement, in subjects with morbid obesity (MO). **Methods:** Fifty one MO subjects, mean age of 43 years, with a BMI of 51,8 ± 8,7 kg/m^2 (mean ± SD), were all evaluated using two different techniques of BP measurement. Measures were performed, in a supine position, at the forearm level with a standard cuff bladder, and on the opposite forearm using an intra-arterial access. The MO group was evaluated during and after a bariatric surgical procedure, at regular intervals (every 10 to 15 minutes). **Results:** A total of 1286 measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were taken with each technique. A significant difference ($p<0.001$) was observed between the two techniques. The values for the intra-arterial were: SBP 136 ± 27 mmHg and DBP 71 ± 14 mmHg. For the simultaneously cuff assessment, SBP was 144 ± 27 mmHg and DBP was 70 ± 18 mmHg. There were positive correlations between the two techniques for the SBP ($r=0,828$, $p<0,001$) and DBP ($r=0,814$, $p<0,001$). **Conclusion:** Although statistically different, BP measurements at the forearm in MO subjects are clinically useful when compared to intra-arterial radial artery measurement of BP. When upper arm BP measurement is technically difficult or inaccurate, BP taken at the forearm may represent an alternative site and should be favoured in the MO. This may help to better manage BP in this population.

P25

Efficacy of Sibutamine-Induced Weight Loss vs Usual Treatment with Continuous Positive Airway Pressure in Obese Patients with Obstructive Sleep Apnea

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Objective: To compare the efficacy of 1-yr sibutramine-induced weight loss vs. continuous positive airway pressure (CPAP) treatment on cardiac autonomic function, blood pressure and symptoms of sleep apnea in obese patients with obstructive sleep apnea (OSA). **Methods:** Subjects with a body mass index (BMI) ≥ 30kg/m^2 and without previous treatment for OSA underwent either sibutramine (10 or 15 mg) (n=22) or conventional treatment with CPAP (n=19) for 1-yr duration. An overnight polysomnographic study, a 24-hour Holter monitoring and a 24-hr ambulatory blood pressure monitoring (ABPM) were performed on two occasions (baseline and after 1-yr). **Results**: At baseline, there was no significant difference in age, body weight, BMI, blood pressure, resting heart rate, fasting glucose and lipid profile between groups. Sibutramine induced a 5.4±1.4 kg decrease in body weight and a 7% reduction in waist circumference (all $p<0.001$) compared to the CPAP group where no changes in anthropometric variables were observed. Even if mean systolic (SBP) and diastolic (DBP) blood pressure were near to normal at baseline, ABPM showed that neither weight loss nor CPAP treatment influenced mean SBP and DBP over the year (133±2 vs. 132±2 mmHg for SBP and 82±1 vs. 84±2 mm Hg for DPB pre/post sibutramine treatment and 128±8 vs. 125±12 mm

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Hg for SBP and 80±1 vs. 77±5 mmHg pre/post CPAP treatment). No significant difference was also observed in day-time and night-time mean SBP and DBP. There were no changes in indices (VLF, HF, LF, LF/HF, SDNN, SDANN, rMSSD and pNN50) of heart rate variability. Only an increase in the RR interval (mean NN) was observed after treatment in the CPAP group ($p<0.05$). CPAP treatment improved all sleep and respiratory variables ($p<0.01$), whereas weight loss improved nocturnal desaturation only ($p<0.001$). **Conclusion:** These results suggest that neither weight loss nor CPAP treatment improve autonomic cardiac modulation, SBP or DBP. The potential hypertensive effect of sibutramine might have attenuated the beneficial impact of weight loss on these variables, particularly in this group of mild-hypertensive obese subjects. However, sibutramine may be combined safely to a conventional CPAP therapy in order to optimise OSA treatment in obese patients.

P26

Relationship Between Waist Circumference and Adipokines During Puberty

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Background: Increased visceral fat (VF) is associated with increased cardiovascular disease risk. This relationship may be mediated through the production of adiponectin by visceral fat and leptin by global fat. In adults, production of adiponectin decreases while leptin increases with increasing adiposity, resulting in a decreasing A/L ratio. In infants and pre-pubertal children, production of both adiponectin and leptin increase with increasing adiposity so that the A/L ratio remains constant even with increasing adiposity. The timing of the change from the child to the adult relationship between increasing adiposity and the A/L ratio occurs has not been studied. It is likely that the change in adipose tissue function, reflected by the A/L ratio, occurs during puberty. VF can be estimated by measuring waist circumference (WC). **Objective:** Describe the changes in the relationship between the A/L ratio and WC during puberty. **Methods:** We analyzed 61 serum samples (43% female; 79% white) from Project Heartbeat!, a longitudinal cohort of black and white children ages 8 - 18 years, to determine adiponectin and leptin concentrations. WC and blood were obtained every 4 months for 4 years. We calculated Pearson correlation coefficients to determine the relationship between natural log (ln) A/L ratio and WC at each pubertal stage (1 - 5, as described by Tanner). **Results:** The range of the ln A/L ratio was 5.1–11.3. See table for associations between ln A/L ratio and WC. **Conclusion:** The adult pattern of A/L ratio and its relationship to WC occurs most strongly and significantly at pubertal stage 3. There is some indication that the association may weaken at later pubertal stages, though larger studies are needed.

ASSOCIATIONS BETWEEN WC AND LN A/L RATIO DURING PUBERTY

#subjects	Pubertal stage	WC (mean ± SD)	ln A/L ratio (mean ± SD)	r
21	1	60.7 ± 6.9	8.9 ± 1.4	- 0.58*
13	2	66.2 ± 8.3	8.3 ± 1.4	- 0.55
10	3	69.8 ± 13.1	7.8 ± 1.5	- 0.76*
6	4	75.5 ± 7.5	7.8 ± 0.8	- 0.39
12	5	70.6 ± 6.7	7.6 ± 1.5	- 0.49

*$p<0.05$

P27

Cardiac Response to Progressive Cycle Exercise in Young, Overweight Men and Women

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Although obesity has been associated with changes in cardiac structure and function at rest, there is a paucity of data on the influence of overweight on cardiac function during exercise, particularly in young subjects. **Purpose**: To compare cardiac output (Q), stroke volume (SV) and heart rate (HR) at rest and during submaximal exercise in young normal weight (NW) and overweight (OW) subjects. **Methods**: Sixteen young, sedentary men (n = 10) and women (n = 6) participated in the study (age range 21–35 years). Subjects were grouped according to BMI as NW (Mean ± SD: BMI 22.0 ± 2.2 kg/m^2; fat 25.1 ± 8.8%; VO_{2max} 2.4 ± 0.5 L/min) or OW (BMI 29.6 ± 2.7 kg/m^2; fat 33.1 ± 7.7%; VO_{2max} 2.8 ± 0.6 L/min). Groups were matched for VO_{2max} and age. Body composition was measured via DEXA. A baseline maximal exercise test on a cycle ergometer was used to measure VO_{2max}. Forty eight hours following the first visit, Q was measured in duplicate (CO_2 re-breathing method) at rest and during steady-state cycling exercise at 50, 75 and 100 Watts. Differences between groups at rest were analyzed using an independent t-test. Differences between groups during exercise were analyzed using repeated measures ANOVA. **Results**: As expected BMI, fat mass and fat free mass (FFM) were significantly higher in the OW group ($p<0.05$). There were no differences in VO_{2max} between groups when expressed as an absolute value or relative to FFM ($p>0.05$). Resting VO_2 was significantly higher in the OW group compared with the NW group (0.29±0.1 L/min vs. 0.23±0.1 L/min, $p<0.05$, respectively). There was a trend for resting Q and SV to be higher in the OW group but this was not significant ($p>0.05$). During exercise Q, SV and VO_2 were significantly higher at each exercise intensity in the OW group compared with the NW group ($p<0.05$). When FFM, age and sex were added as covariates to the repeated measures ANOVA, Q and VO_2 remained significantly higher at each exercise intensity in the OW group. **Conclusions**: These preliminary findings suggest that young, overweight individuals have a higher VO_2, Q and SV during exercise when compared to normal weight individuals. The increased oxygen uptake and hemodynamic response in overweight subjects is hypothesized to reflect the high metabolic demands of an increased body mass.

P28

No Effect of Acute Exercise on Postprandial Lipemia in Lean and Obese Pre- and Early Pubertal Children

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One factor contributing to the increased risk of coronary heart disease (CHD) in obese adults is an elevation in post-prandial triglycerides (PPTG). As obesity rates continue to increase in children, it is important to determine CHD risk factors that may already be present, such as elevated PPTG, and to evaluate interventions that may improve such risk factors. In adults, a single bout of moderate exercise has been shown to decrease PPTG after a high fat meal, consumed 12–16hrs later. Hence, the aim of this study is to determine if a single bout of exercise can decrease PPTG after consumption of a high fat meal in children. Preliminary data is presented for 27 children (18 lean/9 obese, 13 M/14 F, Tanner 1–3, 10.43 ± 1.69 yrs). Subjects completed two study days; exercise and rest (random order). Each day was preceded by 3 days of diet control and 72 hrs abstinence from planned exercise. The afternoon prior to each study day (5:00pm), subjects either exercised (cycle ergometer, 25 mins at 65% (65 of 100) age estimated max heart rate) or rested for the same time period. On the exercise day, the energy expended (number of kcals) during the exercise bout was added to the diet that day to maintain energy balance. At 7:30 the following morning, a liquid test meal was consumed (49 ± 2% FAT, 19 ± 1% PRO and 30 ± 3% CHO; % of 100). Subjects remained resting for the duration of the study day. Fasting blood samples were drawn before the test meal and hourly through the remainder of the study day (7 time points total). Obese children had greater fasting TG (89 ±30 vs 56 ±26 mg/dl, $p<0.01$) compared to lean children. The integrated area under the curve (IAUC) for PPTG over the study period (6hr) was significantly lower under the rest condition (12053 ± 5559 vs 23153 ± 13981 mg/dl/360 mins, $p<0.05$) and under the exercise condition (11260 ± 4732 vs 22577 ± 15130 mg/dl/360 mins, $p<0.05$) in lean compared to obese children, respectively. There was no difference in PPTG IAUC due to exercise, across groups or within either group. In summary, a single bout of moderate exercise did not reduce PPTGs after a high fat meal in pre-and early-pubertal children. The significantly elevated PPTG's in obese children, however, indicate that this independent risk factor for CHD is apparent at an early age, coincident with the obese state.

P29

An Italian General Practitioners Network Survey on Obesity

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Background: Obesity is increasing at all ages; to evaluate this epidemic a network of 40 GPs interested in health education and preventive care were engaged to perform a screening on a sample of patients randomly selected from their lists. The aim of the present analysis is to describe main results of the survey. **Methods:** Weight, height were measured in 1044 men and 1046 women ages 35–75, without previous cardiovascular disease (CVD). Body mass index (BMI) was computed and categorized in normal weight (BMI 18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2) and obese (BMI>=30 kg/m^2). Food frequency (per day: fruits and vegetables; per week: meat, cheese, fish, pulses, chocolate, fry food, sweet, wholemeal food, rotisserie food and sugar drink), physical activity (at work and during leisure time), smoking and use of medication were investigated through a questionnaire; CVD risk was assessed using the Italian CUORE Project score. **Results:** Prevalence of overweight was 50% in men and 34% in women; prevalence of obesity was 23% in both men and women. Age-adjusted correlation analysis showed that BMI was inversely correlated with consumption of pulses, fish, wholemeal food, rotisserie food, chocolate and sweet, and directly correlated with meat. Women eat vegetables, wholemeal food and chocolate more frequently than do men, and men eat more fry food, meat and sugared drinks than do women. Age-adjusted correlation analysis showed that physical activity during leisure time was inversely correlated with BMI. CVD risk score in 10 years was: 3% for normal weight women, 5% for overweight, 7% for obese; 8% for normal weight men, 11% for overweight, 13% for obese. Age-adjusted ANOVA analysis showed a significant association between CVD risk score and classes of BMI in both men and women ($p<0.001$). **Conclusions:** The major step to implement a preventive strategy in the general population is to involve GPs. In this way they are made aware of the low proportion of normal weight persons in the population and how overweight and obesity are inversely related to low-fat foods and physical activity. Encourage GPs to counsel on healthy lifestyle is an achievable goal. A network of GPs seems to be an appropriate way to monitor overweight and obesity.

P30

Association of Lifestyle Factors with Subcutaneous and Visceral Adiposity: The Framingham Heart Study

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Background Abdominal adiposity is associated with cardiovascular disease (CVD) risk. We sought to determine the relationship between lifestyle factors and abdominal subcutaneous

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adipose tissue (SAT) and visceral adipose tissue (VAT) in a community-based cohort. **Methods** Cross-sectional associations between lifestyle factors and SAT and VAT volumes, as measured by multidetector computerized tomography, were examined in 2926 Framingham Heart Study participants (mean age 50 years, 48.6% women), free of CVD. Multivariable regression was performed to assess SAT and VAT in relation to diet, physical activity, smoking, and alcohol consumption. All models were sex-specific and adjusted for age, menopause, hormone replacement therapy, education, alcohol and smoking. **Results** Adherence to the 2005 Dietary Guidelines for Americans and physical activity were inversely associated with SAT and VAT (p-value$<$0.0001 to 0.002). In men, former smoking was associated with higher mean SAT (2743$\pm$56 cm^3) as compared to current (2629$\pm$88 cm^3) or never smokers (2538$\pm$44 cm^3; p=0.02). Similar results were observed in women, although not statistically significant (p=0.06). Ever smoking was significantly associated with higher mean VAT (p=0.03 in women; p=0.005 in men). Women who consumed $>$7 drinks/week of alcohol had lower mean SAT (2869$\pm$106 cm^3) than those who consumed less (3184$\pm$44 cm^3, p=0.006). In men, alcohol intake of $>$14 drinks/week was associated with higher mean VAT (2272$\pm$59 cm^3) compared to $\leq$14 drinks/week (2139$\pm$25 cm^3, p=0.04). A U-shaped relation with SAT and VAT appeared when alcohol intake was broken down in more categories. An increasing number of healthy lifestyle factors were associated with lower levels of SAT and VAT in women and men (all p-values$<$0.003). **Conclusion** Adherence to dietary guidelines, physical activity, abstinence from smoking, and moderate alcohol consumption are associated with lower volumes of SAT and VAT and may be important factors in the prevention of abdominal obesity.

P31

AHA-Recommended Dietary Intake Patterns and Lipid Responses to Exercise: Findings from the STRRIDE I Study

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BACKGROUND: While the standard approach for reducing cardiovascular risk due to dyslipidemia is to recommend a "healthy" diet plus exercise, the interaction of diet with exercise effects on plasma lipids has not been systematically studied. This is unfortunate since diet and exercise can have distinct effects on lipid sub-fractions. Also, from a behavioral standpoint, both interventions can be challenging and difficult to accomplish simultaneously. Thus in the clinical setting, it would be very helpful to be able to define the optimal lifestyle approach(es) for improving lipid profiles. METHODS: The first Studies of a Targeted Risk Reduction Intervention through Defined Exercise (STRRIDE) measured the effects of a supervised exercise program in the absence of intentional dietary change in 216 sedentary, overweight men and women randomized to 6 months of inactivity or one of three supervised aerobic exercise programs. Lipoproteins and lipids assessed included LDL and HDL size (nm); concentrations of LDL (nmol/L), small LDL and large HDL particles (mg/dl); and LDL cholesterol, HDL cholesterol, IDL cholesterol, and triglycerides (mg/dl). Detailed records of dietary intake were kept throughout the study and analyzed for nutrient content. Overall mean results for selected nutrients were compared to the respective AHA 2006 Diet and Lifestyle Recommendations for total, saturated, and trans fat, cholesterol, omega 3 fatty acids and fiber using a modified z score. Linear models were used to evaluate the effect of diet, exercise, and the interaction between diet and exercise on changes in lipoproteins and lipids.. RESULTS: Independent of diet, the exercise interventions had beneficial effects on LDL size (p = 0.01), triglycerides (p = 0.001) and IDL cholesterol (p = 0.04). However, dietary adherence to the AHA diet was not related to changes in these or any other of the lipid components. Additionally, there was no interaction of diet z scores with the lipid responses to exercise. CONCLUSIONS: Our findings indicate that adherence to the AHA 2006 dietary recommendations does not provide additional lipid benefits to overweight subjects who are following a well controlled aerobic exercise regimen.

P32

Determination of Significant Predictors of Attrition from Cardiac Rehabilitation

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Methods: To be included in this retrospective analysis, cardiac rehabilitation (CR) completers had to complete $\geq$ 6 weeks of CR and have complete pre and post lipid profiles, stress tests, Beck Depression Inventory (BDI), SF-36, and anthropometric measures. Non completers had to have complete entry data and failed to complete CR. Of the 1422 individuals who participated in CR between 1/6/2004 and 6/28/2007, 87.8% (1248) met inclusion criteria (997 completers, 251 non completers). Candidate variables for multivariate analysis were identified using t-tests and chi square analysis. Multivariate analysis was performed using stepwise logistic regression modeling the probability of being a non completer. **Results:** Based on a multivariate analysis, age, diabetes status, BDI score, smoking status, non HDL cholesterol (non-HDL-C) and Physical Component Summary (PCS) scores were identified as significant independent predictors of non completion of CR. Participants $<$ 65 yrs old were at greater risk of non completion compared to older participants as were smokers, diabetics, and those entering not at goal for non-HDL-C. Compared to minimal depressive symptoms, increasing levels of depressive symptoms led to increased risk of non completion. Conversely, when compared to the lowest level of physical function, increasing levels of physical function indicated by the physical component summary score decreased the risk of non completion. **Conclusions:** Reasons for attrition from CR are multifactoral in nature. With the exception of age, all variables identified by the multivariate analysis have the potential for intervention by an interdisciplinary team approach to CR.

ODDS RATIOS FOR SIGNIFICANT PREDICTORS OF CR ATTRITION

Comparison	Odds Ratio:Point Estimate	95% Wald Confidence Limits	
$<$ 65 yrs of Age	1.76	1.30	2.39
Diabetes	1.42	1.04	1.93
BDI: Mild to Moderate Symptoms*	1.39	1.00	1.93
BDI: Severe Symptoms*	2.96	1.68	5.21
Smokers	2.08	1.30	3.32
PCS: Fair**	0.58	0.39	0.85
PCS: Good**	0.52	0.35	0.79
PCS: Excellent**	0.47	0.31	0.72
Non-HDL-C at goal ($<$ 130 mg/dl)	0.71	0.52	0.96

*BDI scores: $\leq$ 4 = minimal symptoms; $>$ 5 and $\leq$ 20 = mild to moderate symptoms; $>$ 20 = severe symptoms **PCS scores: $<$ 33.85 = poor; $\geq$ 33.85 and $<$ 41.2 = fair; $\geq$ 41.2 and $<$ 48.41 = good; $\geq$ 48.41 = excellent

P33

Changes in Global Gene Expression Profiles During a Lifestyle Change Program for Heart Disease Reversal Correlate with CAD Risk Factor Improvement

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Background: Coronary artery disease (CAD) is a leading cause of death, disability, and healthcare burden. Many patients with ischemic CAD receive surgical interventions and lipid-lowering drug therapy as the main component of their treatment regime. An alternative, noninvasive approach to CAD management involves intensive risk factor modification through comprehensive lifestyle changes. Although lifestyle change is effective in improving traditional CAD risk profiles, little is known about molecular responses that may form the basis for disease progression. **Methods:** Patients (n=48) participated in a prospective, nonrandomized, lifestyle change program designed to stabilize or reverse progression of CAD through dietary changes, exercise, stress management, and group support. Nonintervention controls were matched to patients based on age, gender, and disease status. CAD risk factors and risk for future coronary events were assessed over the course of one year. Global gene expression profiling was conducted on peripheral blood samples at each time point using Affymetrix U133A 2.0 arrays containing ~14,500 genes. **Results:** Most patients showed significant improvements in BMI, lipids, blood pressure, and exercise capacity, as well as cardiovascular risk. In addition to physiologic responses, we identified a subset of 414 genes exhibiting highly significant changes in expression among patients in the lifestyle modification program. Of note, genes LTA4H, DPYSL2, CD36, EIF4EBP1, BRD4, and RIOK3 showed increasing expression, while levels of HLA-F decreased during the intervention. These changes in gene expression were significantly correlated with improvement in important CAD risk factors. **Discussion:** These results suggest that fundamental molecular changes occur during intensive cardiovascular lifestyle modification. Differentially expressed genes may contribute to CAD risk factor improvement because they function in diverse biological processes such as plaque stability, fatty acid transport, and blood pressure regulation. Defining genes associated with changes in CAD risk factors may improve our understanding of the molecular biology of CAD and aid in the development of more effective therapies for reducing cardiovascular risk.

P34

Effect of Lifestyle Modification on Metabolic Coronary Heart Disease Risk Factors in Korean Women with Metabolic Syndrome

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Background: The metabolic syndrome (MetS), with associated increased CHD risk, is highly prevalent among postmenopausal women in Korea. Although therapeutic lifestyle modification (TLM) has been recommended as a cornerstone therapy, studies investigating the effects of TLM on metabolic CHD risk factors in women are limited. **Purpose**: This study was to examine the effects of a six-month TLM on metabolic parameters in Korean women with Mets. **Methods:** A randomized controlled design was used. Fifty four women with Mets were recruited from community health centers and randomly assigned to the intervention (N=32) or control (N=22) groups. The subjects in the intervention group participated in a supervised weekly TLM session for six months. The TLM was consisted of health monitoring, education, aerobic exercise (40-min/session, 200 Kcal/day), and a low calorie diet with low carbohydrate ($\approx$1300Kcal/d). Those in the control group received a booklet about MetS and were instructed to maintain their usual diet and activities. Anthropometric measures, blood pressure, and serum metabolic parameters were measured at before and at completion of the intervention. Repeated measure ANOVA and paired t test were used to analyze the data. Age and baseline values were included as covariates in the ANOVA. **Results**: Fifty three women (mean age of 63.2 y) completed the study. The changes of the anthropometrics were significantly different between the intervention and control group ($p<0.05$ respectively): waist circumference (-11.32 and -2.56 cm); body weight [-5.17 (8.3%) and -2.08 (3.6%) kg]; BMI (-1.98 and -0.56kg/m^2); fat free mass (-3.15 and -0.20 kg). Fasting blood sugar (-12.45 and -6.73mg/dl), systolic (-15.0 and -10.86mmHg) and diastolic blood pressures (-8.55 and -11.73 mmHg), and LDL-C (-17.02 and -16.39 mg/dl) have significantly decreased after the intervention within each group ($p<0.05$ for all). The changes in HDL-C (0.45 and -2.14 mg/dl) and triglycerides (23.66 and 24.23 mg/dl) were not statistically different between the two groups ($p > 0.05$ for both). **Conclusion**: The results indicate that 6-month systematic TLM have considerable beneficial effects on metabolic CHD risk factors in Korean women with MetS.

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P35

Intensive Lifestyle Changes Program Improves Endothelial Function and Inflammatory Markers of Atherosclerosis

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Background: Endothelial dysfunction is the earliest and most important factor in the pathogenesis of atherosclerosis. Inflammation has been shown to contribute to endothelial dysfunction. Intensive lifestyle changes have been shown to regress atherosclerosis, improve cardiovascular risk profiles and reduce cardiac events. We evaluated the influence of intensive lifestyle changes on endothelial function and inflammatory markers of atherosclerosis. Methods: A total of 24 participants, 12 (58%-men, 50%-CAD) were enrolled in an intensive lifestyle program (low fat, whole foods diet; exercise, stress management; group support) and 12 historically matched controls participated in the study. Endothelial dependent brachial artery flow mediated dilatation (FMD) was assessed in both groups at baseline and after 3-months. Inflammatory markers were measured only in the intervention group at the baseline and after 3-months. Results: The intervention group had significant improvement in FMD at 3-months (11.70 +/- 1.3 Std. error, $P < 0.0001$) compared to controls (-3.3 +/- 1.80 Std. error, $P = 0.95$). An analysis of variance between experimental and control group at baseline and after 3-months was performed for FMD which was significantly improved in experimental group with p value < 0.0001. The intervention group did not show significant reduction in inflammatory markers (E-selectin, Intra Cellular Adhesion Molecule, Interleukin-6, C-reactive protein and Interleukin-10) although there was a downward trend in IL-6 and CRP. The subgroup with CAD in the intervention group showed significant improvement in IL-6 (mean 1.43 pre to mean 0.03 ng/ml post, $p=0.03$) and CRP (mean 0.483 pre to mean 0.319 mg/dl post, $p=0.01$), but no significant change in other inflammatory markers (IL-10, ICAM and E-selectin). Conclusions: Significant improvement of endothelial function was observed among subjects making intensive lifestyle changes, but not in the control group. These findings, along with observed improvement in CRP and IL-6 in the intervention group with CAD, suggest one or more potential mechanisms linking lifestyle changes to improved cardiac outcome.

P36

Lifestyle Intervention Improves Microvascular Reactivity and Increases Adiponectin Levels in Overweight Hypertensive Patients

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We investigated the impact of regular aerobic training on skin microvascular reactivity and adiponectin levels, as biomarkers for lifestyle-induced improvements in hypertensive patients. In 24 overweight patients (18 men, age 41+/-7 years, body mass index 27+/-2 kg/m2) with grade 1 hypertension, we determined cutaneous microvascular blood flow by laser-Doppler method(Periflux System 5000, Perimed, Sweden) and serum adiponectin levels (ELISA), before and after 8 weeks of moderate-intensity aerobic exercise. The training consisted of walking, stationary bicycling, or any combination of these activities for 30 minutes, 4 times a week, at 65–80% maximal heart rate. Twenty four age- and sex-matched hypertensive subjects, who were examined twice at 8-week interval in the absence of treatment, served as controls. The two groups did not differ by age, blood pressure, and sex distribution. After exercise training, no significant change was observed in office and 24-hour blood pressure. The area under the curve, after postocclusive reactive hyperemia (PRH), evaluated by laser-Doppler, improved significantly (from 876±539 PU/sec to 1468±925 PU/sec, $p<0.001$). Rest flow, peak flow, their ratio, and half recovery time all showed a non-significant improvement. Lifestyle intervention induced a significant reduction in waist circumference (from 97.2±9 cm to 95.2±9, $p<0.05$) and an increase in serum adiponectin (from 11.9± 3.4 mg/mL to 12.4±3.8 mg/mL, $p<0.05$). A positive correlation emerged between exercise-induced variations of PRH and adiponectin levels ($r=0.44$, $p<0.05$). In conclusion, moderate aerobic training improves cutaneous microvascular reactivity in patients with mild hypertension, independently of blood pressure reduction. Cutaneous endothelial function and serum adiponectin concentrations may serve as biomarkers of the efficacy of non-drug treatment in hypertensive patients.

P37

Association Between Adherence to Treatment Components and Weight Change in a Behavioral Weight Loss Program

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Adherence to the treatment protocol is essential for short-and long-term success in any weight-loss program. The purpose of this study was to examine how adherence to the five components of a behavioral weight loss treatment regimen influenced weight loss during the 12-month intervention period of PREFER, a randomized clinical trial. Adherence to the five treatment components included: attending group sessions; meeting the daily calorie goal, the daily fat gram goal, and the weekly exercise goal; and self-monitoring eating and exercise behaviors. The study included 176 overweight and obese adults, who were first randomly assigned to one of two preference conditions (Yes or No). Participants randomized to the Peference-No condition were further randomly assigned to one of two diet conditions (standard calorie- and fat-restricted diet (STD-D) or a calorie- and fat-restricted lacto-ovo-vegetarian diet (LOV-D)). The Preference-Yes group received their preferred diet, either STD-D or LOV-D. The cognitive-behavioral intervention focused on lifestyle modification was delivered in 33 group sessions over 12 months followed by a 6-month, no-contact maintenance period. Adherence was measured objectively for attendance and subjectively by self-report for the four other components. Results from mixed modeling analyses showed a significant interaction between attendance and preference for weight change ($p=.023$). Higher attendance at group sessions was associated with a significant weight loss in both Preference-Yes groups ($ps<.001$). No significant weight change was observed among non-attenders in the Preference-No group ($p=.912$). We did not find significant associations between adherence to self-monitoring, adherence to the dietary and exercise goals and weight change overtime. Attendance seems to be crucial for participants to acquire the knowledge and skills related to lifestyle modification. Future studies should focus on strategies to improve attendance, which in turn could lead to improved clinical outcomes.

P38

Exercise Effects of the Healthy Lifestyle Change Program, A Novel Intervention for Adults with Developmental Disabilities

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Introduction: Few fitness interventions have been designed for people with developmental disabilities, even though this population is at high risk for obesity, hypertension and cardiovascular disease due to inactivity, mobility limitations, and possible medication side effects. Our goal was to evaluate the effect on exercise and weight loss of a novel intervention for adults with developmental disabilities. **Methods:** We used a pre-post test design to evaluate the Healthy Lifestyle Change Program (HLCP), a 7-month healthy lifestyle fitness program designed to help adults with developmental disabilities achieve long-standing health changes. Clients of Westside Regional Center with a BMI≥25 were recruited to participate in the HLCP. Participants attended health education and exercise sessions twice weekly. Peer mentors served as exercise leaders and primary motivators. Sixty-eight participants began the HLCP, 45 completed the 7-month objective (66%), and 19 continued the program to 20 months. Measures reported here include 7-month change in physical activity, abdominal girth, weight and perceived exercise self-efficacy. **Results:** An increase in overall physical activity was reported by 61% (27/45) of participants. At pre-test, 55% of participants reported moderate physical activity at least 3 times a week, and post-program, 75% reported this amount. Participants' confidence in their ability to exercise regularly also increased significantly. Two-thirds of participants maintained or lost weight loss and weight loss ranged from 2 to 24 lbs. Change in participants' average weight was -3 lbs ($p=0.03$). Abdominal girth decreased in 74% (29/39) of participants and among these participants, the mean loss was 1.9 in. For the entire cohort, abdominal girth decreased by 1 in. on average ($p=0.005$). At 20-months, average weight loss among the 19 participants was -9.5 lbs (weight loss range: 2–57 lbs). **Conclusions:** The HLCP, uniquely designed for adults with developmental disabilities, resulted in increased physical activity and weight loss. This program should be expanded and evaluated for larger populations with developmental disabilities because of their unique susceptibility to behavioral risk factors for cardiovascular disease

P39

Possible Interaction Between Gender and Cardiovascular Risk Factors in First- and Second-Generation Turkish Migrant Women

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In the third year of a CVD prevention program aimed at both second- and first-generation Turkish migrant women in rural Austria 910 participants completed a questionnaire on self-assessed CVD risk factors. Second generation was defined as having gone to school in Austria. More than half of the participants (477) were young adult women between 20 und 40 years of age. As expected, results varied widely between first and second generation. The greatest differences were found in gender- and lifestyle-related risk factors. BMI> 30 (first 26.3%/second 6.2%), exercise 3 times a week (36.3%/71.3%) and healthy diet (61.7%/83.6%) showed significantly better results among second-generation women. Smoking (16.7%/38.5%) showed significantly worse results in second-generation women (see fig. 1). Having fewer language barriers, twice as many second- as first-generation migrants consume German-language media. Even though fewer language barriers led better awareness of health risk factors to be expected in second-generation migrants, they were less informed about their clinically measured risk factors like blood pressure, cholesterol and blood glucose levels than was the first migrant generation in the same age group. Thus, culturally coded gender expectations might be a stronger impetus for health behavior than health information for second-generation migrant women. Healthcare providers should strengthen positive health behavior of the culture of origin and the host culture to support good CVD health of women whose gender roles are in transition.

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P40

Relationships Between Social Support for Exercise and Physical Fitness by Sex and Race

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Many lifestyle interventions seek to increase physical activity (PA) by encouraging social support (SS). However, efforts to increase SS can be received differentially by race and sex. In PREMIER, 810 adults [34% African American(AA), 62% women, 50% ≥ 50 yrs old] with pre- or stage 1-hypertension were randomized to 1) Advice, 2) Established, or 3) Established + DASH diet. Groups 2 and 3 were behavioral interventions that promoted weight loss, diet, increasing PA to 180 min/week, and developing SS for target behaviors. SS and fitness were assessed at baseline and after 6 months. The Sallis SS for Exercise scale, previously validated, ranged from 20 (low SS) to 100 (high SS). Fitness was assessed by heart rate response to a submaximal treadmill test. Change values were calculated as 6 month minus baseline. Improved fitness is indicated by negative fitness change values (i.e., lowered heart rate at a given workload). Data were analyzed by subgroups defined by sex and race (AA and non-AA) and controlled for group assignment, site and cohort. Among Non-AA women, change in SS was significantly associated with change in fitness (Table). Among AA men there were significant SS-fitness relationships at baseline and month 6, although change in SS was not associated with change in fitness. In Non-AA men and AA women, there were no significant SS-fitness associations. These results highlight the challenges in developing effective interventions that influence SS for diverse populations.

CORRELATIONS AMONG SOCIAL SUPPORT AND FITNESS BY SEX AND RACE

Correlations	Non-AA		AA	
	Men	Women	Men	Women
	r(p)	r(p)	r(p)	r(p)
SS Baseline & Fitness Month6	.00(.98)	. 09(.16)	-.43(.00)	.09(.26)
SS Change & Fitness Month 6	-.02(.74)	-.13(.05)	-.23(.11)	-.02(.81)
SS Month 6 & Fitness Month 6	-.02(.80)	-.02(.73)	-.31(.03)	.08(.35)
SS Baseline & Fitness Change	.00(.98)	.13(.04)	-.16(.27)	.10(.22)
SS Change & Fitness Change	-.06(.39)	-.15(.02)	-.07(.62)	-.08(.29)
SS Month 6 & Fitness Change	-.05(.50)	-.01(.93)	-.29(.05)	. 02(.81)

Note: r = partial correlation adjusted for site, cohort, group assignment, p = p value

P41

Predictors of Sexual Activity Among Patients Living with Heart Failure

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Objectives: Sexual activity, as a component of physical activity, is an area of concern by heart failure patients and their partners. Existing evidence suggests that sexual activity is adversely affected in heart failure patients, although the factors that contribute to this are largely unknown. This study examined selected risk factors and demographic variables as predictors of sexual activity in heart failure (HF) patients. **Methods**: Logistic regression was used to examine potential predictors of sexual activity among married or cohabiting HF patients. The regression model used 6 risk factors (tobacco use, alcohol use, diabetes, exercise, number of medications) and 4 control variables (age, gender, education, BMI) to predict whether the respondent was sexually active. **Results:** The HF sample (N=97) was largely male, Caucasian, and had some college education. Most had an ischemic heart failure etiology (59%, 57 of 97), and most were NYHA Class II or III heart failure (81 of 97), and had a mean EF of 34% ±13. Four of the 6 risk factors, tobacco use (p=.001), alcohol use (p=.016), having diabetes (p=.023), and number of medications (p=.012), were statistically significant in showing decreased odds of being sexually active, when controlling for age, gender, education, and BMI. These variables accounted for 33% (R^2=.33) of the variance in sexual activity. Non-exercisers and hypertension were not significant predictors of sexual activity. Among control variables, only age (p<.001) had a statistically significant negative impact on sexual activity. Among cardiac medication classes, there were no statistically significant differences between those HF patients who were or were not sexually active. **Conclusions:** Tobacco and alcohol use, diabetes, and number of medications were significant predictors of sexual activity in heart failure. The specific class of medication was not as influential on sexual activity as number of medications taken. Further research is needed to validate these findings. Health professionals need to be mindful of these predictive factors as they provide sexual counseling to patients with heart failure.

P42

Personal Habits Are Independently Associated with a Positive Attitude Toward Healthy Lifestyle Counseling Among Colombian Medical Students

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Patient counseling practices and personal healthy behaviors are positively associated in practicing physicians and medical students in the U.S; however, this relationship has not been established in developing countries. **Methods** A cross-sectional study was conducted among first (n=407) and fifth (n=254) year voluntary medical students (62% (410 of 661) female) attending 8 schools in Bogotá, Colombia. A "Healthy doctor-Healthy patient" anonymous web-based survey was administered (78% (516 of 661) response rate). Students' counseling attitudes on healthy lifestyles (main outcome) and personal habits (main predictor) were addressed. Students' perception of their school environment, basic knowledge and perceived training on healthy lifestyles (medical training related factors) were also assessed. Associations between student's personal habits and their attitudes towards preventive counseling on each related habit were assessed by logistic regression analyses stratified by year of training and for 5th year students further adjusted by gender and medical training related factors. **Results** A direct association between reporting a personal healthy habit and having a positive attitude towards counseling on each related habit was found in all students for alcohol consumption and in 5th year students for nutrition and smoking. Seniors reporting engaging in ≥ 150 min/week of moderate-to-vigorous physical activity, consuming ≥ 5 daily servings of fruits and/or vegetables, being non-smokers and alcohol abstainers were more likely to have a positive counseling attitude on physical activity (OR=1.73; p=0.25), nutrition (OR=4.71; p=0.006), smoking (OR=2.62; p=0.022) and alcohol consumption (OR=2.61; p=0.009) respectively, independently of gender and medical training related factors. **Conclusion** Personal healthy behaviors are associated with a positive counseling attitude on healthy lifestyles, particularly among 5th year students, where the association was also independent of medical training related factors. These findings suggest that promoting healthy behaviors among medical students in developing countries has the potential to improve future physician's attitudes towards preventive counseling on healthy lifestyles.

P43

The Effect of 6-Year Changes in Physical Activity on Plasma Lipid Profile in the Atherosclerosis Risk in Communities (ARIC) Study

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Background. Many studies have established that high levels of physical activity (PA) are linked to lower levels of morbidity and mortality from cardiovascular disease. This relationship is possibly partially mediated through the effect of PA on plasma lipids. While a number of studies have investigated the effect of PA on lipids, the evidence is still inconclusive. Our objective was to investigate the association between 6-year changes in PA and changes in triglycerides (TG) and HDL, LDL, and total cholesterol (TC) in the ARIC study, a community-based cohort of middle-aged white (N=11478) and African American (AA) (N=4211) individuals. **Methods**. PA from sports-related activities was measured using the Baecke questionnaire, resulting in a semi-continuous index ranging from 1 (low) to 5 (high). Linear models were used to investigate the effect of change in PA on change in lipids, stratified by race and sex, and controlling for age, field center, education, smoking, change in alcohol intake, change in Keys score, and time between visits. After excluding diabetics (N=747) and those on cholesterol-lowering medications (N=534) at both visits, participants included all individuals with complete activity, risk factor, and covariate data at baseline (1987–89) and visit 3 (1993–95). **Results**. Change in PA had no significant effect on change in HDL for all four race/sex groups. Change in PA was significantly inversely associated with change in TG (mg/dL) in white men (β=-3.28 (-6.51, -0.05)) and AA women (β=-3.32 (-6.56, -0.08)). In white women, change in PA showed a significant inverse effect on change in LDL (mg/dL) (β=-1.42 (-2.58, -0.27)) and TC (mg/dL) (β=-1.52 (-2.72, -0.32)). Interestingly we found an unexpected direct association in AA men for LDL (β=3.22 (0.41, 6.03)), TC (β=3.50 (0.48, 6.52)), and, although not statistically significant, TG (β=4.37 (-5.12, 13.86)). **Conclusion**. Although results differ by race/sex groups, increased PA generally results in improvements in lipid profile. The ARIC cohort, unique in its large sample of African American individuals, allowed us to examine race- and sex-specific effects. The unexpected inverse results for African American men are novel and should be investigated further.

P44

Recreational Physical Activity and Incident Ischemic Stroke

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Despite the well known health benefits of increased physical activity with many chronic diseases, including cardiovascular disease, few studies have evaluated physical activity and risk of ischemic stroke among women. Those studies that have investigated this association are inconclusive, perhaps due to small numbers of strokes difficulty in accurately assessing physical activity and/or the relatively young ages of the women studied. In a case-control study of biomarkers and incident ischemic stroke among postmenopausal women (mean ± SD age: 68.7 ± 6.4 years), from the Women's Health Initiative Observational Study, we assessed whether level of physical activity was associated with risk of incident ischemic stroke among 954 case control pairs matched on age and race. Physical activity was calculated as total energy expenditure in metabolic equivalents, measured in hours per week based on frequency and duration of self-reported recreational activities and ranged from 0 to108 mets/week. Odds ratios (ORs) [95% CI] for stroke associated with baseline levels of physical activity, categorized in quintiles, were estimated using conditional logistic regression controlling for body mass index, waist circumference, diabetes, alcohol use, aspirin use, education, smoking, high cholesterol requiring pills, hormone therapy use, systolic blood pressure and antihypertensive medication use. Approximately 13% (n=122) of controls and 16% (n=149) of cases reported no recreational physical activity. Mean ± SD (median) levels of total METS per week were lower among cases (12.4 ± 13.9 (8.3)) than controls (14.3 ± 14.1 (11.0); p-value <0.01). Risk of ischemic stroke was lowest among those in the middle quintiles (Q3, Q4) of physical activity. Compared to Q_3 as the referent, the risk of ischemic stroke was higher with lower levels of physical activity (Q_1 OR=1.48 [1.11–1.97]; Q_2 OR=1.72 [1.29–2.29]). There was a suggestion of a U shaped relationship between ischemic stroke and physical activity (Q_5 OR=1.28[0.93–1.76]). Increased recreational physical activity level was associated with decreased risk of incident ischemic stroke in this large case control study of older women.

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P45

Association Among Sleep Parameters, Physical Activity, and Fitness in Middle-Aged Adults: CARDIA Sleep and Fitness Studies

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Background: Sleep duration is inversely associated with body mass index (BMI) and metabolic disorders in prior studies. Mechanisms relating short sleep duration with high energy intake have emerged, but few studies have investigated the association between sleep duration and activity related energy expenditure. We tested whether objectively-measured sleep duration and quality were positively associated with physical activity (PA) and cardiorespiratory fitness (CRF). **Methods:** Chicago participants aged 38 - 50 from the Coronary Artery Risk Development in Young Adults (CARDIA) Sleep study underwent 3-day actigraphy on 2 separate occasions to determine sleep duration (hours) and efficiency (% of time in bed sleeping) in 2003–2005. In 2005 - 2006, average daily minutes of moderate (MPA $>$ 1950 counts/min) and vigorous activity (VPA $>$ 5700 counts/min) were determined using accelerometers for 7-days; participants underwent a maximal graded exercise treadmill test (GXT) using a modified Balke protocol to assess CRF. **Results:** On average, men (n = 222) slept for 5.8 hrs/night (SD = 1.1) and 80.1% (SD = 11.2) of time in bed was spent sleeping. Women (n = 280) slept for 6.4 hrs/night (SD = 0.9) and sleep was 83.4% (SD = 7.5) efficient. Sleep duration was not associated with MPA or VPA in men or women. Among women, 10% higher efficiency was associated with an odds ratio = 2.0 (95% CI: 1.2, 3.2) for falling in the uppermost quartile of VPA ($>$ 8 minutes/day) which attenuated to non-significance following adjustment for age, race, and smoking status. Sleep duration and efficiency were positively associated with CRF (**Table**), but only the association of efficiency with CRF in men persisted following adjustment for covariates. **Conclusions:** Sleep efficiency is positively associated with CRF in men, independent of BMI and PA levels. Women with more efficient sleep may engage in higher levels of VPA, but sleep efficiency was not associated with CRF.

TABLE: DIFFERENCE IN TREADMILL DURATION (PER MIN) BY SLEEP DURATION AND EFFICIENCY

	Men		Women	
	Duration (per 1 hour)	Efficiency (per 10%)	Duration (per 1 hour)	Efficiency (per 10%)
GXT Duration†	β (SE)	β (SE)	β (SE)	β (SE)
Unadjusted	0.59 (0.13)**	0.64 (0.12)**	0.47 (0.97)**	0.89 (0.18)**
Model 1	0.33 (0.14)*	0.40 (0.14)**	-0.14 (0.14)	0.10 (0.18)
Model 2	012 (0.12)	0.27 (0.11)*	-0.19 (0.11)	0.09 (0.13)
Model 3	0.24 (0.13)	0.47 (0.13)**	-0.10 (0.15)	0.15 (0.17)

*p$<$0.05 **p$<$0.01 † Mean GXT duration in men = 8.9 min (SD = 2.3), women = 6.3 min (SD =2.3) **Model 1:** Adjusted for age, race, smoking status (2005 - 2006). **Model 2:** Adjusted for Model 1 + BMI (2005–2006). **Model 3:** Adjusted for Model 2 + minutes of vigorous and moderate activity

P46

Withdrawn

P47

Correlates of Heart-Healthy Lifestyles in African Americans of the Jackson Heart Study

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BACKGROUND: To help reverse health disparities in CVD for minority populations, it is important to understand the correlates of healthy lifestyles (HLS) in addition to the risk factors for disease. A cross-sectional study of U.S. population found only 5% with a HLS, using BRFSS 2000 data for smoking, physical activity, and diet. In the BRFSS study, HLS was associated with being female, older age, and having more education and higher income, and nonwhite race. METHODS: Correlates of 4 HLS indicators ($\leq$ 35% % daily calories from fat, non-smoking, none to moderate alcohol consumption, and regular physical activity) were examined in the Jackson Heart Study (JHS) sub-sample (N=2557, mean age 53, 64 % female) with psychosocial data and sufficient information to determine HLS and socio-economic status. Stepwise logistic regression models were utilized to explore potential covariates of HLS components. RESULTS: In this sub-sample, 55% were married, 40% had at least college education, 47% had $\leq$ 35% % calories of their daily diet from fat, 88% did not currently smoke, 91% were non-drinkers or light to moderate drinkers, and 51% reported regular leisure time physical activity. 21% led HLS (all 4 indicators). Overall, college education (odds ratio OR 1.32, 95% 1.08 to 1.61), experiencing no stress due to racial discrimination (OR 1.29, 95% CI 1.02 to 1.65), and older age (OR 1.02 per year, 95% CI 1.01 to 1.03) were associated with HLS; while more depression symptoms and discrimination stress were associated with smoking and increased fat consumption (in addition to traditional socioeconomic factors). Although a fifth of the sample had all 4 HLS indicators, other results showed that $<$1% met all 3 of the AHA heart healthy diet recommendations for fiber, fat, and sodium intake CONCLUSIONS: Healthy lifestyle as defined in this JHS sub-sample was more frequent than in the BRFSS national sample, but still relatively low and consistent with national data suggesting higher prevalence in nonwhites. Correlates of HLS indicators in the JHS participants were generally consistent with the national sample. These findings provide new information about psychosocial correlates of HLS in an African American sample that can inform health promotion efforts and policies for reducing CVD risk.

P48

Leisure-Time Physical Activity and the Incidence of Type 2 Diabetes in Patients with Manifest Arterial Disease or Poorly Controlled Risk Factors

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Objective In the present prospective study, we investigated the independent effect of physical inactivity and the combined effect of physical inactivity and obesity on the incidence of type 2 diabetes in patients with manifest arterial disease, or a poorly controlled risk factor. **Methods** Prospective cohort study (Second Manifestations of ARTerial disease(SMART)) of patients with manifest vascular disease or vascular risk factors. Data were used of 3940 patients, mean age 55.2$\pm$12.2 years, with manifest arterial disease, hypertension or hyperlipidemia. Patients with diabetes at baseline were excluded from analyses. Leisure-time physical activity was measured with a questionnaire and MET hours per week(MET/h/wk) were calculated. Incident type 2 diabetes was self-reported. **Results** Leisure-time physical activity $<$2.5 MET/h/wk was spent by 2550(65%) patients (inactive patients) and, 1390(35%) patients spent $\geq$2.5 MET/h/wk (active patients). The prevalence of metabolic syndrome was 35% in the physically inactive and 26% in the physically active group. During a mean follow-up of 4.7 years, 194 incident cases of type 2 diabetes occurred. Physically inactive patients had a higher incidence of diabetes, with age-and sex adjusted hazard ratio (HR) 1.6,95% confidence interval(CI) 1.2–2.3. Additional adjustment for BMI partly explained the association (HR 1.4, 95%CI 1.0–1.9). Patients who are physical inactive and obese are at the highest risk for developing type 2 diabetes (HR 5.6,95%CI 3.6–8.6) in comparison with patients who are physical active and have a BMI$<$30kg/m^2. The excess risk on diabetes attributable to the combined effect of BMI$>$30 kg/m^2 and physical inactivity on additive scale was 1.0 (95%CI -1.5–3.5), so the combined effect of physical inactivity and obesity has greater effect than the sum of the two separate effects. **Conclusion** Leisure-time physical inactivity is independently associated with an increased risk of type 2 diabetes in patients with manifest arterial disease, or a poorly controlled risk factor. However, the combined effect of physical inactivity and obesity poses the greatest risk for the development of type 2 diabetes.

P49

Joint Contributions of Cardiorespiratory Fitness and C-Reactive Protein to Individual and Clustered CVD Risk in Adolescents

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Introduction: low cardiorespiratory fitness (CRF) and states of chronic low-grade inflammation are risk factors for CVD; however their joint contribution to CVD risk has not been determined in adolescents. **Methods**: Complete data on CRF and CVD risk factors were available for 1,360 adolescents between 12 and 19 years as part of the 1999–2000 and 2001–2002 NHANES rounds. Individuals with CRP $>$ 1 (n=5) were not includedA sub-maximal walking treadmill test created. Abnormal values for waist circumference (WC), blood pressure (BP), fasting glucose, HDL cholesterol (HDLc) and triglycerides (TG) as well as the presence of the metabolic syndrome (MetS) were determined by age and gender-specific cut-offs linked to the ATPIII adult

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criteria. Logistic regression analyses were used to assess the association between categories of CRF and CRP and the presence of individual risk factors and the MetS after adjusting for, gender, age race and socio-economic status. **Results:** Abnormal values were found for WC in 19.9% (270 of 1360), BP in 8.8% (119 of 1360), fasting glucose in 8.3% (113 of 1360), HDLc in 37.5% (510 of 1360) and TG in 10% (136 of 1360). The prevalence of Mets was 6.6% (90 of 1360) and of low CRF was 33.9% (461 of 1360). Mean CRP values where lower among fit vs. unfit adolescents in both elevated and normal WC categories (both p<.001). **Conclusion**: The additive influence of low fitness and elevated CRP on MetS appears to be primarily mediated by its effects on WC. Fitness attenuates the CVD risk associated with high CRP levels and is associated to lower levels of low-grade inflammation, independently of abdominal adiposity status.

ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR THE PRESENCE OF ELEVATED CVD RISK FACTORS AND METS.

	WC	Glucose	BP	HDLc	TG	MetS
LowCRP-Fit (referent)	1	1	1	1	1	1
LowCRP- Unfit	2.3 (1.5–3.6)	2.4 (1.5–4)	1.3 (0.8–2.3)	1.2 (0.8–1.6)	3 (1.8–4.8)	2.7 (1.4–5.4)
HighCRP- Fit	7.1 (4.6–11.1)	1.6 (0.9–3)	3 (1.7–5.2)	2.1 (1.5–2.9)	2.1 (1.2–3.8)	5.5 (2.8–10.8)
HighCRP-Unfit	20.2 (12.5–32.8)	1.6 (0.8–3.2)	2.8 (1.6–5)	2.2 (1.5–3.2)	4.4 (2.6–7.7)	9.9 (5.1–19.3)

P50

Endurance Training Increases IL-10 Levels in Skeletal Muscle Tissue of Post-MI CHF Rats

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Endurance exercise training programmes has recently been reported as positive immunomodulator of proinflammatory cytokines overproduction in patients with chronic heart failure (CHF), however, few studies have addressed the role of endurance training in muscular anti-inflammatory cytokine production in rats with Post-MI CHF. **Purpose:** To determine the effect of training exercise in IL-10 protein level and NFκ-B gene expression modulation in soleus skeletal muscle. **Methods:** Control (sham-operated) and myocardial infarction by LAD ligation (MI) animals were assessed for transthoracic echocardiogram 4 weeks after operation and were randomly assigned to either a sedentary or training group (Sham-S, n=7 and MI-S, n=10) and some underwent an aerobic training protocol groups (Sham-T, n=8 and MI-T, n=8). Trained rats ran in a treadmill (0% grade at 13–20 m/m) for 60 min/day, 5 days / week for 8–10 weeks, whereas sedentary rats had only limited activity. Maximal oxygen uptake (VO_{2max}) normalized for body weight (ml kg^{-1} min^{-1}), as well as skeletal muscle citrate synthase activity, were determined to determine the effect of training program in the IL-10 levels and relative expression of mRNA NFê-B. **Results:** Post-MI rats were indicated by an increase in the left ventricular end-systolic diameter, and wet/dry weights lung and liver ratios compared with sham-operated rats with no training effects. IL-10 levels in the *soleus* muscle was reduced in Sham-S when compared with MI-S (197 $\pm$ 75 versus 122 $\pm$ 24 pg/mg protein, respectively, p<0.05) whereas the training protocol increased significantly (1.6 fold) in MI-T animals (316 $\pm$ 72 pg/mg protein; p < 0.001). Using real-time PCR, NFκ-B gene expression was restored by training in MI rats (0.6 $\pm$ 0.1 versus 0.9 $\pm$ 0.3 arbitrary units, MI-S x MI-T, p<0.05). VO_{2max} normalized for body weight (ml kg^{-1} min^{-1}), as well as skeletal muscle citrate synthase activity, were found to be greater in trained rats when compared with sedentary rats. **Conclusion:** These results demonstrate that moderate intensity endurance training produces positive immunomodulation on skeletal muscular mRNA expression of IL-10 along with beneficial metabolic effects in rats with moderate CHF. These effects may be mediated by exercise training in NFκ-B response.

P51

Effects of a Hospital-Based Exercise Program on Children with HIV

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OBJECTIVE: There are few known interventions to prevent increased cardiovascular risk, gains in trunk fat, and loss of lean tissue in HIV-infected children exposed to highly active antiretroviral therapy (HAART). The purpose of this study was to evaluate the effectiveness of a hospital-based, supervised aerobic and resistance training program for improving these parameters in children with HIV. METHODS: Subjects with HIV infection participated in a 24-visit, hospital-based aerobic and progressive resistance training program designed to last 12 weeks at one of two centers. Outcome measurements included: upper body strength; lower body strength; muscular endurance; flexibility; aerobic capacity; total and regional lean body mass and % fat by dual x-ray absorptiometry (DXA). Measures were collected at baseline and after 24 visits. RESULTS: Thirty patients enrolled, and 16 completed the intervention. The 14 biologically unrelated subjects analyzed completed the intervention in a median of 16 weeks (range: 11- 21 weeks). There were 8 males, median age 15 years (range: 6–23 years), 10 subjects on protease inhibitors, and median CD4 % of 22 (range: 0- 41) at baseline. Median BMI z-score was 1.13 (range: -1.70- 2.57) in patients ≤20 years of age. The median increases in eight measures of upper body strength were between 11% and 36% (Bonferroni minP = 0.002), and the median increases in three measures of lower body strength were between 26% and 48% (Bonferroni minP = <0.001). Muscle endurance measured by sit-ups increased a median of 32% (P = 0.004), and aerobic capacity measured by relative VO2 max increased by a median of 3.0 ml/kg/min (P = 0.001), which was 12% of the baseline median. Median increases in total and regional lean body mass were between 3% and 6% (P < 0.02 for total, arms, and legs). Median changes in total and regional DEXA % fat were small and did not achieve statistical significance. No adverse events or effects were seen during the intervention. CONCLUSION: A supervised hospital-based fitness program is safe and effective for improving cardiovascular and general fitness as well as lean body mass in persons with HIV.

P52

Impact of β-Blockers on Glucose and Hormonal Counterregulation During Exercise in Patients with Type 2 Diabetes

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Objective: The objective of this study was to evaluate the impact of a β-blocker (βb) treatment on glucose, insulin and counterregulatory hormone responses during exercise performed in different dietary states (fasting [FS] or 2 h after a standardized meal [2hr-PS]), either with or without atenolol treatment, in patients with type 2 diabetes. **Methods:** Ten sedentary men with type 2 diabetes, free of cardiovascular complications, were randomly assigned to 4 aerobic exercise sessions (FS, FS βb; 2hr-PS, 2hr-PS βb), performed at 60% of their VO2peak. Atenolol regimen consists of 100 mg daily for 5 consecutive days, prior to the experimental procedures. Glucose, insulin, glucagon, cortisol and catecholamines (epinephrine, norepinephrine and dopamine) levels were measured at the following times; 15 min prior to the exercise session (baseline), 0, 15, 30, 45, 60 min, during the exercise period, and at 75 and 90 min while recovery. **Results**: Baseline plasma glucose and insulin levels were higher in the 2hr-PS compared to the FS situations (p<0.01), without any differences with or without βb. The 2hr-PS situations induced an important fall in glucose and insulin levels in response to exercise (Table). A similar increase in glucagon, cortisol, epinephrine, norepinephrine and dopamine levels were observed in response to exercise (P<0.001) under all conditions. At the end of exercise, glucagon levels were higher in the 2hr-PS situations compared to the FS with βb (p<0.01). **Conclusion:** A short treatment with atenolol has no significant impact on insulin responses to exercise in patients with type 2 diabetes. However, in situations where insulin decrement were small, such as the FS, βb might influenced the normal physiological increment in glucagon levels.

	Glucose (mmol/L)		Insulin (pmol/L)		Glucagon mmol/L	
	Baseline	60-min	Baseline	60-min	Baseline	60-min
FS	7.2±1.0*	7.0±0.9	40±31 *	16±15	226±129	297±145 †
FS βb	7.6±2.2*	7.9±1.4	34±26 *	17±12	215±97	278±123
2hr-PS	10.8±2.1	6.1±1.5 †	140±95	33±29 †	229±129	351±94 †
2hr-PS βb	11.7±3.2	5.9±1.6 †	179±140	43±43 †	220±118	302±126 †

* p<0.01 FS vs. 2hr-PS ; † p<0.001 Baseline vs. 60-min

P53

Physical Activity Levels on Entry and Exit from an Early Outpatient Cardiac Rehabilitation Program

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The typical number of exercise training sessions patients referred to an early outpatient cardiac rehabilitation (CR) program receive has been reduced from a standard 36 to as few as 6 sessions. Although recent studies have reported on the physical activity (PA) profile of patients in maintenance outpatient CR, little is known about PA levels of patients completing an early outpatient CR program. The objective of this project was to determine if the PA levels change through the course of early outpatient CR and if the PA levels differ on days patients attend CR vs. days they do not attend CR. Subjects (14 male, 8 female; age: 65.6 $\pm$ 12.7 years, BMI: 29.1 $\pm$ 4.5 kg/m^2) were required to wear an Actigraph GT1M accelerometer during both the first and final week of an early outpatient CR program and met minimum accelerometer criteria. Patients in this early outpatient CR program completed between 3–8 weeks of exercise training (12 patients only received 3 weeks of CR). Activity counts, inactive time, and light intensity and moderate intensity time were compared both between entry and exit from CR and between days patients attended CR and days they did not attend CR (mean $\pm$ SE). These data suggest that although patients are performing more PA at exit from an early outpatient CR, the amount of increase in PA is relatively small. Moderate intensity PA was higher and inactivity time was less on CR days. It is also noteworthy that no patients achieved accelerometer criteria for vigorous levels of PA. As with previous studies of maintenance CR programs, we observed that patients' PA was higher on CR days vs. non-CR days. Therefore, it was concluded that an early outpatient CR program although helpful, is likely not sufficient in length of time to provide substantial improvements to a patient's PA status. Thus, it is important for clinicians to counsel their patients to continue in maintenance CR programs.

	Daily activity (counts/min)	*Light (minutes/day)*	*Moderate (minutes/day)*	*Inactivity (% observed minutes)*
CR Entry	216.4 ±17.2[a]	93.4 ±5.4	53.1 ±4.9[a]	78.8 ±1.3 [a]
No-CR Entry	172.4 ±13.1	83.3 ±6.7	34.4 ±3.8	82.7 ±1.2
CR Exit	231.6 ±16.9[b]	90.6 ±6.0	45.3 ±3.8	79.7 ±1.3
No CR Exit	204.9 ±19.6	91.3 ±5.9	40.3 ±4.8 [c]	79.4 ±1.7 [c]

a = CR vs. No-CR p < 0.05; b = Entry vs. Exit p < 0.05; c= interaction p < 0.05

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P54

A Tool for Measuring "Insufficient Level of Physical Activity" in Field Settings

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Background: Questionnaires developed elsewhere need to be culturally adopted and their reliability and validity established in the target population prior to its use in local settings. Aim was to examine the reliability and validity of short form IPAQ (International Physical Activity Questionnaire) when applied to an adult population within a primary-care-setting in the district of Colombo, Sri Lanka. ***Method***: IPAQ was administered to volunteers within four study-groups (N=30 each) stratified by two age groups (≥30; <30 years) and two types of occupation (sedentary; active). Validity of the questionnaire in differentiating 'insufficient' from 'sufficient' level of physical activity (PA) was assessed using the following methods: judgemental validity (cultural adaptation of IPAQ into Sri Lankan settings); construct validity (testing hypotheses on 'insufficient' levels of PA of participants against theoretically related 'constructs' of occupation, age and illness); and convergent validity (testing IPAQ against the PA-logs that were maintained for one week by the participants of <30 years of age, in relation to energy expenditure of their physical activities). Seven-day-reliability was assessed using test-retest method (N=110). ***Results***: IPAQ and PA-log data correlated well for energy expenditure [Spearman rho=0.544 (overall PA); 0.82 (vigorous PA); 0.46 (moderate PA); and 0.25 (walking)] ($p<0.05$). Hypotheses on having more 'insufficiently active' persons among the sedentary occupations compared to active occupations, and among the oldest age group compared to younger age groups were partially confirmed ($p<0.05$). Hypotheses on having more 'insufficiently active' persons among the ill persons irrespective of their age or type of occupation compared to non-ill persons were totally confirmed. Repeatability of categorical data was significantly high [Kappa=0.8 (overall); 0.9 (vigorous); 0.74 (moderate); 0.7 (walking)] ($p<0.05$). ***Conclusion***: Though not perfect, IPAQ provides a valid and reliable tool for assessing 'insufficient level' of PA in field settings in Sri Lanka and therefore is recommended for rapid use by health care workers during their practice.

P55

Development of an Evaluation Scale for Self-Management Behavior Related to Physical Activity by Patients with Coronary Heart Disease in Japan

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Objective Self-management education aims to enable patients to acquire knowledge and skills to improve their coronary risk factors, identify barriers that hinder improvement and attain problem-solving and coping skills to achieve effective self-care behavior. To provide patients with effective self-management education that takes their lifestyle into account, medical personnel need to provide education and evaluation of self-management behaviors which patient can apply to their daily life in addition to the frequency, duration, intensity and type of physical activity they should perform. This study aimed to assess the reliability and validity of an evaluation scale for self-management behavior related to physical activity by patients with coronary heart disease (ES-SMBPA-CHD), which is thought to be practical for CHD patients. **Research Design and Methods** Male outpatients with coronary heart disease (n = 97) completed a self-administered questionnaire supported by a semi-structured interview based on literature review. The content, factor, and concurrent validity and internal consistency and reproducibility of the scale were analyzed. Spearman's correlation coefficients for the ES-SMBPA -CHD and International Physical Activity Questionnaire (IPAQ) subscale scores were calculated to evaluate the concurrent validity. This protocol was approved by Kobe Univ IRB **Results** The ES-SMBPA-CHD was divided into two parts, the first dealing with self-management behavior to enhance physical activity in daily life and the second with self-management behavior to maintain the level of physical activity. Factor analysis showed that the first part comprised four factors such as "Increasing the number of steps by shopping activity" and the second five such as "Exercising to stimulate the enjoyment of eating" and "Creating situations to enhance active behavior". The ES-SMBPA-CHD correlated with the IPAQ subscales. Cronbach's α coefficient was between 0.72 and 0.89 and the intraclass test-retest correlation coefficient of the subscales was between 0.75 and 0.91. **Conclusions** The ES-SMBPA-CHD is reasonably reliable and valid and we expect that will prove useful for the assessment of patients' self-management behavior and for individualized instruction.

P56

Trends in Stages of Change for Physical Activity

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Objective. This study evaluated trends in stage of change for physical activity. **Methods.** A random sample of adult residents of Rhode Island was surveyed during the years 1998 and 2000, and stage of change for physical activity was determined. We compared the trends for stage of change over the two-year period. A subgroup analysis to determine trends according to demographic and socioeconomic characteristics was also performed. **Results.** Persons were less likely to be in maintenance in 2000 compared with 1998, but a somewhat higher proportion of persons were in action. Compared with 1998, a positive shift in the distribution of persons in the pre-action stages occurred, such that a smaller proportion of persons were in precontemplation and a greater proportion in contemplation and preparation. This shift to contemplation and preparation was most pronounced in men, older adults, whites and blacks. There were a relatively high proportion of persons who believe they meet the physical activity recommendations of the US Surgeon General in both years surveyed. **Conclusions.** The proportion of persons in maintenance declined, and a forward shift in persons in the pre-action stages occurred over the two-year period. More people were in contemplation, preparation and action. These shifts were most pronounced in older persons, men and persons of minority status, and support the efficacy of public health efforts to improve physical activity.

P57

Effects of an Aerobic Capacity–Based Program on Cardiovascular Risk Factors in Spanish High Schools

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Aerobic capacity is an important factor for health and for reducing the risk of cardiovascular diseases (Swain & Franklin, 2006). The aim of this study was to improve aerobic capacity in Spanish adolescents through a specific program applied in physical education (PE) classes in a high school. Serum cholesterol was measured with a blood test before and after intervention (after obtaining all necessary consents and permissions). Sample of 74 adolescents (av.age= 15) from 2 high schools in Granada (Spain) were divided into control group (CG, n= 38) and experimental group (EG, n= 36). A quasi-experimental design with pre and postest measurements was used. During 16 PE sessions of 55' each, an intervention program consisting of physical activity at 75–80% of maximum heart rate (153.75–164 of 205) was applied to EG. We also established a minimum motor engagement time of 45% (24'45" of 55') in each session (Siedentop et al., 1982). The CG kept to the usual PE program. The Heart rate of both groups was controlled with Polar Team System. Aerobic capacity in pre and postest was measured with Leger test. At postest, we found a significant increase in aerobic capacity in EG (p= .001) as compared with CG (p= .000), while CG did not improve this variable (p= .513). There was no significant difference in serum cholesterol between pre and postest for both groups. In line with other research, results showed that intervention was not suitable to reduce serum cholesterol, an important indicator of cardiovascular risk (Aadahl et al. 2007). Intervention should perhaps have been applied for longer to find significant results, or extracurricular factors, such as nutritional habits or physical activity at leisure time should have been applied at the same time on. Results also showed that aerobic capacity can be improved with a specific PE program, an important issue for teachers. In fact, during intervention EG worked on 75–80% of maximum heart rate (M= 161.19 Bpm) and with a high motor engagement time (M= 52.1 % of total time in each session; 28'38" of 55'); CG could not reach these percentages. Developing an appropriate PE program using these parameters may be important in the future to obtain positive effects and reduce the risk of cardiovascular diseases in adults.

P58

Yoga as a Choice of Physical Activity Among Adults with Type 2 Diabetes: A Pilot Study

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Introduction: Yoga, a form of physical activity, appears to be especially effective in the reduction of blood pressure, glucose and cholesterol levels. Moreover, the number of people who have adopted the practice of yoga has increased significantly. **Purpose:** The purpose of this pilot study was to assess the degree to which yoga is currently being used by adults with type 2 diabetes and if there are differences in types of physical activity performed between those who practice yoga and those who do not. **Methods:** We used a cross-sectional, descriptive design for this pilot study. After the study has received approval by Human Subjects, a sample of 38 adults with type 2 diabetes was recruited from the Obesity Nutrition Research Center Clinical Registry and the General Internal Medicine Clinics. The level of physical activity was measured by the International Physical Activity Questionnaire. **Results:** The mean age of participants was 56.7 years old (SD = 5.6) and the mean Body Mass Index was 37.08 ± 7.83 kg/m^2. Despite having diabetes, 74% (n=28) reported that their health was good or very good. Sixteen percent (n = 6) have used yoga in their lifetime and four had used yoga for illness prevention and maintenance of health. The total physical activity scores ranged from 80 to 25,326 MET-minutes/week. Yoga users showed smaller amounts of leisure time physical activity and greater amounts of total physical activity than those who did not report yoga usage, but there were no significant differences. **Conclusions:** People with type 2 diabetes reported practicing yoga more than what is reported by the U.S. adults (16% vs. 5%), but their practice of yoga did not contribute to a significant difference in the total amount of physical activity performed. However, this preliminary study demonstrated the popularity of yoga as a form of physical activity by people with type 2 diabetes, indicating that a yoga program would be a very viable option for this group.

P59

Masterly Inactivity by the Cardiologist

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Background The epidemic of obesity driven by inactivity is accentuated by obstacles in the workplace such as calorie-saving lifts and escalators. Hospitals are not exempt from such temptations and doctors as a profession face challenges to maintain adequate levels of physical

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activity. Hypothesis We assessed whether all members of a hospital Cardiology team experienced similar levels of physical activity in the workplace, or whether seniority, which brings with it higher levels of sedentary sessions, predisposes to physical inactivity. Method Pedometers of the same brand and type were given to each member of the Cardiology team, comprising the House Officer, Senior House Officer, Clinical Fellow, Specialist Registrar and Consultant, in a Teaching Hospital, to be worn during the working day, for five days. Results In order of seniority, the most junior team member (39354 steps) amassed the greatest number of steps each day, and over the five day period was found to walk more than the senior house officer (21148), who walked more than the Clinical Fellow (18567), who walked more than the registrar (14393), who walked more than the Consultant (7291). Conclusion In conclusion, there is a clear and significant trend towards decreased levels of activity with increasing seniority within the Cardiology team. Some would argue that it is not the role of the workplace to offer physical activity, yet many would argue that the workplace should encourage physical activity in all its members for the well-being of its workforce. Extra activities, where provided, should be encouraged, such as fitness classes and on-site recreational clubs, and more senior doctors should be encouraged to avoid lifts and use stairs. In addition, perhaps this finding will justify the need for good music to keep senior feet tapping in the cardiac catheterisation laboratory.

P60

Determinants of Physical Inactivity Among Men and Women from Greece: A 5-Year Follow-up of the Attica Study

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OBJECTIVE: To evaluate factors that are associated with physical activity changes among adults within a 5-year period. **METHODS**: From May 2001 to December 2002 we randomly enrolled 1514 men and 1528 women, without any evidence of cardiovascular or any other chronic disease. The sampling was stratified by the age-gender distribution of the greater area of Athens. Weekly energy expenditure assessed by considering frequency, duration and intensity of sports-related physical activity. During 2006, the 5-year follow-up was performed in 1955 participants, which included, among others, current physical activity status. **RESULTS**: 587 (61%) men and 673 (68%) women were classified as physically inactive at baseline, whereas 661 (69%) men and 728 (73%) women were classified as physically inactive at follow-up; thus, a 13% increase in physical inactivity rate was observed in men and a 7% in women during the follow-up period ($p<0.01$). Multivariate analysis revealed that male sex, non-smoking, healthy eating, better self-reported quality-of-life and lower prevalence of hypercholesterolemia and incidence of cardiovascular disease were the characteristics of people that remained physically active; advanced age, anxiety and depression, increased body mass, and low quality-of-life, were the baseline predictors of physical inactivity among initially active participants, which also had the higher incidence of cardiovascular disease. **CONCLUSIONS**: Gender, aging, psychological disorders, body mass, smoking, dietary habits, perceived health status and quality-of-life were the most important discriminating factors of physical activity changes.

P61

Low Birth Weight Is Associated with Elevated White Blood Cells in Black and White Young Adults: The Bogalusa Heart Study

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Introduction - Low birth weight, an indicator of intrauterine growth restriction, is associated with adult cardiovascular disease, type 2 diabetes and adverse levels of cardiovascular risk factor variables. This study assessed the hypothesis that low with weight is related to elevated white blood cell (WBC) which is recognized as an important marker of systemic inflammation. **Methods** - The study cohort consisted of 1004 black and white subjects (29.4% black, 39.1% male) aged 19–38 years enrolled in the Bogalusa Heart Study. Birth weight and gestational age information on the study cohort were obtained from the Louisiana State birth certificates. **Results -** White versus black subjects had higher birth weight (3.394 kg vs 3.025 kg, $p<0.001$) and higher WBC (6680 /μL vs 6089 /μL, $p<0.001$). Birth weight was negatively associated WBC in whites (regression coefficient $\beta=$ - 342, $p=0.017$). Black subjects showed a similar but nonsignificant association ($\beta=$ - 346, $p=0.150$). No race difference in the regression coefficients was found ($p=0.842$). In the total sample lower birth weight was significantly associated with higher WBC count ($\beta=$ - 330, $p=0.007$), adjusting for race, age, sex, gestational age, body mass index and smoking. With respect to WBC differential counts, Pearson correlation coefficients between birth weight and neutrophils were -0.093 ($p=0.014$) for whites, -0.082 ($p=0.168$) for blacks and -0.084 ($p=0.008$) in total sample, after adjusting for covariates. Birth weight was not correlated with other leukocyte subtypes. Moreover, mean values of WBC decreased with race- and sex-specific quintiles of gestational age-adjusted birth weight (p for trend $=0.0009$). **Conclusions** - The findings from this study suggest that low birth weight is associated with cardiovascular disease in adult life through mechanistic link between fetal growth retardation and increased systemic inflammation.

P62

Treatment Goals for Cholesterol in Patients with Coronary Artery Disease: A Diminishing Gender Gap but Still a Failing Grade

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Background: The effectiveness of lipid lowering therapy in slowing the progression of coronary artery disease (CAD) and preventing subsequent events is well established, and most now advocate a goal of LDL cholesterol of <70 mg/dl. Previous studies have demonstrated a gender difference in the treatment of cardiovascular disease. However, over the past few years, the risk of CAD in women and its treatment have received more attention. The purpose of the present study was to determine what percent of persons with established CAD are at their LDL goal and whether the gender gap in the knowledge and treatment of patients with established CAD has decreased. Methods: This study involved a structured survey of 100 inpatients, mean age 66+/- 12 (SD) yrs, who had an established diagnosis of CAD. A total of 48 women and 52 men were evaluated. Each patient was interviewed using a structured survey to determine knowledge of lipid goals. Data including the patient's knowledge of these goals, fasting lipid levels, and use of anti-lipid medication were analyzed. Results: Overall, only 69% of men and 67% of women with established CAD were on cholesterol lowering medications. Only 45% of patients (48% of men, 42% of women) with established CAD were at a goal cholesterol of LDL < 70 mg/dl. Of the patients who were not at goal cholesterol, only 19% of men and 18% of women stated they had been educated about their cholesterol goals. Conclusion: Our study demonstrates that the gender gap has diminished in the treatment of patients with established CAD with regards to use of anti-lipid therapy. This is likely due to improved publicity regarding women's cardiovascular health. However, only 45% of this study population with CAD were at goal cholesterol levels and only 68% were on anti-lipid medications suggesting the need for continued aggressive education and treatment of patients with CAD.

	% Knowing LDL Goal	% on Anti-Lipid Medication	% Meeting LDL Goal
Men	19%	69%	48%
Women	18%	67%	42%
P value	NS	NS	NS

P63

Protective Effect of Moderate Alcohol Drinking on Subclinical Coronary/Aortic Calcification in Japanese Men Ages 40s and 60s

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Alcohol consumption can be both protective and harmful for atherosclerosis. Epidemiological studies suggest protective effects of mild to moderate drinking on coronary heart disease. Coronary artery calcification has been found to reflect the atherosclerotic burden. The protective amount of alcohol consumption may vary across age groups, because atherosclerosis becomes severer with aging. The purpose of our study was to elucidate the protective amount of alcohol consumption against coronary/aortic calcification in Japanese men aged 40's and 60's in a community-based sample. Such studies are particularly feasible in Japanese populations, because their amount of alcohol consumption is comparatively large. Participants of the study were 699 men (313 aged 40's and 386 aged 60's) without past histories of myocardial infarction or angina pectoris were analyzed. The participants were randomly selected from Kusatsu City, Shiga, Japan (response rate: 50%). Scanning for coronary/aortic calcification were done using GE-Imatron C150 electoron-beam tomography scanner. Calcification was evaluated by widely accepted Agatston scoring procedure. In this study, Agatston score of 10 or more was defined to be calcification present, with a notion that low Agatston score may be due to artifact. Participants were classified as never drinkers or current drinkers who consume -23, -46,-69, or 69- grams of ethanol per day on average. Odds ratios of calcification were obtained by logistic regression, adjusted for age, body-mass index, systolic blood pressure, total cholesterol, fasting plasma glucose, and current smoking, having never drinkers as the reference. The risk of coronary calcification were J-shaped for both groups of age 40's and 60's. The J-shape for aortic calcification was observed only in those aged 40's, possibly because the aortic calcification prevalence in the age group of 60's was too high to be affected by the amount of alcohol consumption. The amount of alcohol consumption protective against coronary calcification was 23–46 grams/day for those in 40's and -23 grams/day for those in 60's Mild to moderate alcohol consumption is protective against coronary calcification, but the ideal amount may be different across age groups.

P64

Relation of Follicle-Stimulating Hormone to Central Arterial Stiffness and Endothelial Function in Young and Middle-Aged Women

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Background. The risk for cardiovascular disease in women increases during the perimenopausal period when follicle-stimulating hormone (FSH) concentration is steadily rising but before estrogen begins to decline. Therefore, it is possible that FSH may play an important role in the development of cardiovascular disease. We hypothesized serum FSH, but not estradiol concentrations, to be associated with central arterial stiffness and endothelial function independent of age. **Methods.** Eleven young (25±4 yrs) and 10 middle-age (45±2 yrs) healthy, recreationaly active women in the follicular phase of their menstrual cycle were assessed for the traditional CVD risk factors as well as carotid-femoral pulse wave velocity (cfPWV) and brachial artery flow-mediated dilation (FMD). **Results.** FSH concentrations were ~3-fold higher in the middle-age compared to the young women ($p<0.05$) but estradiol concentrations were similar ($p=0.20$). Carotid-femoral PWV (779±108 cm/s vs. 635±77 cm/s; $p<0.01$) was significantly greater and FMD (9±5% vs. 4±5%; $p<0.05$) significantly lower in the middle-age women compared to the young women despite similar levels of self-reported leisure time physical activity (International Physical Activity Questionnaire), percent body fat (DEXA), and carotid artery pulse pressure (applanation tonometry). Carotid-femoral pulse wave velocity was strongly associated with FSH concentrations ($r=0.67$; $p<0.01$) but not estradiol ($r=0.08$; $p=0.37$); however, when controlled for age, the association

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of FSH with cfPWV was reduced (r= 0.39; p=0.06). Brachial FMD was not associated with FSH or estradiol concentrations independent of age. Total cholesterol (197±23 mg/dl vs.163±36 mg/dl; p<0.05) and LDLc (114±24 mg/dl vs. 92±40 mg/dl; p= 0.06) were also elevated in the middle-age women but were not related to FSH or estradiol concentrations independent of age. **Conclusion.** At a time when FSH concentrations are rising, but estrogen status remains normal, middle-age women are experiencing subtle increases in central arterial stiffness.

P65

Risk Factors for Peripheral Artery Disease in US Adults: The 1999–2004 National Health and Nutrition Examination Survey

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Background: The risk factors for peripheral artery disease in a large US population remain incompletely explored. **Objectives**: We investigated the risk factors for peripheral artery disease in 4700 healthy US men and women aged 40 to 85 years from the National Health and Nutrition Examination Survey (1999–2004). **Methods**: Systolic blood pressures were measured twice at the right brachial vessel and posterior tibial vessels in both legs, and right and left ankle-brachial indexes (ABI) were calculated as ankle systolic blood pressure at right and left, respectively, divided by brachial systolic blood pressure. Peripheral artery disease (PAD) was classified as ABI <0.9 in either leg, excluding ABI ≥1.5. Cigarette smoking, alcohol intake, physical activity, and educational level were assessed by means of standardized questionnaires. Stepwise logistic regression procedure was used to identify important predictive variables for PAD with statistical significance set at p<0.05. **Results**: To identify PAD risk factors, age, sex, race, education, cigarette smoking, physical activity, alcohol intake, body mass index, high-density lipoprotein and total cholesterols, systolic blood pressure, diabetes mellitus, and antihypertensive medication use were included in the logistic regression model. The stepwise variable selection procedure identified that cigarette smoking, female sex, physical inactivity, diabetes mellitus as significant risk factors for PAD. The odds of having PAD were highest for current smoking (OR = 3.7, 95% CI: 2.48, 5.42), female sex (OR = 2.1; 95% CI: 1.19, 3.60), physical inactivity (OR = 1.52, 95% CI = 1.04, 2.22), and diabetes mellitus (OR = 1.65, 95% CI = 1.04, 2.60). Population attributable risk also documented that the prevalent PAD in this population might have been reduced by 35% if participants had not been cigarette smoking; might have been reduced by 19% if they had been physically active, and might have been reduced by 23% if they had not been associated with diabetes mellitus. **Conclusions**: Cigarette smoking, female sex, physical inactivity, and diabetes mellitus are strong risk factors for PAD in US adults.

P66

Gly82Ser Polymorphism in the RAGE Gene in Diabetic and Prediabetic Subjects: From Population-Based Studies to Functional Relevance. Results from the KORA S2000 Study

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Background: The receptor for advanced glycation end-products (RAGE) seems to play a pivotal role in the initiation and development of atherosclerotic lesions in patients with type 2 diabetes mellitus (T2DM). We sought to investigate whether the RAGE Gly82Ser polymorphism (G/A, rs2070600) is associated with impaired glucose tolerance (IGT) and T2DM in a representative middle-aged population from Southern Germany. In addition, we tested the hypothesis that the 82 Ser allele could amplify ex-vivo a cellular perturbation in a pro-inflammatory environment (e.g. in the diabetic milieu with increased S100 accumulation). Methods: Rs2070600 was genotyped using MALDI-TOF MS in 254 patients with T2DM, 353 subjects with IGT and 878 age and gender-matched controls. Circulating concentrations of 14 acute phase reactants, cytokines and chemokines were also determined. Human peripheral blood monocytes were isolated from 5 T2DM patients with rs2070600 GA genotype and 5 age- and gender- matched controls, bearing the rs2070600 GG to assess ex-vivo cytokine expression in supernatants as well as phosphorylation of p38 MAP kinase after stimulation with S100 (10μg/mL). Results: Neither in crude, nor in multivariable analyses, the 82Ser allele was independently associated with increased risk of IGT (OR 1.16; 95% CI 0.67–2.02) or with T2DM (OR 0.48; 95% CI 0.16–1.46). There was no consistent association between GG or GA+AA genotypes and various systemic biomarkers. Furthermore, no statistically significant differences were observed in the induction of TNF-α and IL-6 expression in supernatants under stimulation with S100 in subjects bearing GG vs GA genotypes. Similar findings were obtained with respect to activation of phospho-p38 MARK. Conclusions: Our data indicate that the RAGE Gly82Ser SNP is not associated with increased risk of IGT or T2DM in this population. Furthermore, we found that the RAGE 82 GA genotype had no impact on the amplification of cellular perturbation in a pro-inflammatory environment.

P67

11β-Hydroxysteroid Dehydrogenase Type 1 Gene Polymorphisms and Metabolic Syndrome in Urban Japanese Cohort

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Objective: 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1), one of the isoforms of the 11β-hydroxysteroid dehydrogenase enzymes, acts as an oxo-reductase to reactivate cortisone to cortisol, plays a critical role in tissue-specific corticosteroid reactions, and is therefore a key molecule associated with the development of metabolic syndrome. We investigated whether variations in the 11β-HSD1 gene correlated with metabolic syndrome. Research Design and Methods :We performed case-control study using a population-based urban Japanese cohort. Among 3,005 urban residents, we diagnosed 431 subjects diagnosed as metabolic syndrome according to the Japanese definition and 777 subjects with none of metabolic syndrome criteria as control. We genotyped 3 single nucleotide polymorphisms (SNPs) (+9410T>A, +17925C>T, +27447G>C) across the 11β-HSD1 gene in them and analyzed the associations of SNPs and haplotypes with metabolic syndrome. Results: We found a significant higher risk of metabolic syndrome in people with the +9410A allele (OR=1.5 for dominant model, 95%C.I., 1.0 -2.3; P=0.047). Moreover, the ATG and TTG haplotypes (comprising +9410T>A, +17925C>T, +27447G>C) were significantly associated with an increased (OR=1.82, 95%C.I., 1.01–3.25; P=0.042) and decreased (OR=0.74, 95%C.I., 0.57–0.98; P=0.033) risk of metabolic syndrome in Japanese men, respectively. Conclusion: We identified a risk-conferring SNP and haplotype of the 11β-HSD1 gene for metabolic syndrome in a Japanese population. Our data suggested that the 11β-HSD1 gene is a susceptibility gene for metabolic syndrome in Japanese.

P68

High Blood Pressure in Pregnancy and Arterial Stiffness Later in Life

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Background: Hypertensive disorders of pregnancy are the second leading cause of maternal mortality. Contradicted to some earlier studies, surmounting evidence suggests that hypertensive disorders of pregnancy are associated with augmented future cardiovascular risk. Endothelial dysfunction is proposed to play a major role in both pathophysiology of preeclampsia and pathogenesis of atherosclerosis. Objective: To test the hypothesis that arterial stiffness measured by pulse wave velocity, as a surrogate marker for atherosclerosis, is higher in women whose pregnancies were complicated by high blood pressure previously. Methods: A cross-sectional study among 259 healthy post menopausal women selected from a population-based cohort was performed. 68 women who had experienced high blood pressure during pregnancy were compared with a control group of 191 women who did not report previous pregnancy hypertension. Information on high blood pressure during pregnancy was obtained using a questionnaire. The Sphygmocor system was used to non-invasively measure stiffness of the aorta. Results: Women with a history of high blood pressure during pregnancy had significantly higher arterial stiffness compared with controls: PWV 9.63 m/s (1.91) and 8.84 (2.20), respectively with a mean age adjusted difference of 0.92 m/s (0.34, 1.51). Adjustment for the differences between the two groups as well as classic risk factors did not change the result. Women with prior hypertensive pregnancy were also more hypertensive and had a higher insulin resistance and lower B-cell function. History of high blood pressure during pregnancy, age, and mean arterial pressure were the independent predictors of arterial stiffness in all multivariate models. Conclusion: High blood pressure in pregnancy is independently associated with higher arterial stiffness later in life. This study supports other data indicating that these women are at high risk of development of coronary calcifications and coronary heart disease. Pregnancy as such can be seen as a cardiovascular stress test able to identify women at increased CVD risk.

P69

Association Between Blood Pressure and Carotid Intima-Media Thickness Among Healthy Korean Adolescents

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BACKGROUND: Associations between high blood pressure and carotid intima-media thickness (C-IMT) have been reported among hypertensive, diabetic, or obese children and adolescents. However, it is still unclear whether high blood pressure in adolescence can increase C-IMT independently from other morbidities. This study is performed to determine whetherblood pressure is associated with C-IMT among healthy Korean adolescents. **METHODS:** The study participants were 285 (147 male and 138 female) high school students aged 14 to 16. Systolic and diastolic blood pressure (SBP and DBP) were measured with an oscillometric automated blood pressure monitor. Carotid arteries were evaluated using a high-resolution B-mode ultrasonography with a 7.5MHz probe. The mean IMT value was defined as the mean of the maximal IMT of each common artery, and increased C-IMT was defined as values above the sex-specific 75th percentile. Using multiple linear and logistic regression models, independent associations between blood pressure and increased C-IMT was tested. **RESULTS:** The study population had relatively low C-IMT between 0.43mm and 0.67 mm (mean 0.54 mm). After adjustment for age, sex, body mass index, waist circumference, total/HDL cholesterol ratio, and fasting plasma glucose, SBP was positively associated with C-IMT. However, the association between DBP and C-IMT was significant only in women. **CONCLUSION:** These findings suggest that high blood pressure in relatively healthy adolescents can increase C-IMT.

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ODDS RATIO FOR INCREASED C-IMT

		Men (n=147)		Women (n=138)		All (n=285)	
		Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
SBP 10mmHg Incrase	Unadjusted	1.26	0.95–1.68	1.71	1.09–2.67	1.38	1.09–1.76
	Adjusted	1.36	0.95–1.93	2.21	1.31–3.70	1.63	1.15–2.03
DBP 5 mmHg Increase							
	Unadjusted	0.98	0.76–1.26	1.44	1.06–1.95	1.15	0.95–1.40
	Adjusted	1.00	1.75–1.32	1.45	1.06–1.98	1.17	0.96–1.43

P70

Long-Term History of Vascular Risk Factors Before Cardiovascular Mortality: A Nested Case-Control Study

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BACKGROUND: Epidemiologic studies assessed the associations between change of vascular risk factors and deaths from cardiovascular disease (CVD), but information on the long-term risk factor change before CVD mortality with repeated measurements is limited. We investigated the change of major vascular risk factors over 14 years before CVD mortality, in a large prospective cohort study. **METHODS:** A nested case-control study was performed in the Korea Medical Insurance Corporation Study cohort. The cohort consisted of 172580 men and women who were aged 35–59 years in 1990. Major vascular risk factors including body mass index, blood pressure, fasting blood glucose, total cholesterol, and smoking habits were measured every two years from 1990 to 2000. Causes and dates of deaths were obtained from the National Statistical Office. Cases were 1636 people who died from CVD between 1993 and 2004. Two controls per each case (totally 3272 controls) were sampled among survivors at the time of case's death, using incidence-density sampling methods with matching for sex and age. Risk factors were compared between cases and controls, by the time span between case's death and risk factor measurement. **RESULTS:** Body mass index was not strongly associated with CVD mortality. Difference in blood pressure between case and control had been significant from 14 years before death, and it widened progressively until the year of death. Fasting glucose, total cholesterol, and smoking rate were different between case and control, but the differences attenuated to non-significant at the year of death. **CONCLUSION:** People who dying from CVD experience relatively higher level of blood pressure, glucose, cholesterol, and cigarette smoking for a long period. However the strengths of association are different by the time span between risk factor measurement and CVD deaths, and also by the kind of risk factors.

MEAN DIFFERENCES OF VASCULAR RISK FACTORS BETWEEN CASE AND CONTROL

Years before case's death	BMI (kg/m^2)		Ssystolic BP (mmHg)		Fasting glucose (mg/dL)		Total cholesterol (mg/dL)		Smoing rate (%)	
	Difference	P	Difference	P	Difference	P	Difference	P	Difference	P
0	-0.42	0.194	14.8	<0.001	4.4	0.288	3.0	0.542	7.4	0.227
1–2	-0.02	0.830	12.5	<0.001	4.4	0.006	4.7	0.023	10.4	<0.001
3–4	0.12	0.289	11.5	<0.001	7.2	<0.001	5.9	<0.001	13.1	<0.001
5–6	0.15	0.131	11.3	<0.001	10.7	<0.001	8.1	<0.001	10.6	<0.001
7–8	0.07	0.499	10.0	<0.001	11.5	<0.001	9.2	<0.001	11.7	<0.001
9–10	0.20	0.059	11.1	<0.001	9.3	<0.001	8.3	<0.001	12.7	<0.001
11–12	0.28	0.019	9.0	<0.001	7.9	<0.001	6.1	0.003	10.1	0.003
13–14	0.32	0.063	8.6	<0.001	6.2	0.007	1.0	0.706		

P71

Cardiovascular Primary Prevention in Lombardia Region, Northern Italy: Can Accuracy of GP Absolute Risk Calculation Improve Prevention Guidelines Adherence in High-Risk Subjects?

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Background. In Europe the frequently reported low compliance in drug treatment of dislipidemic high risk subjects is an outstanding concern in CVD primary prevention. An extensive CVD primary prevention programme (CPPP), involving general practitioners (GP) and focused on the absolute risk (AR) calculation, is ongoing in Lombardia. **Aims.** We report on risk factor prevalence and treatment compliance of subjects recruited in CPPP in 2006 (85,595 records), when a quality assessment score based on accuracy of AR calculations (AAR) is taken into account. **Methods.** In 2006, GPs were asked to assess AR of at least 1% of their patients adopting the Italian CUORE risk chart or risk score (www.cuore.iss.it). Records with missing or out-of-range values for CVD risk factors (RF) (age, 35–69 yrs; systolic blood pressure, 90–200 mm Hg; total cholesterol, TC:130–320 mg/dl; smoking status; diabetes; HDL-cholesterol, 20–100 mg/dl; and hypertension drug treatment) were excluded. Subjects without a valid identification code or ineligible to AR assessment because of positive history of CHD or stroke were also excluded. The accuracy quality score was based on the agreement between ARs reported by GPs and ARs calculated applying published predictive equations. Lipid-lowering drug treatment prescriptions (LDT) in the first 6 months following AR evaluation were accessible from the regional drug database. **Results.** After exclusions, 47,093 patients were first assessed for AR in 2006, by 1,820 GPs of 14 Health Districts (HD). In the entire sample, 53% were men, 20% diabetic, 19.3% current smokers and 36.4% under hypertension drug treatment. GP's ARR improved when more patients were recruited. Considering the sub-sample with optimal ARR (N=34,891), large variations in RF means and prevalences were detected among HDs, attributable to GPs different patients' selection criteria. Within this restricted high quality dataset, 79.5% of high-risk subjects (AR≥20%) had a TC of more than 200 mg/dl, and only 2.1% were under LDT. In the follow-up, the percentage of subjects under LDT accordingly to European guidelines, as well as the compliance to LDT, improved for subjects with the highest ARR scores. **Conclusions**. Accuracy of GPs AR calculation is an important factor in CVD primary prevention.

P72

Anemia and Renal Failure: A Deadly Duet in Acute Coronary Syndromes

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Introduction: Anaemia and renal failure are common comorbidities in patients with acute coronary syndrome (ACS), being associated with adverse outcomes. Aim: To determine, in an acute coronary syndrome (ACS) population, the impact of anaemia and renal failure regarding in-hospital mortality. Population and methods: Retrospective analysis of a database containing 475 patients consecutively admitted to a single coronary care unit for ACS between May 2004 and December 2006. Our population was divided into two groups: A - patients with (n=249), and B - patients without anaemia and renal failure (n=226). Results: Group A patients were more elderly and had more frequently higher TIMI score, diabetes, heart failure, valve disease and previous myocardial infarction, stroke, nephropathy or peripheral neuropathy. These patients had more severe acute events, showed by higher Killip class, peak levels of necrosis and inflammation biomarkers, worse metabolic control, lower left ventricular ejection fraction and longer hospitalization. Morbidity and mortality were significantly higher in this group. After multivariate regression analysis (figure 1), Killip class >1, BMI < 24.5 Kg/m2 and the association anaemia and renal failure were independent predictors of in-hospital mortality. Conclusion: In ACS, anaemia and renal failure is associated with a worse clinical profile, being an independent predictor of in-hospital mortality.

Variables	p-Value	Beta	OR	IC 95% of OR
Female	0.477	0.382	1.465	(0.512 - 4.192)
Diabetes	0.799	0.141	1.152	(0.389 - 3.412)
Killip class > 1	0.034	1.123	3.074	(1.087 - 8.698)
BMI < 24,5	0.021	1.242	3.464	(1.203 - 9.971)
Anaemia + Renal failure	0.035	1.659	5.254	(1.126 - 24.515)

C-Statistics 0.815

P73

Excess Mortality Among Individuals with Impaired Fasting Glucose/Impaired Glucose Tolerance Is Limited to Those Who Develop Diabetes: The San Antonio Heart Study

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It is not known if the excess cardiovascular disease (CVD) risk among individuals with impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) is confined to individuals who develop diabetes. If elevated glucose levels themselves are atherogenic or are a marker for a common antecedent of diabetes and CVD, then individuals with IGT or IFG should be at increased cardiovascular risk whether or not they progress to diabetes. Therefore, our objective was to examine the relationship between baseline IFG status and baseline IGT status, stratified by future diabetes status, and all-cause and cardiovascular mortality in the San Antonio Heart Study (SAHS), a cohort of Mexican Americans and non-Hispanic whites. Our analysis included 3,685 individuals between the ages of 25 and 64 who participated in two clinical examinations an average of 7.7 years apart. IFG (fasting glucose ≥ 100 mg/dL), IGT (2-hour glucose ≥ 140 mg/dL) and diabetes (fasting glucose ≥ 126 mg/dL or 2-hour glucose ≥ 200 mg/dL) status were determined at each clinical examination. We compared all-cause and cardiovascular mortality in individuals stratified by baseline IFG and whether or not they progressed to diabetes. We examined IGT in a parallel analysis. Subsequent to the second SAHS clinical examination participants were followed on average an additional 8.0 years, during which time 265 deaths occurred, 135 from CVD (death certificate ICD-9 codes 401–447 with the exclusion of 427.5). The all-cause and cardiovascular mortality hazard ratios (and 95% confidence intervals) for IGT and IFG adjusted for age, sex, ethnic group, a history of CVD, HDL cholesterol, total cholesterol, hypertension and smoking status are found in the following table. In summary, when IFG or IGT did not progress to diabetes we did not find an increased risk of all-cause or cardiovascular death.

COX HAZARD MODELS COMPARING IFG AND IGT EXPOSURE CATEGORIES FOR ALL CAUSE AND CVD MORTALITY

	All Cause Mortality HR (95% CI)	Cardiovascular Mortality HR (95% CI)
Model 1		
NFG to ND	1.00	1.00
IFG to ND	1.34 (0.88, 2.03)	1.26 (0.66, 2.39)
NFG to D	1.27 (0.71, 2.28)	2.12 (1.05, 4.27)
IFG to D	1.70 (0.97, 3.00)	2.54 (1.25, 5.13)
D	2.62 (1.93, 3.55)	3.66 (2.40, 5.57)
Model 2		
NGT to ND	1.00	1.00
IGT to ND	0.93 (0.59, 1.45)	1.04 (0.54, 2.01)
NGT to D	1.55 (0.90, 2.67)	2.82 (1.47, 5.39)
IGT to D	1.19 (0.64, 2.20)	1.69 (0.78, 3.66)
D	2.45 (1.81, 3.32)	3.52 (2.31, 5.37)

Separate models were used for IFG and IGT; NFG, normal fasting glucose; ND, non-diabetic; D, diabetic; NGT, normal glucose tolerance

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P74

The Association of Insulin Resistance with TNF-α Is Mediated by Low Adiponectin and High Resistin Levels in the Framingham Offspring Study

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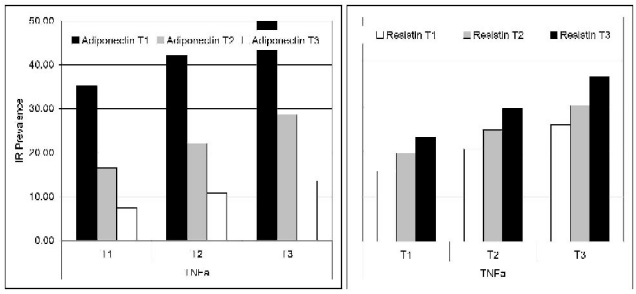
Insulin resistance (IR) is associated with TNFα pro-inflammatory pathways, an association that might be mediated by adipokines with putative IR-protective effects (adiponectin) or IR-promoting effects (resistin). We tested this hypothesis in data from 2131 attendees free of diabetes from the Framingham Offspring Study exam 7 (1998–2001; 54% women, mean age 61 years). We classified subjects by tertiles of TNFα and adipokines. We used age-sex-adjusted logistic regression models to estimate prevalence and trends for IR (defined as homeostasis model IR >75%ile) associated with TNFα tertile. We then tested the adipokine mediating effect on the IR-TNFα association. The prevalence of IR increased across rising tertiles of TNFα (trend p<0.0001; after adjustment for BMI, p=0.0002). The prevalence of IR was lower with higher levels of adiponectin in each TNFa tertile (Figure; P for both TNFa and adiponectin =<0.0001) The prevalence of IR increased with higher levels of resistin in each TNFa tertile (P for both =<0.0003) Adipokines had an additive effect on the IR-TNFa association (p>=0.15 for both TNFα x adiponectin and TNFα x resistin). Associations were similar in linear regression models that tested mean log(HOMA) instead of IR prevalence. We conclude that in this community-based sample there is a positive IR-TNFa association that is mediated by the additive effect of adipokines: resistin adding a weak IR-promoting effect and adiponectin adding a moderate IR-protective effect that seems to weaken, to a large degree, the IR-TNFα association. The lack of TNFα-adipokine interactions suggests that IR is the additive result of several defects in adipose tissue inflammatory regulation.



P75

Inflammation and Not Oxidate Stress Mediates γ Glutamyl Transferase Relationship to the Metabolic Syndrome: Implications for Primary Prevention

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Background: Gamma glutamyl transferase (GGT) has been suggested as a marker for oxidative stress and recently has been reported to predict cardiovascular disease. Our aim was to assess whether GGT predicts the prevalence of metabolic syndrome and its components in a representative cohort of 60 year old men and women. In particular, we posed the question of whether oxidative stress and inflammation account for the effects of GGT on the metabolic syndrome. ***Methods:*** A population-based cross-sectional study of 3605 well-characterized individuals, 1686 men and 1919 women, aged 60 years, in Stockholm County, Sweden. Furthermore, in a subset of 294 healthy men, we investigated whether oxidative stress (urinary 8-iso-Prostaglandin F-2α) and inflammation (CRP) could account for the effects of GGT on the metabolic syndrome. ATP-III updated metabolic syndrome definition was applied. Sex-specific GGT quartiles were calculated. Insulin resistance was defined as the upper quartile of HOMA-2. ***Results:*** High GGT was independently associated with insulin resistance (OR, 4.88 - 95% CI, 3.80–6.30), the metabolic syndrome (OR, 5.58 - 95% CI, 4.21–7.46) and each of its components after adjustment for sex, education, physical activity, smoking, cholesterol and alcohol intake. Diagnostic accuracy, judged by AUC, of insulin resistance to detect the metabolic syndrome was 0.78, but increased to 0.83 when GGT was added (p<0.01). The subset analysis of 294 healthy men, revealed that the quantitative trait of GGT improved the prediction of each of the metabolic syndrome components, independently of oxidative stress and inflammation (p<0.001). Nonetheless, CRP explained a significant percentage of variation of GGT for all of the metabolic syndrome components. Conversely, urinary 8-iso-Prostaglandin F-2α explained a much smaller percentage of variation of GGT for just 2 components. ***Conclusions:*** GGT is significantly associated with the metabolic syndrome in elderly asymptomatic subjects, independently of other risk factors. Our results indicate that GGT plays an important role in the development of the metabolic syndrome which might be mediated, at least in part through inflammation.

P76

Elevated Body Iron Stores Predict the Conversion of Impaired Glucose Tolerance to Type 2 Diabetes

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Background Iron may contribute to the etiology of type 2 diabetes (T2D) by inducing oxidative stress, impeding hepatic insulin extraction or impairing insulin secretion. Elevated levels of ferritin (a marker of body iron stores) much lower than in hemochromatosis are associated with increased risk of T2D in apparently healthy individuals. However, it is yet unknown if ferritin levels predict the development of T2D among high-risk individuals with impaired glucose tolerance (IGT). Further, there are limited data on transferrin receptors (TfR) levels, a novel marker of iron status, and the risk of T2D. **Methods and Results** The Diabetes Prevention Program (DPP) was a randomized clinical trial conducted among overweight and obese individuals with IGT and elevated fasting glucose. We designed a prospective nested case-control study within the placebo arm of the DPP to evaluate the association between baseline levels of ferritin and TfR and the risk of T2D. Study population included 280 incident cases of T2D during a 2.8-year follow-up and 280 controls matched on age, gender and race. Incident T2D was ascertained by annual 75g oral glucose tolerance test and semi-annual fasting plasma glucose. Compared to controls, cases had higher levels soluble TfR (3.5 $\pm$ 0.07 vs. 3.3 $\pm$ 0.06 mg/L; p<0.0001) but ferritin levels were similar (116.0 $\pm$ 7.0 vs. 104.3 $\pm$ 6.3 ng/ml; p=0.16). Further, the odds ratios (OR) and 95% confidence intervals (CI) for incident T2D, adjusted for baseline body mass index, family history of diabetes, physical activity, glycosylated hemoglobin and ferritin, with increasing quartiles of TfR were 1.00, 1.54 (95% CI: 0.89, 2.66), 1.67 (95% CI: 0.95, 2.96) and 2.26 (95% CI: 1.37, 4.01) (p-trend: 0.008). The association between ferritin and incident T2D was less clear and suggested a possible threshold effect; the OR comparing the highest quartile of ferritin to the remaining three quartiles was 1.82 (95% CI: 1.14, 2.90). **Conclusion** Modest increase in iron stores are associated with elevated risk of T2D in adults with IGT, independent of established risk factors. These results indicate a potential benefit in reducing iron stores in high-risk individuals. Future studies should evaluate factors that determine body iron levels in those at high-risk for T2D.

P77

Variations in Prevalent Cardiovascular Disease and Future Risk Among Different Classifications of the Metabolic Syndrome in the REasons for Geographic And Racial Differences in Stroke (REGARDS) Study

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Introduction: The International Diabetes Federation (IDF) and Adult Treatment Panel (ATP) III define the metabolic syndrome (MS) differently with unclear implications for CVD risk. **Methods:** REGARDS is a national prospective cohort study recruiting 30,000 individuals, half African American, half women. We included 22,719 participants enrolled by June 2007 with complete data for MS components. We classified participants as: 1) no MS, 2) MS by both ATP III and IDF criteria, 3) MS by ATP-only, or 4) MS by IDF-only. To assess baseline prevalent CVD, we determined the odds of self-reported CVD by MS category using multivariable logistic regression, controlling for sociodemographic and behavioral risk factors. To assess future risk, we calculated Framingham 10-year CHD risk scores (FRS) in those free of baseline CHD. **Results:** Mean age was 65.2 +/- 9.3 years, 41% were African American, 55% were women, and 22% reported baseline CVD. Overall, 10,785 individuals (47%) met at least one MS definition. Of these, 8,571 (79%) had MS by both definitions, 686 (6%) by ATP-only, and 1,528 (14%) by IDF-only. While ATP-only individuals had the highest odds of baseline CVD and largest proportion of people with a FRS > 20%, IDF-only individuals had significantly increased odds of CVD and twice as many individuals with a FRS > 20% as those without MS (table). **Conclusion:** Individuals meeting only ATP III MS criteria are at higher risk for prevalent and future CVD than those meeting other criteria. Those meeting only IDF MS criteria, albeit at lower risk, are still at notably higher risk than those without MS. The IDF MS definition identifies a clinically important number of additional individuals at excess CVD risk.

	Odds Ratios for Baseline Cardiovascular Disease		Framingham Risk Score		
				FRS > 20%	
MS Category	Number in each MS Category (n=22,719)	Adjusted OR (95% CI)	Number Free of Baseline CHD (n=17,670)	n	%
None	11,934	Referent	9,665	571	6
IDF-Only	1,528	1.40 (1.23–1.60)	1,163	151	13
Both	8,571	1.74 (1.62–1.87)	6,347	1,301	21
ATP-Only	686	1.77 (1.49–2.11)	495	167	34

P78

Heart Rate Variability, Ambient Particulate Matter Air Pollution (PM), and Glucose Homeostasis: The Environmental Epidemiology of Arrhythmogenesis in the Women's Health Initiative (EEAWHI)

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Background Whether impaired glucose homeostasis affects the PM-coronary heart disease (CHD) association remains unclear. We therefore examined whether it modifies the effect of PM on heart rate variability (HRV), a predictor of CHD. ***Methods*** We conducted our examination in EEAWHI, an ancillary study of Women's Health Initiative clinical trial participants. We focused on an exam site- and race-stratified, 6% random sample of women with a 6:1 over-representation of ethnic minorities among whom resting standard 12-lead ECGs and blood

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draws were repeated at 3-yr intervals from 1993–2004. We estimated the mean of, standard deviation of and root mean square of successive differences between normal-to-normal RR intervals from the ECGs (RR; SDNN; RMSSD). We used data from EPA Air Quality System monitors and national-scale log-normal kriging to spatially interpolate daily mean residence-specific concentrations of PM $<$ 10 μm in diameter (PM_{10}) at geocoded addresses over 2 days before each ECG. We assayed fasting glucose enzymatically and insulin by stepwise sandwich ELISA. We computed insulin resistance according to the homeostatic model assessment (HOMA-IR). We identified assayed values $>$ 90th percentile as high after excluding women with diabetes, users of anti-diabetics or anti-arrhythmics, and ECGs with signal:noise ratios $<$ a pre-specified threshold, $<$ 5 or 50% normal-to-normal RR intervals, AV conduction defects or arrhythmias. ***Results*** At the time of their 1st included ECG, the women (n = 3902) were aged 50–86 yr and 84% non-Hispanic White. In multi-level, mixed, longitudinal models weighted for sampling design, PM_{10} was inversely associated with HRV. Adjusted inverse associations were stronger for RMSSD $>$ SDNN $>$ RR and at high $>$ low values of insulin and HOMA-IR, but not glucose. For example, 10 $\mu g/m^3$ increases in PM_{10} were associated with -7% (95% CI = -10%, -2%) v. -1% (-3%, 1%), -5% (-8%, -2%) v. -1% (-2%, 0%) and -2% (-6%, 2%) v. -2% (-3%, 0%) decreases in RMSSD at high v. low insulin (p = 0.007), HOMA-IR (p = 0.028) and glucose (p = 0.907). ***Conclusions*** The findings suggest that insulin and insulin resistance modify the adverse effect of ambient particulate matter air pollution on cardiac autonomic control and thus risk of CHD among non-diabetic postmenopausal women.

P79

Lifetime Total Pack-Years of Cigarette Smoking Is Associated with Conversion from Normoglycemia to Prediabetes: The Western New York Study

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Objective: to determine whether lifetime pack-years of cigarette smoking is associated with the conversion from normoglycemia to pre-diabetes. **Methods**: Between 2003 and 2004, 1,455 participants from the Western New York Health Study who were free of Type 2 diabetes and known cardiovascular disease at baseline (1996–2001) were reexamined (58% response rate). An incident pre-diabetes case was defined as a subject who had a fasting plasma glucose (FPG) at baseline of $<$100 mg/dl and FPG $\geq$ 100 and $\leq$ 125 mg/dl at the follow-up examination. Lifetime total pack years smoked was assessed at baseline by asking participants about frequency and amount of smoking in each decade of life beginning at age10–19 yrs. up through their current age. Pack-years was categorized as: zero (n=451), 1–39 pack-years (n=410) and $\geq$ 40 pack-years (n=52). **Results**: Over a mean follow-up of 6 years**,** 101/927 subjects converted from normoglycemia to pre-diabetes. Subjects who converted to pre-diabetes were at baseline significantly older (58 vs. 55 years), had a greater BMI (28.1 vs. 26.6 kg/m^2) and a higher fasting glucose (94 vs. 90 mg/dl) (all P $<$ 0.05) than non-converters. Compared to non-converters, subjects who became pre-diabetic were at baseline more likely to be hypertensive (37% vs. 21%, P=0.001), more likely to currently smoke (16.8% vs. 11.4%, P =0.027), and more likely to have a family history of NIDDM (41% vs. 30%, P=0.036). The mean lifetime total-pack years smoked among subjects who remained normoglycemic was 9.2 compared to 15.3 among converters to pre-diabetes (P = 0.01). The multivariate logistic regression analysis fully adjusted for age, sex, year of baseline interview, alcohol intake, BMI, family history of NIDDM, and HTN demonstrated a positive linear association between increased pack-years of smoking and conversion from normoglycemia to pre-diabetes (P_{trend} =0.036). The OR of conversion to pre-diabetes comparing 1–39 pack-yrs vs. zero was 1.66 (95% CI 1.01–2.76). The OR of conversion comparing $\geq$40 pack-years vs. zero was 1.94 (95% CI 0.83–4.54). **Conclusion**: This prospective data show that pack-years of smoking was positively associated with conversion to pre-diabetes even after accounting for several putative risk factors for NIDDM including family history and obesity.

P80

Metabolic Syndrome and the Risk of Incident Stroke: The ARIC Study

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To identify particular clusters of Metabolic Syndrome (MetS) components that carry the highest risk of incident stroke, we analyzed the public use data from the population-based Atherosclerosis Risk in Communities (ARIC) study. The baseline (1987–1989), stroke-free middle-aged individuals (N=14,993) were followed over 9 years for incident stroke. We defined baseline MetS according to AHA/NHLBI criteria: persons having $\geq$ 3 of the following were classified as MetS: waist circumference $>$102 CM for men & $>$ 88 for women; blood pressure (BP) $\geq$ 130/85 mmHg or on antihypertensive medication; fasting glucose $>$ 100 mg/dl or using hypoglycemic medication; triglyceride $\geq$ 150 mg/dl; and HDL-cholesterol $<$ 40 mg/dl for men & $<$ 50 mg/dl for women. Proportional hazard models were used to assess the hazard ratio (HR and 95% CI) of ischemic stroke associated with MetS and its different clusters, adjusting for age, sex, race, education, and smoking status. At baseline, the mean age was 54 (SD=5.7), with 26% African American and 55% females. The overall prevalence of MetS was 39% (40%, 34%, 34% and 50% for white men, white women, black men, and black women, respectively). The HR of incident ischemic stroke associated with MetS among women (HR 2.41, 95% CI 1.69–3.49), and men (HR 2.11, 95% CI 1.56–2.85) was similar. There was a dose-response relationship between the numbers of MetS components and the risk of incidence stroke: the HR (95% CI) were 1.36 (0.77, 2.42), 1.72 (0.99, 3.00), 2.48 (1.44, 4.23), 3.59 (2.08, 6.21), and 4.82 (2.68, 8.68), for persons with 1 to 5 Mets components, respectively. Furthermore, persons with either elevated BP or elevated fasting glucose in the clusters to form a MetS had the highest risk for incident stroke (HR 2.74 - 4.16 comparing to persons without any MetS components) than MetS without these two components (HR $<$ 2.00 comparing to persons without any MetS components). **Conclusions:** Persons with MetS have a significantly higher risk of incident ischemic stroke than those without MetS. Furthermore, persons with MetS that had either elevated BP or elevated fasting glucose have the highest risk of stroke. These data support the needs to target MetS, especially MetS with these two highest risk components in the clusters, in order to reduce the burden of stroke.

P81

Life Course Socioeconomic Conditions and Metabolic Syndrome in Adults: The ARIC Study

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Metabolic syndrome (MetS), a condition defined as a cluster of risk factors including impaired insulin sensitivity, dyslipidemia, hypertension, and central adiposity, is associated with an increased risk of diabetes and vascular disease. Inverse associations of socioeconomic status (SES) in adulthood and the MetS are reported, but less is known about the impact of SES across life on MetS. We examined the association of childhood, adulthood and cumulative SES (cumSES) on the prevalence of MetS in mature adulthood (baseline) in the Atherosclerosis Risk in Communities (ARIC) Study. Participants were 2461 black and 8536 non-diabetic white men and women ages 45–64 years at baseline (1987–89). Using 2005 ATP III criteria, MetS was identified in 39% of black women, 28% of white women, 29% of black men and 34% of white men. Measures from childhood [parental education, occupation type (manual/nonmanual) and role (managerial/non-managerial), and home ownership], early (education, occupation type and role, and home ownership) and mature adulthood (income, occupation type and role, and home ownership) were used to create a cumSES score (range: 0–15). Childhood SES, adult SES and cumSES scores were grouped into two categories. Age- and center-adjusted prevalence ratios (PR) and 95% confidence intervals (CI) for MetS by SES were estimated by log-linear regression for race-gender groups. There was no association of childhood SES, adult SES or cumSES with MetS in black or white men. Associations for women are presented below. Our findings suggest that socioeconomic disadvantage early in life and across the life course influence risk of the MetS in women.

TABLE: ASSOCIATIONS (PR AND 95% CI) BETWEEN SES AND METS IN WOMEN, BY RACE *

	Childhood SES	AdultSES†	CumSES
Black:			
High	1.00	1.00	1.00
Low	1.3 (1.0,1.5)	1.4(1.2, 1.6)	1.6 (1.3,1.9)
White:			
High	1.00	1.00	1.00
Low	1.3 (1.2,1.4)	1.3 (1.2,1.4)	1.4 (1.2,1.5)

*Adjusted for age and ARIC center; †Based on both early and mature adulthood

P82

Racial Disparities in Metabolic Syndrome Prevalence in the REasons for Geographic And Racial Differences in Stroke (REGARDS) Study

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Introduction: Historically, metabolic syndrome (MetS) prevalence has been similar in African Americans (AA) and whites. In the US, obesity and diabetes prevalence have been increasing, and are disproportionately impacting AA's. How these increases affect MetS prevalence differences by race and gender is unknown. **Methods:** REGARDS is a nationwide population-based cohort study enrolling 30,000 AA and white participants $>$ 45 years of age from 2003 to present. We included 22,719 of 28,224 enrolled participants with complete data on MetS components. To assess the association between race and prevalence of ATP III defined MetS and its components, we used multivariable logistic regression, stratified by gender, adjusting for region, age, education, income, physical activity, alcohol use, and smoking status. **Results:** A total of 9,257 (41%) participants had MetS by ATP III criteria. MetS was most prevalent in AA women (50%). In women, the adjusted odds of MetS was 40% greater in AA's than whites, while in men, AA's had significantly lower odds. Among the MetS components, AA's had significantly greater odds of elevated blood pressure and hyperglycemia and significantly lower odds of hypertriglyceridemia and low HDL-C than whites. AA women were twice as likely as white women to be centrally obese while white men were significantly more obese than AA men (table). **Conclusion:** In contrast to earlier studies where prevalence estimates were similar between AA's and whites, AA women in REGARDS have a significantly higher prevalence of MetS due to higher rates of central obesity, elevated blood pressure, and hyperglycemia. Interventions targeting these factors, especially in AA women, are necessary to reduce MetS prevalence.

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PREVALENCE AND ADJUSTED OR OF METS OR ITS INDIVIDUAL COMPONENTS BY RACE AND GENDER

	Prevalence				Odds Ratios for MetS and its Individual Components in AA's compared to whites	
	White Men (n=6682)	White Women (n=6745)	AA Men (n=3499)	AA Women (n=5793)	Women	Women
	%	%	%	%	OR_{adj} (95% CI)	OR_{adj} (95% CI)
Metabolic Syndrome	38.8	37.0	36.9	49.7	1.7 (1.6, 1.85)[a] 1.4 (1.25, 1.48)[b]	1.7 (1.6, 1.85)[a] 1.4 (1.25, 1.48)[b]
Individual Components	%	%	%	%	OR_{adj} (95% CI)[b]	OR_{adj} (95% CI)[b]
Elevated blood pressure	63.9	57.0	78.0	79.4	2.7 (2.48, 2.99)	2.7 (2.48, 2.99)
Hyperglycemia	40.2	28.7	49.0	46.8	2.0 (1.81, 2.15)	2.0 (1.81, 2.15)
Hypertriglyceridemia	33.9	34.3	19.5	14.6	0.3 (0.25, 0.30)	0.3 (0.25, 0.30)
Low HDL-cholesterol	39.9	34.9	29.1	34.8	0.9 (0.79, 0.93)	0.9 (0.79, 0.93)
Central Obesity	36.9	47.7	35.5	69.8	2.0 (1.88, 2.22)	2.0 (1.88, 2.22)

a) adjusted for region of residence and age; b) adjusted for region, age, education, income, physical activity, alcohol use, and smoking status

P83

Impact of Diabetes and Gender on Survival After Acute Myocardial Infarction in Quebec (Canada): A Population-Based Study

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Objective - Women with AMI experienced a higher mortality compared to men. Diabetes is one of strong risk factor for coronary artery disease. The purpose of this study was to examine the impact of diabetes on gender difference in 30-day and 5-year mortality post-AMI according to three age groups (20−64, 65–74 and ≥ 75 years) in the province of Quebec, Canada. **Methods -** A population-based study included 24,520 patients ≥ 20 years (5,449 and 19,071 patients with and without diabetes respectively) hospitalized for AMI in any medical center in the province of Quebec between April 1st 1995 and March 31th 1997. AMI hospital admissions were selected using the principal diagnosis (ICD-9: 410) in the Quebec hospital discharge database. Diabetic patients were identified through the Quebec diabetes surveillance system database. Cox proportional-hazard models were used to estimate the relative risk of death adjusted for socio-economic status and co-morbid conditions. **Results -** According to diabetes status and below age 75 years, both women with and without diabetes experienced greater 30-day mortality than their men counterparts. This excess mortality in women was however independent of diabetes status (p=0.926 for diabetes-gender interaction). Within the 5-year follow-up period, in 30-day survivors, a significant gender difference was found in only younger (20−64 years) women with diabetes, who were at 1.36 times more likely to die than men with diabetes (p=0.009). Younger women without diabetes had similar risk of death than men (p=0.522), with a significant interaction between diabetes and gender in the < 65 years age group (p=0.018). **Conclusions -** We found that the higher 30-day mortality post-AMI in younger (20−64 years) and middle-aged (65–74 years) women compared to men was not influenced by the diabetic status. However, in surviving the first 30-day, the higher 5-year mortality in younger women may be explained by a deleterious impact of diabetes on long-term following AMI.

P84

Change in the Contribution of Renal Disease to the Incidence of Cardiovascular Disease

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We have recently reported declining trends by year of type 1 diabetes diagnosis for renal failure, although no such favorable changes were observed for coronary artery disease (CAD). As renal disease is an important risk factor for CAD development, we evaluated whether the changing trends in overt nephropathy (ON) may reduce the influence of renal disease on CAD development using data from the Pittsburgh Epidemiology of Diabetes Complications study, a prospective cohort of childhood onset type 1 diabetes. At study entry, mean age was 28 and diabetes duration 19 years. ON was defined as albumin excretion rate >200 μg/min in 2/3 timed urine samples and CAD as EDC physician diagnosed angina, myocardial infarction (MI) confirmed by Q-waves on ECG or hospital records, revascularization, or ischemia. Insulin resistance was determined by a regression equation with terms for waist to hip ratio, hypertension and HbA1, derived from hyperinsulinemic euglycemic clamps in 24 subjects. During 16 yrs of follow-up, 140 persons developed CAD (23.2%). Information on ON at the time of CAD incidence was lacking for 13 persons. Of the remaining 127, 51 (40.2%) did not have ON before CAD. The CAD diagnosis for these 51 persons was: angina (n=24), ischemia (n=13), revascularization (n=6) and MI (n=8). We also categorized participants by diabetes diagnosis yr into 3 cohorts: 1950−59, 1960−69, and ≥1970. The age at CAD incidence declined by cohort (46.3 vs. 40.8 vs. 34.1 for cohorts 1950−59, 1960−69 and >1970, respectively, p-trend<0.0001). The proportion of incident CAD cases without prior ON was 42.3%, 30.9% and 60.0% in the 1950−59, 1960−69 and ≥1970 cohorts respectively. In multivariable Cox models, diabetes duration, female gender and HDL cholesterol were significant baseline predictors of developing CAD without prior ON compared to remaining CAD free (all p-values <0.05). Similarly, diabetes duration, BMI, insulin resistance, HDL and non-HDL cholesterol, white blood cell count and fibrinogen predicted developing CAD with prior ON compared to remaining CAD free (all p-values <0.05). These data suggest that the influence of ON on CAD incidence may be declining in the recent diabetes diagnosis cohorts. Furthermore, insulin resistance may underlie CAD incidence that is preceded by ON.

P85

Circulating Retinol Binding Protein-4, Cardiometabolic Risk Factors, and Prevalent Cardiovascular Disease in a Community-Based Sample of Elderly Men

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Background: Retinol binding protein-4 (RBP-4) has been associated with obesity, insulin resistance, and diabetes in small study samples. Associations with cardiometabolic risk factors and overt cardiovascular disease (CVD) in the community are largely unexplored to date. **Methods:** We evaluated the cross-sectional relations of serum RBP-4 to cardiometabolic risk factors including anthropometrical measures, blood pressure, lipid measures, fasting glucose and insulin, HbA1c, body fat distribution measured with dual-energy x-ray absorptiometry (DXA), and to the metabolic syndrome (MetS) in 511 men at age 82 participating in the community-based Uppsala Longitudinal Study of Adult Men (ULSAM) in 2003–2005. We also examined the associations of RBP-4 concentrations with prevalent CVD. **Results:** RBP-4 concentrations were positively associated with body mass index (r=0.10; P=0.030), sagittal abdomen diameter (r=0.12; P=0.010), waist circumference (r=0.13; P=0.004), serum triglycerides (r=0.30; P<0.0001), total cholesterol (r=0.12; P=0.009), fasting glucose (r=0.13; P=0.004), HbA1c (r=0.10; P=0.022) and trunk fat mass measured by DXA (r=0.13; P=0.004), but not significantly correlated with fasting insulin, systolic or diastolic blood pressure. Serum RBP-4 were associated with MetS (odds ratio [OR], 1.49; 95% confidence interval [CI], 1.23–1.80 per 1-standard deviation [SD] increase; P<0.0001), and increased with the number of MetS components (56.8 and 68.2 μg/mL for 0 and 5 components, respectively; P for trend<0.0001). RBP-4 concentrations were associated with prevalent CVD in multivariable models adjusting for all cardiometabolic risk factors significantly correlated with RBP-4 (OR, 1.32; 95% CI 1.08–1.61 per 1-SD increase; P=0.006). RBP-4 was significantly associated with prior cerebrovascular disease (OR, 1.54; P=0.003), and borderline significantly associated with prior ischemic heart disease (OR, 1.23; P=0.080). **Conclusions:** In our community-based sample of elderly men, RBP-4 concentrations were associated with several cardiometabolic risk factors, MetS, and prevalent CVD. These findings are consistent with the hypothesis that circulating RBP-4 may be a marker of cardiometabolic risk and prevalent CVD.

P86

Increased Risk of CVD Mortality Associated with Elevated Blood Pressure Levels and Diabetes for African American and White Individuals

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Background: African-Americans (AA) suffer a greater burden of cardiovascular disease (CVD) compared with whites, which is partially explained by greater prevalence's of traditional CVD risk factors including hypertension and diabetes. However, it is unclear if the strength of association involving diabetes and hypertension with CVD varies for AA and whites. Methods: A pooled analysis utilizing NHANES I Epidemiologic Follow-up Study, NHANES II Mortality Follow-up Study, Charleston Heart Study, and Evans County Heart Study was performed, consisting of over 28,000 individuals (5,131 AA) with an average of 16.7 years of mortality follow-up. Individuals were categorized into risk levels derived from baseline blood pressure levels and diabetes status. The referent group consisted of normotensive individuals without diabetes. Diabetes status was combined with each level of blood pressure and compared to the referent group. Stratified Cox proportional hazards models were run to estimate the hazards ratios (HR) of CVD death for each category compared to the referent group while stratifying by study and controlling for age and gender. Interaction parameters were used to determine if the HR varied significantly by race. Results: A greater proportion of AA experienced CVD mortality (24.8 vs. 16.9 p<0.001). HR are shown in the below table. Stage 2 hypertension was associated with nearly a 4-fold increase in CVD mortality risk among AA and white individuals with diabetes and a 2.3 fold increase for both race groups without diabetes. The additional risk associated with diabetes at lower levels of blood pressure was stronger in whites as compared to AA (p-values 0.003 - 0.053). The risk of CVD mortality was nearly doubled for prehypertensive diabetic AA and tripled for prehypertensive diabetic whites. Conclusions: The greatest risk of CVD mortality is seen among the stage 2 hypertensive diabetic individuals. This increased risk is similar for both African Americans and whites.

Diabetes	Blood Pressure	AA HR (95% CI)	White HR (95% CI)	P-value
No	Normal	1	1	
No	Pre	1.10 (0.75, 1.60)	1.17 (1.00, 1.37)	0.397
No	Stage 1	1.45 (1.01, 2.08)	1.55 (1.33, 1.80)	0.229
No	Stage 2	2.31 (1.62, 3.29)	2.32 (2.00, 2.71)	0.326
Yes	Normal	0.80 (0.29, 2.27)	2.40 (1.31, 4.41)	0.034
Yes	Pre	1.95 (1.15, 3.32)	2.96 (2.24, 3.91)	0.053
Yes	Stage 1	2.16 (1.32, 3.53)	4.18 (3.30, 5.29)	0.003
Yes	Stage 2	3.73 (2.47, 5.64)	3.96 (3.18, 4.94)	0.367

Blood pressure levels follow JNC-7 guidelines

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P87

Prevalence of Myocardial Infarction in Older Diabetic and Nondiabetic Icelanders Using Cardiac Magnetic Resonance

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Background: Diabetes is considered a coronary heart disease risk equivalent. We used cardiac magnetic resonance (CMR) to determine the prevalence of myocardial infarction (MI) and unrecognized MI (UMI) in diabetic and non-diabetic participants in ICELAND-MI, a substudy of the AGES-Reykjavik study. Methods and Results: Late gadolinium enhancement CMR studies assessed for MI in nondiabetic (n=627) and diabetic (n=351) subjects. Since the prevalence of diabetes was <11% in the initial random sample of 702 subjects, an additional 276 diabetic subjects were recruited to ensure adequate sample size. Mean age (76 yrs) was similar, but diabetic subjects had a higher frequency of coronary disease risk factors: male (56% v. 45%), hypertensive (69% v. 50%), higher systolic blood pressure (mean 147 v. 141 mmHg), higher creatinine levels (mean 1.1 v. 1.0 mg/dL), and lower HDL levels (mean 53 v. 62 mg/dL). In addition, diabetic subjects had lower LV ejection fraction (mean 59% v. 61%), but had HbA1C values indicating good glycemic control (mean 6.5%). Diabetic subjects had higher ($p<0.001$) prevalence of both MI (30% v. 20%) and UMI (19% v. 12%). Among those with MI, the percent of the left ventricle that was infarcted was not significantly different according to diabetes status (12% v. 13%). ECG was insensitive for detecting MI and only detected 26.7% of clinically recognized MI and only 17.3% of MI detected by CMR. Adjusting for baseline differences in coronary risk profiles in multivariable logistic regression models, diabetes remained significantly associated with both MI (OR 1.45; 95%CI 1.05–2.02) and UMI (OR 1.62; 95%CI 1.12–2.33). Conclusions: CMR detected a high prevalence of MI older diabetic subjects, the majority of which were clinically unrecognized and not detectable by ECG. The higher risk of MI in diabetic subjects–whether recognized or not–strongly supports the designation of diabetic patients as coronary risk equivalents, and also highlights the limitations of current detection and prevention strategies.

P88

Withdrawn

P89

Hepatic Steatosis and Subclinical Cardiovascular Disease in a Cohort Enriched for Type 2 Diabetes

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Background To explore possible mechanisms whereby hepatic steatosis (HS) is associated with increased cardiovascular risk in persons with diabetes, we investigated the cross-sectional relationships between HS, regional fat distribution, inflammatory biomarkers, and subclinical measures of atherosclerosis in the Diabetes Heart Study (DHS), a family study of sibling pairs concordant for type 2 diabetes. ***Methods*** The following parameters were obtained in 623 randomly selected DHS participants: computed tomography (CT) liver attenuation density (a liver:spleen attenuation ratio (L:SAR) < 1.0 is indicative of HS, and decreasing values signify worsening HS); visceral and subcutaneous fat distribution by CT; Body Mass Index (BMI); serum C-reactive protein (CRP) and adiponectin; coronary, aortic, and carotid artery calcium by CT; and carotid atherosclerosis by B-mode ultrasound. Associations between the L:SAR and these factors were expressed as simple or partial Spearman correlations, and generalized estimating equations (GEE) were used to adjust for familial correlations. ***Results*** After adjustment for age, race, gender, BMI, and diabetes status, the amount of HS expressed as the L:SAR correlated with the amount of visceral fat (r: -0.22, $p<0.0001$) and subcutaneous fat (r: -0.13, p: 0.031). HS was positively associated with an atherogenic lipid profile, including lower HDL (r: 0.21, $p<0.0001$) and higher triglycerides (r: -0.25, $p<0.0001$). Higher CRP (r: -0.095, p: 0.004) and lower serum adiponectin (r: 0.34, $p<0.0001$) were observed in the setting of HS, indicating a pro-inflammatory state. There were no statistically significant associations between the L:SAR and coronary, aortic, or carotid calcium or carotid intimal thickness when controlling for age, gender, race, diabetes status, smoking history, visceral adiposity, and CRP. ***Conclusions*** The strong correlations observed between HS and pro-atherogenic biomarkers and characteristics of the metabolic syndrome suggest that HS reflects more than just general adiposity, but represents a systemic, inflammatory, pro-atherogenic adipose state. Our data suggest that HS is less likely to be a direct mediator of cardiovascular disease and may be more appropriately described as an epiphenomenon.

P90

Relationship Between Body Mass Index, Waist Circumference, and Cardiovascular Disease Risk Factors Among US 12- to 19-Year-Olds, 1999–2004

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Objective. To characterize the relationships between childhood body mass index (BMI) and waist circumference (WC) with common cardiometabolic disease risk factors for adult-onset cardiovascular disease (CVD) and to determine optimal threshold values of BMI and WC for detecting elevated risk of CVD in adolescents. **Methods and Patients.** We analyzed the combined 1999 to 2004 National Health and Nutrition Examination Surveys (NHANES) cross-sectional data for 12- to 19-year-olds (N = 2,581). Main outcome measures were the presence of ≥ 3 age-adjusted CVD risk factors (high-density lipoprotein cholesterol; low-density lipoprotein cholesterol; triglyceride; glucose; insulin; and systolic and diastolic blood pressure). The presence of ≥ 3 of these risk factors was predicted from age-adjusted BMI and WC values. **Results.** Using the 80th percentile as a cutpoint for abnormal values for CVD risk factors (20th percentile for HDL) the proportion of adolescents at risk ranged from 17% to 19% in the ethnicity-sex groups. ROC curve analysis showed that both BMI and WC had good diagnostic accuracy, ranging from 0.73 to 0.83, and good sensitivity and specificity, ranging from 0.68 to 0.78. The BMI cutoffs ranged from 19.5 to 25.0 kg/m^2 for boys and from 19.4 to 27.0 kg/m^2 for girls. The WC cutoffs ranged from 66.8 to 87.5 cm for boys and from 71.5 to 87.2 cm for girls. **Conclusions**. This population-based analysis among a multiethnic sample of 12–19 year olds produced threshold values for BMI and WC that may have significant clinical utility in identifying adolescents and teenagers at risk for later cardiovascular disease onset.

P91

Inflammatory Markers Do Not Independently Predict Type 2 Diabetes Mellitus in the Western New York Health Study

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Objective: To determine the incidence of T2DM in Western New York and to investigate whether two inflammatory biomarkers, C-reactive protein (CRP) and interleukin-6 (IL-6) predict incident T2DM. **Methods**: The Western New York Health Study is a prospective, general population study of residents from Erie and Niagara counties, NY. At baseline (1996–2001) participants (ages 35–79 years, mean 59.3) were free of diabetes and self-reported cardiovascular disease. Between February 2003 and September 2004, 1455 participants were reexamined (58% response rate). At the follow-up exam incident Type 2 diabetes was defined as fasting glucose ≥ 126 mg/dl or use of antidiabetic medication: 69 people met the case definition and were individually matched with up to 3 controls on sex, race, year of study enrollment, and baseline fasting glucose (<110 or 110–125 mg/dl). Biomarkers were measured from frozen baseline samples. **Results**: Over a mean follow-up of 6.2 years, the incidence of T2DM among this predominantly white cohort (94%) was 8.02 (95% CI: 6.16–10.12) per 1000 person-years. Compared to controls, cases had larger BMI (32.2 kg/m^2 vs. 29.2 kg/m^2, P =0.001), higher insulin (22 uU/ml vs. 11.8 uU/ml, P=0.05) and were more likely to report a family history of diabetes (55.2% vs. 39.9%, P=0.049). The correlation between both inflammatory markers and BMI was (r= 0.3, P<0.001). Median baseline CRP (2.41 ug/ml) was significantly higher among incident diabetes cases compared the controls (4.4 ug/ml vs.3.2 ug/ml, P=0.018). Median IL-6 (2.06 [g/ml) also was significantly higher among cases than controls (2.89 pg/ml and 2.45 pg/ml, P<0.001). In conditional logistic regression analyses adjusted for age, family history of diabetes, smoking, drinking status, physical activity, and BMI the OR of T2DM (CRP ≥ median vs. < median) was 1.49 (95% CI: 0.67–3.33; P=0.331) The OR of T2DM (IL-6 ≥ median vs. < median) was 0.75 (95% CI: 0.36–1.54; P=0.424). **Conclusion**: The incidence of T2DM in this cohort of overweight and obese older Western New Yorkers was somewhat higher than national estimates of whites. Although elevated CRP was associated with an excess risk of T2DM neither biomarker was a significant independent predictor of incident T2DM after accounting for other putative risk factors.

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P92

Changes in Lifestyle Risk Factors for Cardiovascular Disease in Adults with Type 1 Diabetes Over Time

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Objective: Cigarette smoking, physical activity and alcohol consumption influence the risk of cardiovascular disease (CVD). However, little longitudinal data exist concerning patterns of these lifestyle risk factors in persons with type 1 diabetes (T1D) over time. The goal of this report was to compare the amount of physical activity, alcohol consumption, and smoking in a large sample of adults with T1D and comparable non-diabetic controls (non-DM) over a three year period. **Methods:** In 2000–2002 and again in 2003–2004, the Coronary Artery Calcification in Type 1 Diabetes (CACTI) Study applied validated questionnaires for smoking, alcohol consumption and physical activity. Longitudinal data exist for 442 T1D patients (43% male, age 38±9 yr) and 571 non-DM controls (51% male, age 41±9 yr). **Results:** Physical activity (blocks and flights walked, sports, recreation) was measured using average kcal per week. Men and women with T1D reported more physical activity than non-DM controls at baseline (p=.04) but this difference was not seen at the follow up. Smoking was not significantly different between T1D and non-DM for men or women. T1D men and women drank less alcohol at baseline than non-DM controls (p=.02, p=.01 respectively) but this difference was not seen at follow-up. **Conclusion:** Overall, men and women with T1D engage in similar lifestyle risk factors for CVD as non-DM controls. Among subjects who completed both visits, there were no differences between T1D and non-DM men and women in these lifestyle factors at the follow-up visit. However, comparing baseline to follow up by gender and diabetes status, T1D men decreased physical activity, non-DM men decreased monthly alcohol intake, and T1D women increased monthly alcohol intake over time.

	MALES							
	Baseline			Follow up				
	T1D (n=190)	Non-DM (n=289)	p*	T1D (n=190)	Non-DM (n=289)	p*	p†	p††
Smoking (%)	9.0 (17/190)	8.7 (25/289)	0.91	5.8 (11/190)	8.0 (23/289)	0.37	0.17	0.56
Physical Activity mean (top) median (bottom) (IQR)	2781±3322	2207±2237	0.04	2268±2676	2519±6936	0.58	0.02	0.42
	1977 (878, 3616)	1628 (748, 3034)	0.07	1445 (756, 2844)	1570 (784, 2844)	0.71	0.005	0.98
Alcohol drinks/month#	18.1±29.7	25.0±34.1	0.02	19.8±35.5	22.5±31.9	0.39	0.32	0.03

	FEMALES							
	Baseline			Follow up				
	T1D (n=252)	**Non-DM (n=282)**	**p***	**T1D (n=252)**	**Non-DM (n=282)**	**p***	**p†**	**p††**
Smoking (%)	10.3 (26/252)	8.5 (24/282)	0.47	9.1 (23/252)	7.8 (22/282)	0.58	0.41	0.57
Physical Activity mean (top) median (bottom) (IQR)	1804±1998	2065±2521	0.18	2238±4821	2115±3221	0.73	0.12	0.82
	1121 (448, 2463)	1484 (700, 2624)	0.04	1078 (448, 2315)	1445 (506, 2753)	0.10	0.68	0.88
Alcohol drinks/month#	9.4±15.1	14.0±26.0	0.01	13.8±25.4	14.7±24.7	0.69	0.001	0.61

* p-values comparing T1D subjects to non-DM controls within sex, †p-values comparing T1D subjects at baseline to T1D at follow up within sex, †† p-values comparing non-DM controls at baseline to non-DM at follow up within sex, #among those who drink

P93

The Cardiovascular Epidemiology of Abdominal Aortic Diameter

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This study aimed to determine the associations between the diameter of the abdominal aorta at three anatomic sites and both traditional cardiovascular disease (CVD) risk factors and calcified atherosclerosis in different vascular beds. Methods: Subjects were 504 individuals who underwent computed tomography (CT) scanning from the base of the skull to the pubic symphasis. Measurements of aortic diameter were conducted just inferior to the superior mesenteric artery (SMA), just superior to the bifurcation (BIF) and at the mid-point between these two sites (MID). At the same visit as the CT scan, study subjects completed a standardized medical examination. Results: The mean age, body mass index (BMI) and percent body fat were 57.8 years, 27.1 kg/m2 and 29.8%, respectively, and 41% were female. The prevalence of dyslipidemia, hypertension and diabetes mellitus was 31.7, 38.1 and 2.8%, respectively. The mean diameter at the SMA was 21.3 mm, 19.3 mm at the MID and 18.6 mm at the BIF. At all 3 locations, the aortic diameters were significantly larger in men than women ($p < 0.01$ for all). In a multivariable linear regression model containing age, sex, BMI, diabetes, dyslipidemia, smoking and hypertension, only age ($\beta = 0.96$), male sex ($\beta = 3.06$) and BMI ($\beta = 0.68$) were significantly associated with increasing aortic diameter at the SMA ($p < 0.01$ for all). The significance of the associations for these variables was unchanged for aortic diameter at the MID and BIF. Notably, there was an inverse significant association between diabetes and aortic diameter at the BIF only (-1.10, $p = 0.02$). On average, a 1-unit increment in calcium due to atherosclerosis in the abdominal aorta and iliac arteries was associated with 0.13 ($p < 0.01$) and 0.09 ($p = 0.02$) mm increases, respectively, in aortic diameter at the SMA. The results were similar for the MID ($\beta = 0.19$, $p < 0.01$ and $\beta = 0.12$, $p = 0.01$; respectively) and BIF ($\beta = 0.09$, $p < 0.04$ and $\beta = 0.09$, $p = 0.03$; respectively). Conclusions: Age, male sex, BMI and calcified atherosclerosis in the abdominal aorta and iliac arteries are significantly associated with increasing increments in aortic diameter. As shown previously for abdominal aortic aneurysm, diabetes is inversely associated with the diameter of the abdominal aorta, but only in it's distal segment.

P94

The Prevalence of Peripheral Arterial Disease in US Adults Aged ≥40 with Either Metabolic Syndrome or Low Glomerular Filtration Rates: Estimates from the National Health and Nutrition Examination Survey, 2001–2004

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Peripheral artery disease (PAD) is identified by a low ABI and is a marker of subclinical coronary artery disease. Its presence identifies individuals at high risk for future cardiovascular disease (CVD) events. The prevalence of the metabolic syndrome (MetSyn) is high and its presence is associated with an increased risk of developing cardiovascular disease. Chronic kidney disease (CKD) is an independent risk factor for CVD. The purpose of this study was to determine the prevalence of PAD in patients with MetSyn and CKD. Methods: We analyzed data from two National Health and Nutrition Examination Surveys (NHANES) between the years 2001–2004. The prevalence of the MetSyn as defined by ATP III criteria, the prevalence of cardiac risk factors, and CKD status was determined in 4,023 participants aged 40 years and older. The presence of PAD was defined as an ABI < 0.9. CKD stage was determined using a GFR calculated using the abbreviated Modification of Diet in Renal Disease (MRDR) Study formula. A GFR > 90 was defined as normal, mildly decreased kidney function was defined as 60 to 90, a low kidney function was defined as a 30 to 60, and an impaired GFR was defined as $<$ 30. The non-MetSyn and normal GFR individuals served as a reference category. All estimates were weighted to account for the unequal probabilities of selection from the complex NHANES sampling scheme. Results: The prevalence of PAD in U.S. adults aged 40 or older with and without MetSyn was 9.4% and 4.5%. The likelihood of PAD dramatically increased as the GFR decreased. A person without MetSyn and a GFR of $<$ 30 is 11 times as likely to have PAD as a person without MetSyn and a normal GFR. There are an estimated 1.8 million U.S. adults with $30 \leq GFR < 60$. Conclusions: This data provides a nationally representative sample of PAD prevalence stratified by presence of MetSyn and GFR. The likelihood of PAD dramatically increased as the GFR decreased. This effect was greatest in individuals with the MetSyn.

TABLE 1. PREVALENCE OF PAD

	Non-MetSyn		MetSyn	
	Prevalence	OR (95% CI)	Prevalence	OR (95% CI)
GFR > 90	3.4%	1.00 (reference)	3.5%	1.03 (1.02 - 1.03)
60 ≤ GFR ≤ 90	3.7%	1.10 (1.09 - 1.10)	10.3%	3.29 (3.28 - 3.30)
30 ≤ GFR < 60	15.5%	5.25 (5.24 - 5.27)	19.3%	6.84 (6.81 - 6.86)
GRF < 30	28.4%	11.4 (11.3 - 11.5)	47.1%	25.5 (25.3 - 25.7)

P95

Costs and Effectiveness of Coronary Computed Tomographic Angiography for Individuals with Diabetes Mellitus: A Matched Comparison to Myocardial Perfusion SPECT

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Background: Coronary computed tomography angiography (CCT) identifies coronary artery disease (CAD) by visualization of coronary plaque, while myocardial perfusion imaging (MPS) identifies CAD by assessment of myocardial perfusion defects. To date, no cost effective analysis has been performed comparing these modalities in diabetic patients. Using the Centers for Medicare Services recently-assigned transaction codes (T-codes) for CT dedicated to coronary angiography, we examined CAD-related costs and clinical effectiveness for diabetic patients (pts) undergoing CCT under T-codes, compared to matched diabetic pts undergoing MPS testing. Methods: We examined ICD-9 codes within multicenter payer claims in order to identify 142,535 pts who underwent CCT or MPS. For each pt, data was collected for 9 months before and after the test. MPS pts were matched to CCT pts by multilevel modeling of 11 demographic and clinical risk states. Cost and clinical effectiveness was assessed by: 1) downstream CAD costs (2006 US dollars), and 2) clinical events including myocardial infarction (MI), angina, and CAD-related hospitalization. Results: Diabetic CCT pts (n=246) were matched 1:4 to diabetic MPS pts (n=984) for age (56.5 v 56.5 yrs), gender (43.9% v 43.9% female), hypertension (73.6% v 73.6%), hyperlipidemia (79.3% v 79.3%), known CAD (32.5% v 32.5%) and 5 additional variables. In multivariable analysis, 9-month CAD costs were similar amongst diabetic pts undergoing CCT and MPI (cost difference, $703, 95% CI $-1209 - $1618, p=0.11). Similarly, for diabetic pts without known CAD, no difference existed for 9-month CAD costs (cost difference, $-213, 95% CI $-386 - $645, p=0.43). Among individuals undergoing CCT or MPS, rates of MI (1.2% vs. 1.3%, p=NS), incident angina (8.1% vs. 7.7%, p=NS), and CAD-related hospitalization (1.0 vs. 0.6, p=NS) were also similar. Conclusion: Nine-month downstream CAD-related costs do not differ for diabetic individuals who undergo coronary evaluation by CCT compared to MPS, with equivalent clinical outcomes. For diabetic patients without known CAD, costs and clinical outcomes are also similar. These results suggest that CCT may be an effective alternative for coronary evaluation of diabetic patients with suspected CAD.

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P96

Intra-abdominal Fat Increases with Testosterone in African Americans and in Caucasians

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It has been shown that intra-abdominal fat (IAF) is lower in African-American (AA) than in white women. These results were obtained in small samples or in only pre- or post-menopausal women, and have not included hormonal factors. The Diabetes Risk Study, an ancillary study of the Study of Women's Health Across the Nation (SWAN), was designed to assess the dependence of ethnicity and reproductive hormones on IAF, controlling for age and % body fat. We hypothesized that i) AA women would have lower IAF after adjusting for % body fat, age, and other known risk factors, and ii) IAF would be positively related to the free testosterone index (FTI). Participants were selected from the 431 women in the total cohort if they were pre-, peri-, or post-menopausal, never took hormone therapy, and did not undergo a hysterectomy or double oophorectomy. IAF was measured by CT scan, total fat by DEXA scan. Physical activity was assessed by the Kaiser Physical Activity Score (KPAS), depression with the CESD. The free testosterone index(FTI) was calculated from T and SHBG. Out of the 363 women eligible for this study, 170 (46.8%) were African American (AA). Women of both ethnicities were comparable in age (mean$\pm$SD=50.4$\pm$3.8 years), menopausal status (13.5% pre-, 48.5% peri-, 38.0% post-menopausal), and the hormonal profile (E2=56.9pg/mL, T=43.1ng/dL, SHBG=53.6nM, FTI=4.0). Both groups were similar in education and smoking. AA women had significantly higher % body fat (45.8% vs. 41.5%, $p<0.001$), higher Framingham Risk Score (FRS) (10.8 vs. 9.9, $p<0,05$), and lower KPAS (7.3 vs. 8.2, $p<0.001$). A higher percentage of AA women were depressed (17.2% vs. 8.8%, $p<0.05$). In a multivariate model, IAF was signifiantly related to % body fat (β =2.8, p<.001), FRPT (β =3.6, p<.001), smoking (β = -18.0, p=.016), CESD (β =21.6, p=.001), KPAS (β = -4.7, p=.001), and FTI (β =16.6, p<.001), after adjusting for age (ns) and education (ns). The model explained 53.3% of the variance. AA women had significantly lower IAF after adjustments (84 vs. 99cm^2, both SE=3). Interactions with ethnicity were not significant. We conclude that increasing testosterone in women going through the menopausal transition is related to increases in IAF in AA and white women despite lower overall IAF levels in AA women.

P97

Increased QT Interval Temporal Variability in Elderly Subjects with the Metabolic Syndrome

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Background: A prolonged QT interval, as well as increased QT dispersion and QT temporal variability (QTVI) has been shown to be associated with increased risk of arrhythmias. This study investigates if these QT variables are altered in the metabolic syndrome, a known risk factor for cardiovascular morbidity and mortality. **Methods:** A populations-based sample of 1016 subjects aged 70, living in the community of Uppsala (the PIVUS study), were investigated with a 6-precordial lead ECG during 5 min of controlled breathing to calculate the mean QT interval, QT dispersion and QTVI. **Results**: Occurrence of the metabolic syndrome (n=172) was associated with an increased QTVI (-0.58$\pm$0.73 (SD) vs -0.76$\pm$0.56 in those without, p=0.0004), being significant also after correction for heart rate, mean QT interval and cardiovascular diagnosis and medication. QTVI increased in relation to the number of components of the metabolic syndrome present (p=0.003). Mean QT interval and QT dispersion were not related to occurrence of the metabolic syndrome. **Conclusions**: Temporal variability of the QT interval, but not the mean value of the QT interval, was increased in subjects with the metabolic syndrome, possibly indicating an increased risk of arrhythmias in these subjects.

P98

Change in Hemoglobin A1c and C-Reactive Protein Levels in Patients with Diabetes Mellitus

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Objectives: High C-Reactive Protein (CRP) levels have been associated with increased cardiovascular risk, but little data is available for its use as a prognostic marker in patients with diabetes. We studied the effects of an intensive intervention to reduce hemoglobin A1C on CRP levels among patients with diabetes. **Methods:** The 109 enrolled patients with Type 2 DM were randomly assigned to either a group behavioral and pharmacologic "intervention" for cardiac risk reduction for 4 weeks or to continue with "usual care" at the Providence VA Medical Center during 2004–2007. A1C levels were related to CRP levels before and after the intervention and adjusted for demographic (age, sex, race), and clinical (smoking, weight, blood pressure, lipid profile, serum creatinine) factors, and medications (aspirin, ACE inhibitors, angiotensin receptor blockers, thiazolidinediones and statins) using linear regression modeling. **Results:** A1C levels significantly correlated with CRP levels ($r = 0.31$, $P < 0.01$) at baseline, independent of demographic and clinical factors and medications. After 3 months, patients in the "intervention" group (n=58) had a significant decrease in A1C levels (8.1 $\pm$ 1.54% to 7.36 $\pm$ 1.13%, $P < 0.01$), associated with concomitant changes in total cholesterol (-18.70 $\pm$ 38.19 mg/dL, $P = 0.01$), LDL (-12.17 $\pm$ 31.36 mg/dL, $P = 0.048$), and systolic blood pressure (-6.81 $\pm$ 21.02 mm Hg, $P = 0.034$) from the baseline. No significant changes were found in these parameters for the "usual care" group. There was no significant change in HDL levels for either treatment group. CRP levels did not change significantly from baseline in either the "intervention" group (5.25 $\pm$ 4.43 mg/dL to 6.71 $\pm$ 6.54 mg/dL, $P = 0.17$) or the "usual care" group (5.32 $\pm$ 7.94 mg/dL to 5.43 $\pm$ 8.23 mg/dL, $P = 0.95$). Linear regression modeling identified baseline CRP and age as the only predictors of the final CRP levels. **Conclusions:** While CRP correlated with A1C at baseline, a reduction in A1C levels with intensive intervention did not translate into a reduction in CRP levels, despite adjustment for medication use and clinical confounders. The absence of such a corresponding change questions the usefulness of CRP as a short-term modifiable marker of cardiovascular risk in patients with diabetes.

P99

Benign Prostate Hypertrophy: Is It a Component of Metabolic Syndrome?

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Background: The prevalence of benign prostate hypertrophy (BPH), T2DM, HTN, and CAD increases with age and their pharmacotherapy (and its side effects) often overlap. Also, BPH has been proposed as a component of metabolic syndrome (MS). This study looks at the relationship of BPH with CAD and components of MS. **Methods:** Data of 1563 men aged more than 40 years, and without prostate cancer from NHANES 2003–2004 public-use datasets were analyzed. Odds ratios (ORs) of BPH were calculated for history of T2DM, HTN and CAD. Additionally, BMI and waist circumference (WC) were divided into quartiles (Q1-Q4) and OR of BPH calculated for each quartile with reference to the lowest quartile. Also, fasting blood glucose (FBG), fasting serum insulin (FSI), systolic (SBP) and diastolic (DBP) blood pressures, total cholesterol (TC) and C-reactive protein (CRP) were dichotomized at their means and ORs of BPH estimated. Logistic regression was used to calculate the ORs after applying sampling weights and adjusting for age. Finally, serum concentration of prostate specific antigen (PSA) was regressed on age and WC. **Results:** A clinical history of BPH was present in 12.0% (188/1563) subjects. Age adjusted ORs (95% CI) of BPH for T2DM 0.96 (0.62, 1.49), HTN 1.02 (0.69, 1.51) and CAD 1.23 (0.75, 2.03) were not significant. The odds of BPH increased with increase in BMI (p trend <0.001); however, the OR was statistically significant only for Q4 (OR=1.62, 95%CI = 1.03–2.55). Similarly, odds of BPH increased WC (p trend <0.001); and the ORs of Q3 (OR=2.92, 95%CI =1.41–6.04) and Q4 (OR=3.04, 95%CI = 1.73–5.32) were statistically significant. ORs of BPH in individuals with higher SBP (OR=0.77, 95%CI = 0.51, 1.15) or higher DBP (OR=0.96, 95%CI = 0.58, 1.59) were lower than null. OR of BPH for higher FSI (OR=1.97, 95%CI= 1.22–3.20) was significant. However, neither FBG (OR=1.28, 95%CI= 0.62–2.64), CRP (OR= 0.70, 95%CI=0.40–1.32), and TC (OR= 1.28; 0.97–1.69) had significant associations with BPH. Linear regression gave the following equation: PSA (ng/ml) = 0.88 + 0.06* [Age-40yrs] -0.01*[WC - 70cm]; (P<0.001). **Conclusion:** From these results, clinical history of BPH is not associated with diabetes, hypertension or CAD. However, it appears to be associated with obesity and hyperinsulinemia.

P100

More Severe Subclinical Atherosclerosis and More Metabolic Risk Factors Among Men Aged 40–49 Years Without Hypertension, Diabetes, and Dyslipidemia

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Background: It is difficult to examine atherosclerotic outcomes such as coronary heart disease in relatively young age groups. However, some indicators such as carotid artery intima-media thickness (IMT) and coronary calcification (CC) can assess the severity of subclinical atherosclerosis even in those who are apparently healthy. The purpose of this report is to examine the relationship between the accumulation of metabolic factors and subclinical atherosclerosis in apparently healthy Japanese men aged 40 - 49 where prevalent coronary heart is rare. ***Methods***: Metabolic risk factor and subclinical atherosclerosis assessments were made in a population-based random sample of 313 Japanese men aged 40 to 49 years. Subclinical atherosclerosis was assessed by IMT and CC in the following 3 groups; A) as a whole, B) excluding those on medication for either hypertension, diabetes, or dyslipidemia, and C) further excluding those with definite risk factors (systolic and diastolic blood pressures $\geq$140/90mmHg or fasting blood glucose levels $\geq$126mg/dl). Metabolic risk factors were considered as large waist circumference ($\geq$85cm), high blood pressure ($\geq$130/85mmHg), high fasting serum glucose ($\geq$110mg/dl), high fasting serum triglycerides ($\geq$150mg/dl), and low HDL-cholesterol (<40mg/dl). The relationship between the number of metabolic risk factors (0, 1, 2, 3 or more) and subclinical atherosclerosis was examined in groups A, B, and C. ***Results***: The prevalence of the metabolic syndrome (having 3 or more risk factors) was 28.8%, 25.1%, and 17.7% in groups of A, B, and C. In all groups, IMT and the prevalence of CC (Agatston score >0) increased significantly with increasing number of metabolic risk factors. In those who were the healthiest (group C), levels of mean IMT were 0.6024, 0.5970, 0.6214, and 0.6252 mm in the presence of 0, 1, 2, and 3 or more risk factors (p for trend = 0.029). The corresponding prevalence of CC was 14.8%, 27.0%, 37.5%, and 31.7% (p for trend = 0.027). ***Conclusion***: Even in a sample of apparently healthy young Japanese men aged 40–49 years without hypertension, diabetes, and dyslipidemia, those with more metabolic risk factors had an increased likelihood of having subclinical atherosclerosis.

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P101

Lifetime Risks for Cardiovascular Disease by Weight and Metabolic Syndrome Status in Men and Women at Selected Ages

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BACKGROUND: Metabolic syndrome (MetSyn) is associated with cardiovascular (CVD) and coronary (CHD) events in the short term. However, lifetime risks (LR) for CVD in the setting of MetSyn have not been described. METHODS: Using data from the Women's Health Initiative Observational Study as well as NHLBI's public release datasets (ARIC, CHS, Framingham Heart, Framingham Offspring, and Honolulu Heart Studies), we stratified participants (aged 50, 60, and 70 years) according to their body mass index (BMI), waist circumference, waist/hip ratio and MetSyn status. MetSyn was defined as the presence of at least 3 of the following: waist ≥40 inches (≥35 in women), HDL <40 (<50 in women), triglycerides ≥150, BP ≥130/85 or treated, and fasting blood glucose ≥100 or diagnosis of diabetes. Participants were stratified by both MetSyn status as well as the number of MetSyn components present. LR for CVD death to age 95 years was estimated, with death free of CVD as a competing event. RESULTS: In all, 41,342 men and 178,403 women were followed for a total of 1,281,075 person-years; 9,528 CVD deaths occurred. In general, higher BMI, waist circumference and waist/hip ratio were each associated with higher LR for CVD death. At all ages, the presence (vs. absence) of MetSyn was typically associated with modestly higher LR for CVD death. Representative data on remaining LR for CVD death at age 60 are shown in Table 1. Similarly, a greater number of MetSyn components was associated with somewhat higher LR for CVD death in most cohorts. However, participants with MetSyn were also noted to have substantially shorter median survival (1 to 5 years at age 60), which likely limited their LR for CVD death. Results were similar for the endpoint of CHD death/non-fatal MI. CONCLUSIONS: Remaining LR for CVD is somewhat higher in the presence of MetSyn and its components. Furthermore, median survival in the setting of MetSyn is decreased. These results provide the first estimates of LR for CVD in the setting of MetSyn.

TABLE 1: RISK FOR CVD DEATH BY METABOLIC SYNDROME STATUS IN MEN AND WOMEN AT AGE 60.

		Risk for CVD Death % (95% Confidence Interval), Adjusted for Competing Risk of Non-CVD Death					
		Males			Females		
Cohort	Metabolic Syndrome Status	15 years	30 years	Lifetime Risk	15 years	30 years	Lifetime Risk
ARIC	No	7.8 (5.8–8.6)			2.9 (1.9–3.9)		
	Yes	11.1 (8.5–13.6)			8.1 (6.2–10.0)		
FHS	No	18.8 (16.7–20.8)	37.9 (35.3–40.5)	40.5 (37.8–43.1)	9.7 (8.3–11.1)	28.5 (26.3–30.7)	32.1 (29.9–34.4)
	Yes	20.9 (16.8–25.1)	41.0 (35.9–46.1)	42.4 (37.2–47.6)	11.8 (8.7–14.9)	32.1 (27.5–36.7)	34.6 (29.8–39.4)
FOS	No	13.9 (8.7–19.1)			10.0 (5.0–16.1)		
	Yes	16.7 (11.5–21.9)	29.5 (21.7–37.3)		12.4 (5.4–19.4)		
HHP	No	5.4 (4.9–5.8)	19.2 (18.3–20.0)	26.9 (25.6–28.2)			
	Yes	9.5 (7.8–11.2)	23.2 (21.0–25.4)	33.9 (30.6–37.1)			
WHI	No				1.9 (1.3–2.5)		
	Yes				9.9 (6.2–13.6)		

ARIC and FOS have limited follow-up at older ages. HHP was a study in men only and WHI was a study in women only.

P102

Heart Rate Variability and Metabolic Syndrome in Native Canadians

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Background: Heart rate variability (HRV), which represents the cardiac sympathetic and parasympathetic modulation of the autonomic nervous system (ANS) may be impaired in individuals with the metabolic syndrome (MetS). However, this impairment may depend on the criteria used to define the MetS. We assessed HRV in individuals with MetS defined according to the **International Diabetes Federation (IDF) and among those defined according to the** National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria in native Canadians. ***Methodology:*** In fall 2004, the Health Survey «Qanuippitaa?» was conducted in the 14 coastal villages of Nunavik (North of Quebec). Physiological, anthropometrics and HRV measurements were collected among a sub-sample of 206 adults aged ≥ 40 years. Indices of HRV from the time and the frequency domains were derived from a 2-hour Holter monitoring measurement. The MetS was defined according to the **IDF and the** NCEP ATP III criteria. ***Results:*** The prevalence of MetS was 20% using the **IDF criteria** in contrast to 50% using the NCEP ATP III criteria. Waist girth, systolic and diastolic blood pressure and glucose and triglycerides levels were negatively correlated with the standard deviation of the RR intervals (SDNN). Pearson correlation coefficients were: -0.27 ($p < 0.0001$), -0.15 ($p = 0.03$), -0.15 ($p = 0.03$), -0.25 ($p = 0.0003$) and -0.19 ($p = 0.008$), respectively. When **the** NCEP ATP III criteria was used to define the MetS, SDNN was lower in individuals with the MetS. After adjusting for age and gender, SDNN was 70 ms (95% CI: 66–75 ms) in individuals with MetS vs. 88 ms (95% CI: 80–98 ms) in those without the MetS. In contrast, when the MetS was defined according to the IDF criteria, no significant difference was detected in SDNN among individuals with and without the MetS. The adjusted SDNN was 72 ms (95% CI: 64–80 ms) in individuals with MetS vs. 76 ms (95% CI: 73–81 ms) in those without MetS. ***Conclusion:*** The results of the present study suggest that HRV is impaired in individuals with MetS but its detection may be influenced by the criteria used for the definition of the MetS.

P103

Glycated Hemoglobin in Acute Coronary Syndromes: Good Marker of Risk but Poor Predictor of Outcome

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Introduction: Diabetic patients have a high incidence of acute coronary syndromes (ACS) and diabetes is associated with a two-fold increase in hospital mortality. Glycated haemoglobin (HbA1c) is a marker of glucose metabolism in the preceding 6–8 weeks. Its prognosis value in the acute phase of ACS is not well established. Aim: To evaluate, in an ACS population, the relationship between HbA1c and risk factors, therapeutics strategies, in-hospital complications and mortality. Population and methods: Retrospective analysis of a database containing 756 consecutive patients admitted to a single coronary care unit for ACS between May 2004 and December 2006. Our population was divided in four groups, according to the value of HbA1c: A <6%; B 6–6.9%; C 7–7.9%; D ≥8%. Results: There were no significant differences regarding gender, TIMI risk score at admission, reperfusion strategies and prescribed medication. Higher levels of HbA1c were strongly correlated with: hypertension (60.8%, 79.7%, 90.5%, 79.5%, $p<0.003$); dyslipidemia (61.3%, 86.0%, 86.7%, 91.2%, $p<0.001$); obesity (42.3%, 54.5%, 80.0%, 71.4%, $p<0.001$); diabetes (5.1%, 40.3%, 76.2%, 73.8%, $p<0.001$); previous use of insulin (2.3%, 8.2%, 37.5%, 44.4%, $p<0.001$) and oral anti-diabetic drugs (1.1%, 32.7%, 31.3%, 40.7%, $p<0.001$); previous angina (58.9%, 65.6%, 50.0%, 87.5%, $p<0.005$), previous coronary disease (57.7%, 64.2%, 47.6%, 85.7%, $p<0.004$) and length of stay (6.03, 6.65, 6.38, 7.64 days, $p<0.043$). There was no significant association between HbA1c and the extent of cardiac damage, complications and in-hospital mortality. Conclusion: In acute coronary syndrome patients, glycated haemoglobin is a good marker of risk, but a poor predictor of outcome.

P104

Diabetes and the Risk of Sudden Cardiac Death: Atherosclerosis Risk in Communities (ARIC) Study

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OBJECTIVE: Association of diabetes with increased risk of sudden cardiac death has been indicated by several studies, however limitations in study design underscore the need for confirmatory prospective studies. In the current study we used data from the ARIC cohort to examine the association of prediabetes and type 2 diabetes with the risk of sudden cardiac death as compared to the risk of non-fatal myocardial infarction (MI) during follow-up from 1987 through 2001. METHODS: Diabetes was defined as either a physician's diagnosis of diabetes, use of hypoglycemic medications, fasting blood glucose level>126 mg/dL, or nonfasting glucose level>200 mg/dL. Prediabetes was defined as fasting blood glucose level of 100–126 mg/dL. Sudden cardiac death (n=304) was defined as death adjudicated by a physician panel to be a sudden, pulseless condition without a known non-cardiac cause. Non-fatal MI (n=930) was defined as incident definite or probable MI that did not result in a fatal outcome within 28 days. RESULTS: In analyses adjusted for age, gender, race/ARIC center, hypertension, anti-hypertensive medication, and smoking, the Cox proportional hazard ratio of the association of diabetes with sudden cardiac death was 2.53 (95% CI 1.97, 3.25) and it was 2.51 (95% CI 2.15, 2.92) for non-fatal MI. Those effect estimates were not changed by censoring of non-fatal MI cases that subsequently died of sudden cardiac death. We observed a higher risk of sudden cardiac death and non-fatal MI among women with diabetes as compared to men with diabetes; however, adjustment for covariates eliminated gender differences. Stratification by baseline prevalent coronary heart disease, or prevalent heart failure revealed a larger hazard ratio of the association of diabetes with sudden cardiac death among those without these prevalent conditions. A similar pattern was seen for non-fatal MI. The association for prediabetes was stronger with sudden cardiac death than with non-fatal MI in analyses adjusted for age and race; adjustment for the remaining covariates eliminated the statistical significance of those associations. CONCLUSION: Diabetes is associated with an increased risk of both sudden cardiac death and non-fatal MI. The strength of association is similar for both endpoints.

P105

Association of Alcohol Consumption and HDL Subclasses Measured by NMR Spectroscopy: The Rancho Bernardo Study

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Moderate alcohol intake confers cardioprotective benefits such as improved HDL cholesterol and reduced mortality. Limited evidence suggests HDL subclass distribution may help explain how alcohol improves cardiovascular outcomes. This is the first study to evaluate NMR-derived HDL subclasses and alcohol intake among a wide age-range of older adults (50–94 years) with a large proportion of daily drinkers (n=958, 44%) and stratified by postmenopausal hormone

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therapy (HT). We studied 2171 men and postmenopausal women (55%) aged 50 and older (mean age 71 years) who were not on cholesterol medication and had a triglycerides value <400mg/dL. Participants were categorized based on reported alcohol intake (grams per week) and frequency (none, <3 drinks/wk, 3–4 drinks/wk, and daily). The relationship between alcohol intake and lipoprotein fractions was examined with sex-specific linear regression models adjusted for age, BMI, diabetes, current smoking, exercise at least 3 days per week, and HT in women. Women also were stratified by current HT use (n=325) or not (n=872). We found that individuals with the highest weekly alcohol consumption in both genders, regardless of HT use in women, had increased total size and number of medium and large HDL in addition to an overall increase in HDL concentration (all p <.001) (Table 1). As both alcohol consumption and high levels of HDL cholesterol are associated with decreased cardiovascular disease, the current findings suggest that alcohol may decrease cardiovascular disease through an increase in overall HDL cholesterol and a shift from atherogenic small HDL particles to cardioprotective large HDL particles.

	HDL cholesterol, mg/dL Mean ± std dev		HDL size, nm Median (IQR)		Medium HDL, mg/dL Median (IQR)		Large HDL, mg/dL Median (IQR)	
	Women	Men	Women	Men	Women	Men	Women	Men
None (0 drinks/wk)	62±17	48±11	9.1 (8.8–9.4)	8.6 (8.3–9.0)	6 (2–11)	5 (2–9)	22 (11–33)	10 (6–19)
Light (<3 drinks/wk)	64±16	51±17	9.0 (8.7–9.4)	8.6(8.3–9.0)	6 (2–11)	5 (2–8)	22 (13–33)	12 (5–19)
Moderate (3–4 drinks/wk)	72±19	52±13	9.1 (8.8–9.6)	8.7(8.3–9.0)	7 (2–11)	5 (2–8)	20 (18–24)	15 (6–21)
Regular (daily)	75±19	57±15	9.2 (8.9–9.6)	8.8 (8.5–9.1)	9 (4–14)	6 (2–11)	29 (19–41)	15 (8–25)

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P106

The Impact of Increased Statin Use on LDL-Cholesterol Levels and Control Among US Adults: Progress and Shortcomings

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Background: Few data are available on the use of statins after publication of the ATP-III guidelines in 2001. The objective of this study was to determine changes in statin use and its impact on LDL-cholesterol control among US adults from 1999 to 2004. Methods: High LDL-cholesterol and statin use among 1911 participants of the National Health and Nutrition Examination Survey (NHANES) 2003–2004 were determined and compared with 1770 and 2094 participants of NHANES 2001–2002 and NHANES 1999–2000, respectively. Statin use was obtained from review of participants' drug containers. High LDL-cholesterol and LDL-cholesterol control were defined using risk-specific cut-points from the ATP-III guidelines. Results: Statins were taken by 24 million Americans in 2003–2004, an increase from 12.5 million in 1999–2000. In 1999–2000, 2001–2002, and 2003–2004, statins were being used by 19.6%, 27.3%, and 35.9%, of US adults with high LDL-cholesterol, respectively (p-trend<0.001). Age-standardized mean LDL-cholesterol declined from 119.9 to 112.0 to 100.7 mg/dL among statin users between 1999–2000, 2001–2002, and 2003–2004. LDL-cholesterol control to ATP-III recommended targets was achieved by 49.7%, 67.4%, and 77.6% of statin users in 1999–2000, 2001–2002, and 2003–2004, respectively (p-trend<0.001). Among US adults with high LDL-cholesterol, after multivariate adjustment, non-Hispanic blacks were 39% less likely (prevalence ratio =0.61; 95 CI: 0.39 -0.97) than non-Hispanic whites to be taking statins. Conclusions: Statin use continues to increase among US adults and this has lead to substantial improvements in LDL-cholesterol control. Nevertheless, sub-optimal statin use, especially among minorities, continues to prevent the maximal public health benefit from this effective medication.

P107

Associations Between HMGCR Polymorphisms and Lipids in the Multi-Ethnic Study of Atherosclerosis (MESA)

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HMGCR is a rate-limiting enzyme in cholesterol biosynthesis and is the target of statins. Statins reduce LDL-c, triglyceride (TG), and increase HDL-c. Atherogenic lipoproteins (ALP) include higher TG, lower HDL-c and higher small LDL. There are no available data on the association of ALP with the *HMGCR* gene in multi-ethnic populations. To examine the associations between lipid traits and the *HMGCR* gene, 2444 subjects in the MESA study without statin use in 4 ethnic groups (597 African Americans, AA, 612 European Americans, EA, 627 Chinese Americans, CHA, and 608 Hispanic Americans, HA) were genotyped for the same 10 tag SNPs based on the International HapMap data. In each ethnic group, all the SNPs were in Hardy-Weinberg equilibrium, and haplotypes were constructed by Haploview v4, resulting in a single block with 8 haplotypes (consisting of 10 SNPs). Association analyses for haplotypes were tested within each ethnic group using generalized linear models with adjustment for age, gender, BMI, and DM status. To account for multiple testing, empirical p-values were estimated by permutation of 1000 replicates under the same model. We found that haplotype2 (H2) carriers had lower TG levels than non-carriers in AA (p=0.001) and HA (p=0.02). In HA, H4 was associated with lower HDL-c (p=0.004), higher TG (p=0.02), lower large HDL (p=0.001), higher small LDL (p=0.02), and another haplotype, H8, was associated with the lipid traits in the opposite direction, including higher HDL-c (p=0.002), lower TG (p=0.003), higher large HDL (p=0.001), and lower small LDL (p=0.01). In EA, H8 carriers were similar to HA with respect to HDL and HDL subclasses. There was no remarkable association between total cholesterol or LDL-c and any of the haplotypes examined in any of the ethnic groups. The absence of H4 in AA and EA and the absence of H2 in CHA may account for the association differences among ethnic groups. In summary, the *HMGCR* H4 haplotype was associated with ALP in HA. In contrast, H8 conferred protection against these traits in HA and EA, and H2 was associated with lower TG level in HA and AA. These data suggest that in Hispanics, variation in the *HMGCR* gene contributes to lipoprotein phenotype. This *HMGCR* variation may contribute to ethnic differences in statin response of TG and HDL-c.

P108

Cumulative Exposure to Non-Optimal LDL Cholesterol During Young Adulthood Predicts Coronary Calcium Later in Life in CARDIA

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Background: LDL cholesterol is associated with cardiovascular disease, but the consequences of moderate levels during young adulthood are unclear. Methods: Using repeated serum lipid measures from 7 examinations over 20 years in the African-American (AA) and European-American (EA) men and women recruited at age 18–30 for the Coronary Artery Risk Development in Young Adults (CARDIA) Study, we estimated LDL, HDL and triglycerides trajectories for each participant using mixed models. We then estimated *cumulative* exposure to LDL from age 20–35 in "mg/dl-years", similar to "pack-years" of tobacco exposure, and related this to coronary calcium measured in middle age (44±4 years). Results: Among 3569 CARDIA participants (47% Black, 44% male), cumulative exposure from age 20–35 was ≥2400 mg/dl-years (time-averaged LDL>160 mg/dl) in 4%, 1950–2399 (LDL 130–159) in 17%, 1500–1949 (LDL 100–129) in 43%, 1050–1499 (LDL 70–99) in 32%, and only 4% maintained an optimal average LDL<70 mg/dl (<1050 mg/dl-years) through age 35. Coronary calcium was five times more common in participants with time-averaged LDL>160 during young adulthood (44%) than in those maintaining optimal LDL levels (8%). This association remained strong after adjusting for age, sex, race, income and education, habits, CHD risk factors and cumulative exposure to LDL, HDL and triglycerides after age 35, and after excluding participants who used lipid-lowering medications or developed LDL>160 mg/dl at any age (Table). Conclusions: Cumulative exposure to LDL outside of an optimal range during young adulthood is a graded predictor of coronary calcium later in life.

Cumulative LDL exposure, age 20-35 years		Coronary calcium prevalence, age 44±4	Adjusted odds ratios for coronary calcium, in:			
			Full sample		Excluding participants with LDL ever >160 mg/dl or on meds	
mg/dl-years	Time-averaged LDL, mg/dl		N*	OR (95% CI)	N*	OR (95% CI)
<1050	<70	8%	136	Reference	132	Reference
1050-1499	70-99	10%	1134	1.4 (0.7-2.8)	1114	1.7 (0.8-3.5)
1500-1949	100-129	17%	1545	2.1 (1.0-4.4)	1424	2.7 (1.2-5.9)
1950-2399	130-159	27%	619	3.2 (1.4-7.2)	399	3.9 (1.6-9.6)
>=2400	>=160	44%	135	5.7 (2.2-15)	0	--

P109

Changes in Blood Cholesterol Levels Correlate with Concurrent Changes in Adiposity in Children and Adolescents: Longitudinal Findings from Project HeartBeat!

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Objectives: To examine the associations in children and adolescents between the changes of total and LDL-cholesterol levels (TC and LC) and the concurrent changes of commonly used adiposity measures using longitudinal data from Project HeartBeat!. Methods: Three cohorts, comprising 678 children (49.1% female, 79.9% non-black) initially 8, 11, and 14 years of age, were enrolled and followed at 4-monthly intervals for up to 4 years from 1991 to 1995. Plasma concentrations of TC and LC were determined in fasting samples in a standardized laboratory. BMI and one of its two components, the fat mass index (FMI), percent body fat (%BF), and the sum of triceps and subscapular thicknesses (SF2) were derived from anthropometry alone or with bioelectric impedance. Changes over every 4-month interval in cholesterol and adiposity measures were calculated by sequential differences in values over each 4-month interval of follow-up. A multilevel modeling technique was used for examination of the association. Results: Four-monthly changes in TC and LC were closely and positively related to concurrent changes in each adiposity measure. Estimated from separate TC models, the regression coefficients for BMI, %BF, FMI, and SF2 were 2.524, 0.384, 2.096, and 0.332, respectively, all highly significant after adjustment for sex, race, age, and the initial level of TC at the beginning of each 4-month interval. Corresponding regression coefficients for the LC models were 1.356, 0.291, 1.374, and 0.211, respectively; these coefficients were also highly significant and independent of sex, race, age, and the initial level of LC. No significant interactions of the

changes in adiposity with sex or race were found in any of the TC or LC models. Conclusions: Four-monthly changes in TC and LC are positively and independently related to the concurrent changes in adiposity measures in children and adolescents. The associations between concurrent changes in related variables suggest a close biological relation between these variables. Our findings, in context with other evidence, support prevention of overweight and obesity in youth to prevent dyslipidemia and adult heart disease and stroke.

P110

Increased Postprandial Hypertriglyceridemia Among Smokers Is Not Due to Inflammatory Patterns or Insulin Resistance

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Background–Smoking is associated with increased postprandial hypertriglyceridemia (PPT). Inflammation and insulin resistance are potential "drivers" for this phenomenon. Therefore, we tested whether inflammatory patterns and/or insulin resistance explain the effect of smoking on PPT. ***Methods and results–***Men and women in the NHLBI Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study in Utah and Minnesota (n=1036, age 49±16 y) were included. Each study participant was asked to suspend use of lipid-lowering drugs for three weeks and was given a high-fat milkshake (83% fat and 700 kcal/m^2). Triglyceride concentrations at 0, 3.5 and 6 hr after the fat load were measured. Inflammatory markers were measured at baseline. Principal component analysis was used to derive inflammatory patterns from individual inflammatory markers (CRP, IL-2, IL-6, TNF-α and MCP-1). Insulin resistance (IR) was estimated using the HOMA equation. Repeated measures-ANOVA models were used for analyses. Two inflammatory patterns, namely CRP-IL6 pattern and MCP-1-TNF-α pattern, were derived. We found significant main (smoking and time) and interaction (smoking*time) effects ($P<0.01$) for triglycerides. The multivariate-adjusted mean log-transformed triglyceride concentrations for never, past and current smokers were 4.76±0.03, 4.70±0.04 and 4.81±0.07at 0 hr; 5.35±0.03, 5.39±0.04 and 5.59±0.07 at 3.5 hr; and 5.18±0.03, 5.25±0.04 and 5.42±0.07 at 6 hr after the oral fat load, respectively. Smoking remained significant after adjusting for HOMA-IR and/or inflammatory patterns which showed independent associations with PPT ($P<0.05$). ***Conclusion–***These data confirm impaired metabolism of dietary fat among smokers and suggest that mechanisms other than inflammation or insulin resistance may explain the observed hypertriglyceridemia among smokers.

P111

Clinical Utility of a Fingerstick Technology to Identify Individuals with Abnormal Lipid and High-Sensitivity C-Reactive Protein (hsCRP) Levels

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Background: National Cholesterol Education Program (NCEP) ATP III guidelines stress the importance of lipid screening to identify and manage patients at risk for cardiovascular disease (CVD). Point of care measurement of lipids and other risk factors with immediate results could facilitate optimal preventive care and increase adherence to national guidelines. Fingerstick technology is widely used in outreach settings but has not been validated in diverse populations in clinical settings. The purpose of this study was to determine the ability of a commonly used fingerstick technology (Cholestech LDX) to identify individuals with abnormal total cholesterol (TC), calculated low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides (TG) and hsCRP compared to a standardized university core laboratory. Methods: Participants in the NHLBI Family Intervention Trial for Heart Health (F.I.T. Heart) who were randomized to a screening/educational intervention (n=250, mean age 48 ± 13.5y, 66% female, 36% nonwhite) had baseline lipids and hsCRP measured simultaneously by 1) fingerstick technique analyzed by Cholestech LDX and 2) fresh venous blood analyzed by Columbia University General Clinical Research Center Core Lab using standard methods for lipids and ultra sensitive ELISA for hsCRP. Pearson correlation, kappa, sensitivity, and specificity were calculated for fingerstick vs. core lab. Results: As shown in Table 1, sensitivity and specificity of fingerstick to identify those with abnormal lipids and hsCRP ≥1mg/L are all ≥ 75%. Conclusion: Fingerstick screening of lipids and hsCRP has good clinical utility to accurately identify persons at risk for CVD at the point of care.

TABLE 1: COMPARISON OF LIPID AND HSCRP BY FINGERSTICK SCREEN VS. VENOUS SAMPLES ANALYZED BY CORE LAB

Risk Factor[1]	Pearson Correlation (r)*	Clinical Cutpoint	Sensitivity (%)	Specificity (%)	Kappa (k)
Total Cholesterol	.91	> 200	79	95	.75
LDL-C	.88	> 100	93	82	.75
		> 130	76	92	.69
HDL-C	.77	< 40	93	78	.40
Triglycerides	.93	> 150	88	93	.78
hsCRP	.81[2]	> 1	75	95	.58
		> 3	56	99	.58

*p<.05; (1) Lipids as mg/dL; hsCRP as mg/L; (2) hsCRP values >10mg/L (n=47) excluded

P112

Relation Between Serum PUFA and Lipoprotein Subclasses in US White, Japanese, and Japanese-American Men

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Background: Among polyunsaturated fatty acids (PUFA), dietary marine-derived n-3 PUFA (i.e. docosahexaenoic acid [DHA; 22:6n-3]) and linoleic acid (LA, 18:2n-6) have been reported to favorably influence lipoproteins in some, but not all clinical trials. However, patterns of the relation of each serum PUFA to lipoprotein subclasses in different ethnic populations having considerable variability in habitual diet were not known. Purpose: To identify the relation of serum n-3 or n-6 PUFA to lipoprotein subclasses of VLDL, LDL and HDL measured by nuclear magnetic resonance spectroscopy in U.S. white (n=261), Japanese (n=285), and Japanese American men (n=212) aged 40–49 years. Methods: Of original population-based samples (N=926), we excluded those taking lipid-lowering medications or diabetes. Serum fatty acids were analyzed by the capillary-gas-liquid chromatography and then as % of total fatty acids. Multiple regression models as a function of tertile groups of each PUFA were used after adjusting for age, body mass index, smoking, ethanol, glucose, and insulin (model I); further adjusted for n-3 or n-6 PUFA (model II). Results: Marine n-3 PUFA was higher among Japanese than other populations (9.4%; 3.9% and 5.5%, respectively, in whites and Japanese American). Increases in both marine n-3 PUFA and LA had significant associations with decreases in large VLDL particles (or size) and increases in large HDL particles (or size), consistently across populations. An increase in LA was significantly associated with decreases in small LDL particles across populations, but an increase in DHA had an ethnic-specific pattern, showing a significant inverse association only among white men. Conclusion: An increased proportion of LA, like marine n-3 PUFA, is related to favorable shifting of VLDL, LDL and HDL particles. DHA may influence the reduction of small LDL particles within a relatively moderate range of marine n-3 PUFA.

TABLE. RELATION BETWEEN PUFA AND LIPOPROTEIN SUBCLASS

	β coefficient					
	Small LDL (nmol/L)			Large HDL (μmol/L)		
Model	W	J	JA	W	J	JA
Marine n-3						
I	-124.51§	45.12	5.16	.74§	.46	.50*
II	-129.71¶	-44.04	-19.54	.76¶	1.29¶	.66§
DHA						
I	-134.95¶	71.64*	-5.22	.72§	.19	.68§
II	-136.96¶	-6.59	-20.91	.74§	.93§	.78§
EPA						
I	-50.15	26.51	63.29	.75**	.61*	.37
II	-66.70	-22.79	49.76	.84¶	1.03¶	.46*
ALA						
I	-52.16	-63.60	46.52	.09	.56*	-.20
II	-37.95	-48.81	58.63	.01	.45	-.27
Total n-6						
I	-211.18¶	-172.28¶	-103.66*	1.16¶	1.22¶	.68§
II	-223.42¶	-177.37¶	-105.21*	1.23¶	1.85¶	.82§
LA						
I	-175.64¶	-129.46¶	-104.70*	.87¶	.88§	.52
II	-191.32¶	-124.50§	-107.03*	.97¶	1.44¶	.67§

*p<.05, §p<.01, ¶p<.001, W: Whites, J: Japanese, JA: Japanese American, DHA: docosahexaenoic acid, EPA: eicosapentaenoic acid, ALA: alpha-linolenic acid, LA: linoleic acid

P113

Serum Selenium and Serum Lipids in US Adults

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Background: In a randomized controlled trial, there was a higher risk of developing hypercholesterolemia and hypertriglyceridemia in those assigned to a multi-vitamin pill containing selenium compared to placebo. Observational studies, largely conducted outside of the US in populations with relatively low selenium levels, have reported inconsistent associations between serum selenium and total cholesterol. **Objective**: To examine the relationship of serum selenium levels with serum lipids in a representative sample of US adults. **Research Design and Methods:** Cross-sectional analysis of 5,807 adults ≥20 years old, who participated in the morning medical examinations in NHANES III and fasted more than 9 hours. Serum selenium was measured by atomic absorption spectrometry. **Results:** The multivariable adjusted difference in total cholesterol, LDL cholesterol, HDL cholesterol, LDL/HDL cholesterol ratio, and triglycerides (natural log transformation) comparing the highest to the lowest quartile of serum selenium were 17.11 (95% CI 12.68, 21.53) mg/dl, 10.56 (6.77, 14.35) mg/dl, 3.76 (2.07, 5.45) mg/dl, 0.10 (-0.03, 0.22) and 0.12 (0.06, 0.17) ln(mg/dl), respectively. **Conclusion:** In a representative sample of US adults, serum selenium levels were positively associated with

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serum total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides. In addition, serum selenium levels were associated with a more atherogenic profile (increased LDL/HDL ratio). Randomized trials of selenium supplementation should monitor serum lipids to establish the effect of selenium on lipid profile.

MULTIVARIABLE ADJUSTED DIFFERENCE IN SERUM LIPID LEVELS BY QUARTILE OF SERUM SELENIUM (N=5,807)

	Quartile 1 < 113.8 ng/ml	Quartile 2 113.8–123.9 ng/ml	Quartile 3 123.9–134.7 ng/ml	Quartile 4 ≥ 134.7 ng/ml	p-trend
Total Cholesterol (mg/dl)	0.00 (reference)	6.97 (2.54, 11.40)	10.25 (6.68, 13.81)	17.11 (12.68, 21.53)	<0.001
LDL Cholesterol (mg/dl)	0.00 (reference)	4.12 (-0.13, 8.37)	7.41 (3.60, 11.21)	10.56 (6.77, 14.35)	<0.001
HDL Cholesterol (mg/dl)	0.00 (reference)	2.10 (0.77, 3.42)	1.69 (0.28, 3.10)	3.76 (2.07, 5.45)	<0.001
LDL / HDL cholesterol	0.00 (reference)	-0.03 (-0.16, 0.10)	0.08 (-0.06, 0.23)	0.10 (-0.03, 0.22)	0.03
Ln TG (ln (mg/dl)) TG: Triglycerides	0.00 (reference)	0.03 (-0.03, 0.09)	0.07 (0.01, 0.13)	0.12 (0.06, 0.17)	<0.001

P114

Relation of 9-Year Body Weight Change to Change in LDL Particle Size in Japanese Men and Women: The INTERMAP Toyama Sudy

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Background: Elevated LDL-cholesterol is an established major risk factor for coronary heart disease (CHD). LDL particle size determined by nuclear magnetic resonance (NMR) spectroscopy may improve CHD prediction beyond risk assessment provided by conventional enzymatically determined lipid levels. There are few longitudinal studies on long-term change in LDL particle size and its related factors. **Methods:** We examined 9-year change of lipoprotein profile in 248 INTERMAP Toyama participants (ages 40–59 years at baseline, 51% women). Lipoprotein profile was determined by NMR spectroscopy (Liposcience, Inc., Raleigh, NC) in 1997 at baseline examination and at 2006 follow-up. Relationships of change in body weight (BW) to change in LDL particle size were analyzed. **Results:** At 9-year follow-up, BMI was significantly increased in men and women ($p<0.05$). Mean LDL size was increased in men (from 21.1 nm to 21.3 nm, $p<0.05$), but not in women. LDL-cholesterol and small LDL concentrations were significantly increased in women ($p<0.001$ and $p<0.01$), but not in men. In univariate analyses, BW change was correlated positively with change in small LDL concentration ($r=0.38$ in men, $p<0.001$; $r=0.20$ in women, $p<0.05$). BW change was correlated inversely with changes in mean LDL particle size in men ($r=-0.30$, $p<0.001$), and tended to be correlated in women ($r=-0.16$, $p=0.068$). In multiple linear regression analyses (adjusted for age, BMI, and LDL particle size at baseline), BW change was associated positively with change in small LDL concentration ($p<0.001$ in men; $p<0.05$ in women) and inversely with change in mean LDL particle size ($p<0.001$ in men; $p<0.05$ in women). **Conclusions:** This 9-year follow-up study in Japanese showed that long-term BW increase was associated with decrease in LDL particle size and increase in small LDL concentration in both men and women. BW gain may not only increase LDL cholesterol level but also worsen quality of LDL.

P115

Associations of Total and High-Density Lipoprotein Cholesterol with the Risk of Coronary Heart Disease and Total and Type-Specific Stroke

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Background: High serum total cholesterol and low high-density lipoprotein cholesterol (HDL) are well-recognized risk factors for coronary heart disease (CHD). However, their relationship to stroke, particularly to type-specific stroke risk, is less well established. Aim: To examine the associations of total and HDL cholesterol with the risk of CHD and total and type-specific stroke. Methods: Study cohorts included 27642 Finnish men and 30501 women who were 25 to 74 years of age and free of CHD and stroke at baseline. Results: During a mean follow-up of 17.9 years, 5386 people developed an incident CHD event and 3431 people developed an incident stroke event (293 subarachnoid hemorrhage, 430 intracerebral hemorrhagic and 2554 ischemic). After adjustment for age, body mass index, systolic blood pressure, smoking, education, physical activity, family history of myocardial infarction or stroke, and history of diabetes, hazard ratios (95% confidence intervals) for one mmol/l increase of total cholesterol were: for CHD events, 1.27 (1.23–1.30) in men and 1.14 (1.10–1.18) in women; for total stroke, 1.06 (1.01–1.10) in men and 1.00 (0.96–1.04) in women; for ischemic stroke, 1.06 (1.02–1.11) in men and 1.02 (0.97–1.06) in women; for intracerebral hemorrhagic stroke, 0.98 (0.87–1.09) in men and 0.88 (0.78–0.99) in women; and for subarachnoidal hemorrhagic stroke, 1.12 (0.97–1.29) in men and 1.02 (0.89–1.16) in women. After adjustment for all confounding factors, hazard ratios for one mmol/l increase of HDL cholesterol were: for CHD events, 0.58 (0.47–0.71) in men and 0.39 (0.30–0.52) in women; for total stroke, 0.87 (0.68–1.11) in men and 0.59 (0.46–0.75) in women; and for ischemic stroke, 0.78 (0.59–1.03) in men and 0.54 (0.41–0.72) in women. Conclusions: There is clear evidence of potential benefits for CHD from a simultaneous reduction in total cholesterol and an increase in HDL cholesterol. Total cholesterol has a mild direct association with the risk of stroke in men. High HDL cholesterol is associated with lower stroke risk particularly in women.

P116

Relation of Long-Term Body Weight Change to HDL Particle Size Change in Japanese Men and Women: The INTERMAP Toyama Study

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Background: Lipoprotein particle size, determined by nuclear magnetic resonance (NMR) spectroscopy, may improve prediction of coronary heart disease (CHD) beyond conventional enzymatically determined lipid levels. Small HDL particle has been reported to play an important role in development of atherosclerosis, but there are few longitudinal studies on change in HDL particles over the years. **Methods:** We examined 9-year changes of lipoprotein profile in 248 INTERMAP Toyama participants (ages 40–59 years at baseline, 51% women). Lipoprotein profile was determined by NMR spectroscopy (Liposcience, Inc., Raleigh, NC) in 1997 at baseline examination and at 2006 follow-up examination. Relationships of change in body weight (BW) to change in HDL particle size were analyzed. **Results:** At 9-year follow-up, significant increase was observed in BMI ($p<0.05$) and small HDL concentration ($p<0.001$) in both sexes. Mean HDL particle size was significantly decreased in both sexes ($p<0.001$). HDL-cholesterol concentration did not significantly change. In univariate analyses, BW change was correlated inversely with change in HDL-cholesterol concentration in women ($r=-0.24$, $p<0.01$), but not in men. BW change was not correlated with change in small HDL concentration, but was correlated inversely with change in mean HDL particle size ($r=-0.43$ in men, $p<0.001$; $r=-0.42$ in women, $p<0.001$). In multiple linear regression analyses (adjusted for age, BMI, and HDL particle size at baseline), BW change was significantly and inversely associated with change in HDL particle size in both sexes ($p<0.001$).**Conclusion:** This long-term follow-up of Japanese showed that BW gain decreases HDL particle size in both sexes. These changes in quality of HDL due to weight gain may affect risk of CHD.

P117

Lipid-Associated Risk Factors for First Acute Myocardial Infarction in 3 Countries with Extreme Differences in Myocardial Infarction Incidence: The FAMI Study

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The FAMI Study is a project of the prevalence of traditional risk factors in subjects who present with their first Acute Myocardial Infarction (AMI). Strict inclusion criteria were hospital admission and blood sample within 6 hours of symptom onset, and no previous history of ischemic heart disease. Patients were enrolled from urban areas of China, Italy and Scotland. These 3 countries were chosen for their extreme difference in AMI incidence, being highest in Scotland, and lowest in China (8-fold difference), with Italy in an intermediate position. A total of 1002 patients and 710 controls were enrolled (431 patients and 328 controls in China, 353 patients and 260 controls in Italy, and 218 patients and 122 controls in Scotland). Blood samples were taken in all patients just prior coronary recanalization and in controls in a fasting condition. All samples were shipped to a core laboratory in Milan for storage in the biobank and measurements. LDL and HDL cholesterol were significantly lower in Chinese than Italians and Scots, in both patients and controls. HDL cholesterol was significantly lower and apoB/apoAI higher in patients than controls in all 3 groups, independently of ethnicity. Triglycerides (TG) and LDL cholesterol were significantly higher in patients than controls in Italians, but not in the Scots or Chinese. In conclusion, HDL cholesterol and apoB/apoAI are strong risk factors for a first acute myocardial infarction, independently of AMI incidence and/or ethnicity. Triglycerides and LDL cholesterol appear to be risk factors for AMI only in some populations. Potential gene-environment interactions contributing to these ethnic differences are now under study.

	Italy		Scotland		China	
	Patients	Controls	Patients	Controls	Patients	Controls
LDL Median (25th-75th percentile)	166.4§ (132.8–209.3)	154.6 (126.5–186.0)	160.8 (124.1–195.6)	153.1 (113.9–180.4)	133.9 (107.3–164.1)	128.2 (100.7–159.6)
HDL Median (25th-75th percentile)	39.6* (32.7–47.1)	46.5 (40.2–53.9)	40.9* (34.5–49.1)	48.6 (41.6–56.1)	37.4* (33.0–44.1)	42.4 (35.8–48.9)
TG Median (25th-75th percentile)	122.6* (82.0–171.7)	105.3 (72.5–141.2)	121.9 (82.3–191.7)	111.9 (75.1–169.2)	128.9 (87.2–188.3)	128.6 (90.7–175.5)
ApoB/ApoAI	1.15* (0.95–1.35)	0.99 (0.85–1.18)	1.15§ (0.92–1.41)	1.01 (0.80–1.22)	1.10* (0.94–1.30)	1.02 (0.85–1.18)

§$p=0.005$; *$p<0.0001$

P118

Assessing Statin Therapy and Lipid Profile Goals 1 Year After Percutaneous Coronary Intervention at a Veterans Hospital

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Background: A significant proportion of patients undergoing percutaneous coronary intervention (PCI) are not receiving statin therapy or achieving guideline-based lipid profiles. The NCEP-ATPIII advises a minimum LDL level < 100 mg/dL in patients with coronary heart disease (CHD). However, research suggests that a further reduction in LDL is more desirable in this population to reduce adverse CHD endpoints. *Methods*: We conducted a retrospective, observational study on all patients undergoing PCI at an urban Veterans Hospital from

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September 2004 to July 2006. Statin use and lipid profiles at 6 and 12 months post-PCI were compared to pre-PCI values. *Results*: A total of 401 unique patients had PCI during the study period. Approximately 72% (286 of 397) of patients were on statins at baseline, which improved to 88% (339 of 387) at 6 months post-PCI ($p = 0.01$), but fell to near baseline frequency at 12 months. LDL and total cholesterol (TC) levels improved significantly at both time points when compared to pre-PCI levels (Table 1). Additionally, the percentage of patients at the NCEP-ATPIII goal of LDL <100 mg/dL increased from 52% (176 of 338) at baseline to 65% (183 of 281; $p < 0.0001$) and 74% (181 of 245; $p = 0.03$) at 6 and 12 months respectively. However, baseline HDL levels did not differ from a pre-PCI mean of 38 ± 14 mg/dL at each follow-up point. *Conclusion*: Despite improvement in both LDL and TC levels at 12 months post-PCI, statin use curiously decreased. This may be due to premature cessation of lipid modifying therapy once LDL goals are reached or patient misunderstanding of the potential benefits of statin use. Increased attentiveness to use of statins in this population and continued vigilance toward optimal lipid levels are important. Table 1

	Pre-PCI	6 months	Difference	p value (6 months v. pre-PCI)	12 months	Difference	p value (12 months v. pre-PCI)
TC (mg/dL)	171 ± 43	159 ± 43	12 ± 43	< 0.001	154 ± 44	17 ± 44	< 0.001
LDL (mg/dL)	104 ± 33	95 ± 33	9 ± 37	< 0.001	90 ± 38	14 ± 38	< 0.001
HDL (mg/dL)	38 ± 14	37 ± 12		p = ns	38 ± 12		p = ns

P119

Long-Chain n-3 Fatty Acids in Blood and Risk of Nonfatal Myocardial Infarction: The Nurses' Health Study

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Background: Few epidemiologic studies have examined the relationship between intake of long-chain n-3 fatty acids of marine origin and risk of non-fatal myocardial infarction (MI). Objective: To assess the hypothesis that high levels of long-chain n-3 fatty acids of marine origin in plasma and erythrocytes are associated with a reduced risk of non-fatal MI among U.S. women. Design: Baseline blood samples were collected from 32,826 participants of the Nurses' Health Study in 1989–1990, among which 146 incident cases of non-fatal MI were identified and ascertained between baseline and 1996 and matched with 327 controls for age, smoking, and fasting status. Results: Plasma content of long-chain n-3 fatty acids (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) significantly correlated with dietary intake of these fatty acids (Spearman correlation coefficient (r) = 0.42) and fish (r = 0.34). Baseline plasma long-chain n-3 fatty acids were associated with a reduced risk of developing non-fatal MI after multivariate adjustment for established and potential confounders. The multivariate relative risks (95% confidence interval (CI)) contrasting the highest quartile of plasma long-chain n-3 fatty acids to the lowest quartile were 0.34 (0.17, 0.68; P for trend < 0.01) for EPA, 0.53 (0.26, 1.07; P for trend = 0.11) for DHA, and 0.49 (0.24, 0.98; P for trend = 0.04) for total long-chain n-3 fatty acids. Plasma long-chain n-3 fatty acids significantly positively correlated with plasma high-density lipoprotein (r = 0.29) and inversely correlated with plasma triacylglycerol (r = -0.29) and inflammatory markers, such as ICAM-1 (r = -0.19) and E-selectin (r = -0.20). Erythrocyte total long-chain n-3 fatty acids were not significantly associated with the risk of non-fatal MI; compared to women in the lowest quartile, women in the highest quartile had a relative risk of 0.86 (95% CI: 0.44, 1.68; P for trend = 0.40). Conclusions: These biomarker data suggested that high concentrations of long-chain n-3 fatty acids of marine origin in plasma, but not erythrocytes, were associated with a lower risk of non-fatal MI among women.

P120

Long-Term Fish Consumption and N-3 Fatty Acid Intake in Relation to Coronary Heart Disease and Sudden Coronary Death: The Zutphen Study

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Background: Prospective cohort and intervention studies have shown that fish consumption lowers the risk of coronary heart disease (CHD) death. However, little is known about the effects of long-term fish consumption on (sudden) coronary death. **Methods and Results:** The impact of recent and long-term fish consumption and eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) intake, the n-3 fatty acids from fish, on (sudden) coronary death was investigated in the Zutphen Study, a cohort of 1,373 men born between 1900 and 1920, and examined repeatedly between 1960 and 2000. Hazard ratios were obtained from time-dependent Cox regression models. The effects of long-term fish consumption and EPA+DHA intake were stronger than the effects of recent intake. Long-term fish consumption -on average 20 grams per day- was strongly and inversely associated with CHD death (HR: 0.52 [95%CI: 0.32–0.82]); however, the strength of the association decreased from age 50 (HR: 0.19) until age 80 (HR: 1.07). For men with a daily EPA+DHA intake from fish below 250 mg -on average 132 mg- compared to no intake, CHD death risk was reduced to the same extent as for men with a daily intake above 250 mg (on average 483 mg; *p* for trend 0.36). Moreover, long-term fatty fish consumption -on average 6 grams per day- lowered the risk of sudden coronary death (HR 0.45 [0.26–0.78]). **Conclusions:** The strength of the association between long-term fish consumption and CHD death decreases with increasing age. Fatty fish consumption lowers sudden coronary death risk. There is no clear dose-response relationship between EPA+DHA intake from fish and (sudden) coronary death.

P121

Trans Fatty Acid Intake and Risk of Sudden Cardiac Death in Women

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Background: Intake of *trans* fat is associated with the development of coronary heart disease (CHD). Recent reports suggest that different *trans* isomers may have varying effects on risk, most notably for risk of sudden cardiac death (SCD). In populations consisting primarily of men, biomarker levels of *trans*-18:2 were directly related to SCD risk, while levels of *trans*-18:1 were inversely related to risk. It is not known whether these relations differ in women, in whom SCD may be a more heterogeneous disorder less strongly associated with CHD. **Methods and results:** We prospectively examined the association between estimated dietary intake of total *trans*, *trans*-18:1 and *trans*-18:2 fat and risk of SCD among 85,889 women from the Nurses' Health Study, free of cancer and CVD in 1980. Diet and lifestyle factors were updated via questionnaires every 2–4 years, beginning in 1980. Over 24 years, we documented 281 SCD events, validated by review of medical records. Median intakes (% total energy) were 1.5% for total *trans*, 1.2% for *trans*-18:1 and 0.2% for *trans*-18:2 isomers. Overall, we found no association between intake of total *trans* fat, *trans*-18:1 or *trans*-18:2 isomers and risk of SCD. Compared to the lowest quintile of intake, the multivariate relative risk (RR) [95% CI] of SCD in the highest quintile was 1.1 (0.7, 1.8) for total *trans*, 1.2 (0.8, 2.0) for *trans*-18:1 and 1.0 (0.6, 1.6) for *trans*-18:2. When women who reported a diagnosis of cardiovascular disease prior to their SCD were examined separately (n=11,982), total *trans* fat was significantly associated with SCD risk (RR for extreme quintiles: 2.6; 95% CI: 1.1, 6.1; P for trend=0.03), while no association was found among women without prior cardiovascular disease (RR: 1.0; 95% CI: 0.6, 1.8). **Conclusions:** In this large prospective cohort of women, there was no association between intake of total *trans* fat, or individual *trans* isomers, and overall SCD risk. However, *trans* fat may be associated with SCD risk among women with underlying atherosclerosis. Given these results and known associations with SCD risk in men, *trans* fat intake may play a greater role in SCD risk among those with underlying atherosclerosis.

P122

Alcohol Consumption and Risk of Heart Failure in Hypertensive Male Physicians

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Background: Heavy alcohol drinking is associated with an increased risk of hypertension, a major risk factor for heart failure. While moderate alcohol consumption has been associated with a lower risk of heart failure in the general population, it is not known whether light-to-moderate drinking confers a lower risk of heart failure among people with hypertension. Methods: We studied prospectively 5,153 participants from the Physicians' Health Study I (mean age 58.1 years, range 39.7–85.8 years) with prevalent hypertension at baseline. Baseline alcohol consumption was self-reported and we used Cox regression to estimate relative risks of heart failure. Results: About 70% of the participants consumed 1–7 drinks per week whereas only 4.3% reported consumption of 8+ drinks per week. After an average follow up of 18.4 years, a total of 478 new heart failure cases occurred in this cohort. Alcohol consumption was inversely associated with incident heart failure. Compared to subjects consuming less than 1 drink per week, hazard ratios (95% confidence interval) for heart failure were 0.89 (0.70–1.12), 0.72 (0.57–0.91), and 0.38 (0.20–0.72) for alcohol consumption of 1–2, 5–7, and 8+ drinks/week, respectively, after adjustment for age, body mass index, smoking, randomization's group, use of multivitamins, vegetable consumption, breakfast cereal, exercise, and history of atrial fibrillation (p for trend <0.001). Similar results were obtained for heart failure with and without antecedent myocardial infarction and among subjects without diabetes mellitus. Conclusions: Our data suggest that light-to-moderate alcohol consumption is associated with a lower risk of heart failure among hypertensive male physicians.

P123

Withdrawn

P124

Dairy Intake and Incident Hypertension: The Rotterdam Study

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Objective - There is growing interest in the role of (low-fat) dairy in the prevention of hypertension. In the present study we explored the association of total dairy, low-fat dairy and whole-fat dairy intake with risk of hypertension in a cohort of older adults. *Methods* - We used data from the Rotterdam Study, a prospective population-based cohort study in 7983 subjects aged ≥55 y in the Netherlands. Dairy consumption was assessed at baseline with a validated food-frequency questionnaire in 5434 subjects. Blood pressure (BP) was measured at baseline and during follow-up. Hypertension was considered present when systolic BP was ≥140 mmHg or diastolic BP ≥90 mmHg, or when anti-hypertensive drugs were used. Data-analysis was based on 2245 subjects with complete dietary and BP data and no hypertension at baseline. We calculated hazard ratios for the association between quartiles of energy-adjusted dairy intake and 2- and 6-year incidence of hypertension. We used Cox proportional hazard

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models with adjustment for age, sex, BMI, smoking, educational level, intake of alcohol, total energy and dietary factors. *Results* - During 2 years follow-up, 664 new cases of hypertension were identified. Hazard ratios (95%-CI) for low-fat dairy in consecutive quartiles were 0.77 (0.62–0.96), 0.79 (0.64–0.98), and 0.72 (0.57–0.89) compared to 1st quartile (p-trend: 0.005). After 6 years of follow-up, 984 subjects suffered from hypertension. Hazard ratios for low-fat dairy intake were 0.86 (0.72–1.04), 0.81 (0.67–0.97), 0.84 (0.70–1.01) respectively (p-trend: 0.006). Sub-group analysis showed that the association was most pronounced in presence of overweight. We found similar results for total dairy, while whole-fat dairy was not associated with a reduced risk of hypertension. *Conclusion* - A high intake of low-fat dairy may reduce the risk of hypertension at older age, especially in the presence of overweight.

P125

Food Intake Patterns, Markers of Hemostasis and Inflammation, and Carotid Artery Atherosclerosis in the Insulin Resistance Atherosclerosis Study

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Markers of hemostasis and inflammation are associated with cardiovascular disease (CVD) development. We aimed to identify food intake patterns that might operate via this pathway to influence progression of carotid artery atherosclerosis. Baseline and 5-year follow-up ultrasound measurements of the common (CCA) and internal carotid artery (ICA) intimal medial thickness (IMT) in 867 middle-aged, non-diabetic adults participating in IRAS were analyzed. Food group intake was ascertained with a food frequency questionnaire at baseline. Reduced rank regression was used to derive a food pattern from linear functions of foods (predictors) that maximized explained variation in PAI-1 and fibrinogen (FBGN), the response variables. Multivariate regression was used to evaluate the relation of the food pattern to IMT at follow-up adjusting for baseline IMT. We identified a food pattern characterized by high intakes of rice & pasta, other vegetables, poultry, meal replacements, wine, and pastry, and low intakes of low fiber bread & cereal, tomato vegetables, cottage cheese, meat, and regular soft drinks. The pattern was inversely associated with PAI-1 and FBGN, explaining 16.1% and 1.3% of the variance, respectively. A 1 standard deviation higher baseline pattern score was associated with a 19.0 μm lower mean absolute CCA IMT at follow-up (p=0.02), adjusted for baseline IMT, age, sex, race, clinic, glucose tolerance, smoking, blood pressure and waist, and also with a 32.8μm lower mean absolute ICA IMT (p=0.05). The percent change in CCA IMT was decreasing across food pattern quartiles (Q): Q1 7.8%, Q2 7.6%, Q3 2.7%, Q4 2.4%. For ICA IMT, the percent change was of larger magnitude and the trend not monotonic (Q1 17.3%; Q2 18.8%; Q3 8.0%; Q4 7.9%). No interactions with obesity, glucose tolerance, sex, or race were observed. Adjustment for insulin sensitivity or secretion, lipid lowering medication or education had no impact. We identified a healthful food pattern that simultaneously affected levels of CVD risk factors and the progression of coronary artery atherosclerosis. Reduced rank regression seems a highly promising technique for food pattern-based research aimed at developing dietary recommendations with strong cardioprotective potential.

P126

A High Menaquinone but Not Phylloquinone Intake Reduces the Incidence of Coronary Heart Disease in Women

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Objective: Vitamin K dependent proteins have been demonstrated to inhibit vascular calcification. Data on the effect of vitamin K intake on coronary heart disease (CHD) risk, however, are scarce. **Methods:** We used data from the Prospect-EPIC cohort consisting of 16,057 women, enrolled between 1993–1997 and aged 49–70 years, who were free of CVD at baseline. Intake of vitamin K and other nutrients was estimated with a food frequency questionnaire. Multivariate Cox proportional hazards models were used to analyse the data. **Results:** After a mean $\pm$ SD follow-up of 8.1 $\pm$ 1.6 years, we identified 480 incident cases of CHD. Mean vitamin K_1 intake was 211.7 $\pm$ 100.3 μg/d and vitamin K_2 intake 29.1 $\pm$ 12.8 μg/d. After adjustment for traditional risk factors and dietary factors, we observed an inverse association between vitamin K_2 and risk of CHD with a Hazard Ratio (HR) of 0.92 [95% CI 0.85–1.00] per μg/d vitamin K_2 intake. This association was mainly due to vitamin K_2 subtypes MK-7, MK-8 and MK-9. Vitamin K_1 intake was not significantly related to CHD. **Conclusions:** A high intake of menoquinones, especially MK-7, MK-8 and MK-9, could protect against CHD. However, more research is necessary to define optimal intake levels of vitamin K intake for the inhibition of vascular calcification.

P127

Adherence to the DASH Diet and Incidence of Heart Failure Among Men

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Introduction: The DASH diet reduces blood pressure, but the effect on incidence of heart failure (HF), a consequence of hypertension, is not known. **Hypothesis:** We assessed the hypothesis that men who adhered to a DASH diet pattern would have reduced incidence of HF. **Methods:** We measured diet using food-frequency questionnaire in 39,071 men 45–79 years of age who did not have a history of HF, myocardial infarction, or diabetes. We constructed a score (possible range 0–10) that measured adherence to 10 food-based DASH diet recommendations. The mean DASH score was 4.9 (range 1.0–9.0, interquartile range 1.34). We followed participants through the Swedish inpatient and cause-of-death registers from January 1, 1998 to December 31, 2004 for HF. We used proportional hazards models with age as the time scale to calculate the relative risk (RR) of first HF event associated with quartiles and an interquartile range increase of the DASH score. The models were adjusted for physical activity, sodium and energy intake, education, family history of myocardial infarction at $<$ 60 years, cigarette smoking, and marital status. **Results:** During 7 years of follow-up, 577 men developed incident HF. An interquartile range increase in DASH score (1.34 units) was associated with a RR of 1.00 (95% CI 0.89–1.12, p = 0.98) (Table). **Conclusions:** We did not find an association between this DASH score and incidence of HF in this population of middle-aged and older men. This may be because the DASH diet does not influence incidence of HF, because of residual confounding, or because the diet score did not reflect long-term adherence to the DASH diet.

RELATIVE RISK OF HF BY QUARTILE OF DASH SCORE AND FOR AN INTERQUARTILE RANGE INCREASE IN DASH SCORE

	Quartile 1 (0.98–4.23)	Quartile 2 (4.24–4.90)	Quartile 3 (4.91–5.5)	Quartile 4 (5.87–9.00)	Interquartile range (1.34 units)	p-value
Cases	171	146	124	136		
Person-years	65,794	65,982	66,299	66,199		
Relative risk (95% CI)	1.00 (reference)	0.92 (0.74–1.16)	0.83 (0.66–1.05)	1.00 (0.79–1.27)	1.00 (0.89–1.12)	0.98

P128

Adherence to the Mediterranean Food Pattern Predicts the Prevalence of Hypertension, Hypercholesterolemia, Diabetes, and Obesity Among Healthy Adults: The Accuracy of the Meddietscore

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Objective. We sought to evaluate the accuracy of a diet score in relation to hypertension, hypercholesterolemia, diabetes and obesity. ***Methods***. A diet score (range 0–55) has been developed that assess adherence to the Mediterranean diet. For the consumption of items presumed to be close to Mediterranean dietary pattern (non-refined cereals, fruits, vegetables, legumes, olive oil, fish, and potatoes) scores 0 to 5 for never, rare, frequent, very frequent, weekly and daily consumption were assigned, while for the consumption of foods presumed to be away from this pattern (red meat and products, poultry and full fat dairy products) scores on a reverse scale were assigned. Positive and negative predictive values, in relation to hypertension, hypercholesterolemia, diabetes and obesity status of the ATTICA study participants' (n=3042, enrolment 2001–02 in Athens metropolitan area, aged 18–89 y) were calculated and the 10-year CHD risk based on Framingham equations was estimated, too. ***Results***. The positive predictive values of the score regarding hypertension, hypercholesterolemia, diabetes and obesity are: 45% (95% CI 43%–48%), 46% (95% CI 44%–49%), 12% (95% CI 11%–14%) and 33% (95% CI 30%–35%), while the negative predictive values are 86% (95% CI 85%–88%), 71% (95% CI 69%–74%), 98% (95% CI 97%–99%) and 97% (95% CI 96%–98%), respectively. Moreover, a 10-units increase in the diet score is associated with 4% lower 10-year CHD risk ($\pm$0.1%, p $<$ 0.001). ***Conclusion***. The proposed Mediterranean diet score may be useful in detecting individuals prone to the development of nutrition - related health conditions and cardiovascular disease.

P129

Can a Lifestyle Intervention for Family Members of Hospitalized Patients with Cardiovascular Disease Improve Dietary Habits?

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Background: Perceived susceptibility to disease may be an important motivation to make lifestyle changes. We tested the hypothesis that a novel lifestyle intervention during a "motivational moment" when a family member is hospitalized with CVD may result in improved dietary habits after 6 weeks, and sought to identify predictors of successful dietary change. **Methods:** Participants randomized to a screening and lifestyle intervention in the NHLBI **F**amily **I**ntervention **T**rial for **H**eart Health (**F.I.T. Heart**) who completed a 6 week follow up (76%, n=189, 49$\pm$ 13 years, 68% female, 34% non-white) were included in this study. Adherence to the Adult Treatment Panel (ATP) III Therapeutic Lifestyle Change (TLC) diet ($<$7% of calories from saturated fat, $<$30% of calories from total fat, and $<$200mg dietary cholesterol/day) was assessed at baseline and 6 weeks using the MEDFICTS dietary assessment tool (score $<$ 40 points = adherent) previously validated in this population. Demographics, traditional risk factors, psychosocial factors, stage of change, acculturation status, perceived susceptibility/health status, and relationship to hospitalized patient were measured systematically and evaluated as potential confounders/predictors of dietary change. Linear regression models were adjusted for age, race/ethnicity, sex, marital status, and education. **Results:**The lifestyle intervention was associated with a significant increase in adherence to the TLC diet from baseline to 6 weeks (53% vs. 79%, p$<$.001). Overall, 77% of participants who received the intervention improved their diet score (p$<$.001). Significant univariate predictors of dietary improvement were: elevated glucose (p=.01) or increased triglycerides (p=.007) at baseline, lower perceived health status (p=.002), and younger age (p=.04); these remained significant predictors after adjusting for confounders. **Conclusions:**A lifestyle intervention targeted to family members of patients with CVD delivered during a "motivational moment" was successful in improving dietary habits after 6 weeks, especially among those with elevated risk factors at baseline and a lower perceived health status, suggesting that timing and targeting of lifestyle interventions may be important factors in their success.

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P130

Coffee Consumption and Coronary Calcification in Elderly People: The Rotterdam Coronary Calcification Study

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Background: Diet and lifestyle play an important role in the development of coronary heart disease (CHD). The role of coffee in the cardiovascular system is not yet clear. We examined whether coffee consumption was related to severe coronary calcification, a strong predictor for CHD morbidity and mortality. **Methods:** The relation coffee consumption with coronary calcification was examined in 1,570 elderly men and women without CHD who participated in the Rotterdam Study. Habitual coffee use was assessed with a semiquantitative food frequency questionnaire. Coronary calcification was detected with electron beam computed tomography. Severe calcification was quantified as an Agatson calcium score >400. Sex-specific odds ratios (ORs) with 95% confidence intervals (95% CI) were obtained by multivariable logistic regression, adjusted for age, smoking, body mass index, education, and intake of energy and alcohol. **Results:** In multivariable analysis, coronary calcification in women was significantly inversely associated both with moderate (>3 to 4 cups) and high (>4 cups) coffee consumption, compared with a daily intake of 3 cups or less (OR=0.41 (95% CI: 0.25–0.65) and OR=0.54 (0.33–0.87), respectively). The association persisted after additional adjustment for intake of tea, fruit, meat, and saturated fat. No significant association was found in men. **Conclusion:** Coffee was inversely associated with coronary calcification in women, whereas in non-smoking men a direct association was observed. Further studies should clarify the role of gender in the relation between coffee and coronary calcification.

P131

Association Between Fish Intake and Systolic and Diastolic Cardiac Function: The Hoorn Study

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Background: Fish consumption is associated with a lower risk of cardiovascular disease. An increased heart rate is an independent risk factor for cardiovascular death, particularly for sudden cardiac death. Less is known about the relationship between fish intake and cardiac function. Objective: To investigate the association between fish intake and heart rate and cardiac function in the population-based Hoorn study. Methods: The Hoorn Study is a cohort study of glucose metabolism in the general population (n=2484), which started in 1989. For the present study we used data from the follow-up examinations of the population-based Hoorn study and patients with type 2 diabetes from the Hoorn Screening Study. The total study population consisted of 755 individuals. Information on the dietary intake of the participants was obtained by a validated food frequency questionnaire. Participants underwent an echocardiogram and an ultrasound examination in 2000. Outcome parameters are heart rate, ejection fraction, peak E and A velocity, E/A ratio and deceleration time E as indicator for cardiac function. We used multiple linear regression analysis to investigate the associations between fish intake as dependent variable versus heart rate and cardiac functions. Results: The proportion of subjects consuming no fish was 13.7%, less than twice per week was 74.0% and twice per week and more fish was 12.3%, respectively. The regression coefficients showed no significant association between fish consumption and heart rate, ejection fraction, peak E and A velocity, E/A ratio or deceleration time E in our study population. Adjustment for potential confounders did not affect the results. Conclusion: the Hoorn study did not confirm the association between fish intake and reduced heart rate. Also, this study did not show that fish consumption might influence systolic and diastolic cardiac function.

P132

Trans Fat Consumption Linked to Aggression

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Background: Trans fats obstruct production of omega-3s, which in turn reduce negative behaviors including aggression. Thus, we hypothesized that trans fat consumption may be linked to negative behaviors. **Goal**: To assess trans fat consumption in relation to adverse behaviors affecting others. **Design**: Cross sectional and prospective observational study. **Subjects**: 945 broadly sampled adult male and females without heart disease or diabetes. **Measures**: Trans fat consumption from the Fred Hutchinson Food Frequency Questionnaire. Behaviors included the Overt Aggression Scale Modified aggression subscale; Life History of Aggression; Conflict Tactics Scale; and single-item subjective measures of impatience and irritability (scaled 0–10). **Analysis**: Linear regression with robust standard errors was used. Potential confounders adjusted included age, sex, education, alcohol and smoking. **Results**: Trans fat consumption was significantly associated with higher scores on each behavioral measure (i.e. more aggression). The relation was more consistent than that of known aggression predictors, and was retained with adjustment for potential confounders. In addition, trans fats prospectively predicted future aggression (on follow-up) after adjusting for baseline aggression. **Implications:** These findings suggest trans fat consumption may help explain the reported relation of expressed anger to heart disease, since trans fats may contribute to both outcomes. If the connection of trans fats to adverse behaviors is causal, adverse consequences of trans fat consumption may extend beyond the person directly exposed, to others with whom they come in contact.

TABLE 1. TRANS FAT CONSUMPTION IS SIGNIFICANTLY LINKED TO AGGRESSION & OTHER ADVERSE BEHAVIORS

Behavioral Variable		Trans Fats Relation to Behavior*	
Variable Name	Mean value (SD)	Coefficient (SE)	P-value
OASMa	2.50 (4.72)	0.296 (0.092)	0.001
CTS	1.08 (1.70)	0.101 (0.031)	0.001
LHA	10.1 (6.93)	0.277 (0.106)	0.009
Impatience	1.87 (2.12)	0.0953 (0.0372)	0.011
Irritability	1.30 (1.83)	0.084 (0.031)	0.007

OASMa = Overt Aggression Scale Modified aggression subscale; CTS = Conflict Tactics Scale; LHA = Life History of Aggression
* In regression adjusted for age, sex, education, alcohol and smoking

P133

Regular and Moderate Alcohol Consumption Improves Quality of Life and Mood in Older Men and Women: The Rancho Bernardo Study

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Objective: This study examines the effects of light and moderate alcohol intake on health-related quality of life in community-dwelling older men and women. **Methods:** Information on alcohol intake and measures of quality of life were obtained from 1594 participants (n=633 men, n=961 women) aged 50–97 years at a clinic visit between 1992 and 1996 and from yearly mailed questionnaires. Quality of life measures included the Medical Outcomes Study Short Form, Quality of Well Being scale, Life Satisfaction Index-Z scale, and Satisfaction With Life scale. Men and women were stratified into 4 groups based on alcohol intake: abstainer, light drinker (intake <3 wk), moderate drinker (intake ≥3 times but <170g/wk), and regular drinker (intake ≥ 3 times and ≥170g/week). **Results:** Average age was 72 (±10) years in both men and women. Drinking alcohol at least 3 times per week was reported by 54% of men and 40% of women; 18% of the men and 7.5% of the women were considered regular drinkers. In age-adjusted analyses, frequency of alcohol use was associated with better quality of life on 3 of 4 quality of life measures in men, and in all 4 measures in women. Adjustments for known confounders including age, physical activity, smoking, and major chronic diseases including diabetes, hypertension and CVD yielded similar results. Regression analyses showed an independent association between alcohol intake and measures of quality of life. The association was linear for some scales and inversed J-shaped for others, suggesting a ceiling effect. **Conclusions:** Regular and moderate alcohol consumption is associated with an increased quality of life in older men and women.

P134

Adding Weight Status to Cardiovascular Risk Factor Presence in 50- to 59-Year-Old Women Can Help Delineate Coronary Heart Disease Risk in White and Black Women

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Obective: To examine how body weight, hypertension, diabetes and smoking contribute to coronary heart disease (CHD) incidence in White and Black US women aged 50–59 at entry to the WHI (n=49,159; 11% Black). **Methods:** We examined incidence rates of CHD over approximately 8 years in White and Black participants of the Women's Health Initiative (WHI) Observational Study (OS) or Randomized Control Trial (RCT) cohorts (n=1131 incident CHD events). We compared incidence rates by race and risk factor combinations. **Results:** Among women without diabetes, hypertension or smoking history, CHD incidence per 10,000 person-years was extremely low, but increased markedly with weight category (8.49 for 18.5–24. kg/m^2; 13.45 for 25.0–29.9 kg/m^2; 18.77 for 30.0–34.9 kg/m^2; 19.56 for 35.0–39.9 kg/m^2; 27.18 for ≥40 kg/m^2). Likewise, for each weight category, incidence generally increased with the accumulation of baseline CHD risk factors (e.g., incidence for class II obesity women rose from 19.56 to 29.58 with ever smoking; 46.03 with hypertension and ever smoking; and 168.21 with hypertension, ever smoking, and diabetes. Overall, for each weight category, and within each combination of risk factors, CHD incidence was similar for White and for Black women. Similar patterns were seen when the OS women were analyzed separately from those of the RCT, and when RCT women were stratified by hormone treatment arm, placebo or active therapy or diet arms. Both Black and White women with normal body weight and no hypertension, smoking, or diabetes (15% of the sample) had very low risk of CHD (8.49/10,000 person years). Incidence increased by approximately 15-fold for those with diabetes, smoking history and hypertension (1% of the sample; 127.40/10,000 person-years). **Conclusions:** Among 50–59 year old women, in whom the optimal approach for cardiovascular prevention is controversial, body size and traditional CHD risk factors delineate large differentials in CHD risk. Differential distribution of CHD risk factors accounted for most of the racial difference in CHD risk in this group. Focusing on diagnosis and treatment of these preventable risk factors can reduce women's cardiovascular risk, and help eliminate racial disparities in CHD incidence.

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P135

Association of Pericardial Fat and Visceral Abdominal Fat Volumes with the Prevalence of Cardiovascular Disease: The Framingham Heart Study

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Background: Pericardial fat (PF) and visceral abdominal fat (VAT) are correlated with multiple measures of adiposity, risk factors for cardiovascular disease (CVD), and coronary calcification. We tested the association of PF and VAT with the prevalence of CVD. **Methods:** Participants from the offspring cohort of Framingham Heart Study (n=1314, mean age 59.7 years, 52.6% women, 12.1% with prevalent CVD) underwent abdominal and chest multi-detector computed tomography to quantify the volumes of PF and VAT. PF was defined as the amount of fat inside the pericardial sac, VAT as the amount of fat inside the abdominal muscular wall. CVD was defined as myocardial infarction, angina pectoris, congestive heart failure, stroke, or intermittent claudication. In multivariable analyses, the association of PF and VAT with prevalence of CVD was adjusted for age and sex; BMI and WC; traditional CVD risk factors (systolic blood pressure, hypertension treatment, total cholesterol/HDL, lipid lowering therapy, diabetes, smoking) and alcohol use, menopausal status, and hormone replacement therapy; and finally for VAT. **Results:** Per one standard deviation (SD) increase in fat depot, PF was associated with a 33% increased OR of CVD in age-sex adjusted models and VAT was associated with a 37% increased OR (Table). The association of PF with CVD remained after further adjustment for BMI and WC, but not after accounting for traditional CVD risk factors or VAT. **Conclusion:** Both PF and VAT are associated with CVD independent of age, sex, and conventional measures of obesity. Whether both PF and VAT are independent predictors of future CVD events remains to be determined.

TABLE 1: ASSOCIATION OF PERICARDIAL FAT AND VISCERAL ABDOMINAL FAT WITH THE PREVALENCE OF CVD

	Pericardial Fat		VAT	
Model	OR for CVD, 95% CI for 1 SD change	p-value	OR for CVD, 95% CI for 1 SD change	p-value
+ Age and Sex	1.33 (1.13,1.56)	0.0005	1.37 (1.15,1.64)	0.0005
+ BMI and WC	1.34 (1.12, 1.60)	0.001	1.52 (1.19, 1.96)	0.0008
+ BMI, WC, Risk Factors	1.18 (0.97, 1.43)	0.10	1.27 (0.97, 1.65)	0.0779
+ BMI, WC, Risk Factors + VAT	1.11 (0.88, 1.38)	0.38	—	—

P136

Comparison of Body Mass Index and Waist Circumference in Predicting Risk of Coronary Heart Disease: A Prospective Study Among Men and Women

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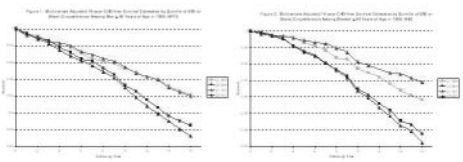
We sought to compare the CHD risk associated with excess weight as assessed by BMI (body mass index) or WC (waist circumference), among men in the Health Professionals Follow-up Study (N = 27,859; 40–75 years old at baseline) and women in the Nurses' Health Study (N = 41,548; 40–65 years old in 1986), using 16 years of follow-up data from 1988 to 2004. We excluded participants at baseline in 1986 with known heart disease, stroke or cancer. A total of 1,823 incident cases of CHD were confirmed among the 27,859 men, and 1,179 among the 41,548 women. Both BMI and WC were strongly and positively associated with CHD risk. Below age 60, using extreme quintiles and multivariate-adjusted proportional hazard models, neither anthropometric measure consistently outperformed the other in predicting CHD risk. Among those aged 60 and above, methods which assessed added predictive ability suggested that WC incrementally predicted CHD risk better than did BMI, as visually depicted in Figure 1 (men) and Figure 2 (women). Further, our results suggest elevated risk of CHD evident within the WHO healthy reference range of < 94.0 cm (men) and < 80.0 cm (women). Compared to men with a WC < 84.0 cm, those with WC of 84.0 to 93.9 cm had a RR of CHD of 1.39 (95% CI 1.11 - 1.74). Compared to women with WC < 71.0 cm, the RR was 1.52 (95% CI 1.22 - 1.88) among those with WC of 71.0 to 79.9 cm. In our cohorts, waist circumference predicted CHD risk better than did BMI in men and women aged 60 years and older. We report evidence that lower WC thresholds may be useful to identify those at increased risk of developing CHD. The findings have broad implications in terms of CHD risk assessment in both clinical practice and epidemiologic studies.



P137

Cross-sectional vs Prospective Associations of Sleep Duration with Changes in Relative Weight and Body Fat Distribution: The Whitehall II Study

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A cross-sectional relation between short sleep and obesity has not been confirmed prospectively. We examined the relationship between sleep duration and changes in body mass index (BMI) and waist circumference using the Whitehall II study, a prospective cohort of 10,308 white-collar British civil servants aged 35–55 in 1985–88. Data were gathered in 1997–9 and 2003–4. Sleep duration and other covariates were assessed. Changes in BMI and waist circumference were assessed between the two phases. The incidence of obesity (BMI≥30 kg/m^2) was assessed among non-obese participants at baseline. In cross-sectional analyses (n=5,021), there were significant, inverse associations ($p<0.001$) between duration of sleep and both BMI and waist circumference. Compared to 7h sleep short duration of sleep (≤5h) was associated with higher BMI ($\beta=+0.82$ units; 95% CI 0.38 to 1.26) and waist circumference ($\beta=+1.88$ cm; 0.64 to 3.12), and with an increased risk of obesity (OR_{adj} 1.65; 1.22 to 2.24). In prospective analyses, short duration of sleep was not associated with significant changes in BMI ($\beta=-0.06$; −0.26 to 0.14) or waist circumference ($\beta=+0.44$; −0.23 to 1.12), nor with the incidence of obesity (OR_{adj} 1.05; 0.60 to 1.82). There is no temporal relationship between short duration of sleep and future changes in measures of body weight and central adiposity.

P138

Nonsubcutaneous Adiposity and Relation to Metabolic Abnormalities: The Multi-Ethnic Study of Atherosclerosis

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Background: We examined the cross-sectional association of non-subcutaneous adiposity with metabolic abnormalities. **Methods:** In the Multi-Ethnic Study of Atherosclerosis, we measured pericardial fat, abdominal visceral fat, liver attenuation and intermuscular fat in 398 white and black individuals (47% men and 43% black), age 47–86 years, selected from Forsyth County, NC during 2002–2005, by CT. An index of non-subcutaneous fat was created by summing the z-scores of the 4 depots. **Results:** In separate logistic regression models, the non-subcutaneous fat index and abdominal subcutaneous fat were associated with metabolic abnormalities (Table 1). However, when both were included in the same models, the index, but not abdominal subcutaneous fat, remained associated with high triglycerides (OR (95% CI): 2.38 (1.7, 3.3) vs 0.85 (0.6, 1.1)), low HDL cholesterol (1.60 (1.2, 2.2) vs 0.93 (0.7, 1.2), high blood pressure (1.75 (1.3, 2.4) vs 1.13 (0.8, 1.5)) and high blood glucose (2.01 (1.5, 2.7) vs 1.01 (0.8, 1.3)). In linear regression analyses, the associations between fat measures and metabolic abnormalities showed similar patterns after excluding users of relevant medications. The relations did not differ by gender or ethnicity. **Conclusion:** Both non-subcutaneous and subcutaneous adiposity correlated with metabolic abnormalities, but only the former remained significant after controlling for both in same model.

Table 1

	OR (95% CI)			
	High triglycerides*	Low HDL cholesterol*	High blood pressure*	High blood glucose*
Model 1‡				
Non-subcutaneous fat index†, 2.9	2.16 (1.7, 2.8)	1.53 (1.2, 2.0)	1.87 (1.4, 2.5)	2.02 (1.6, 2.6)
Model 2§				
Abdominal subcutaneous fat†, 220 mm^2	1.34 (1.1, 1.7)	1.20 (1.0, 1.5)	1.53 (1.2, 2.0)	1.47 (1.2, 1.9)
Model 3#				
Non-subcutaneous fat index†, 2.9	2.38 (1.7, 3.3)	1.60 (1.2, 2.2)	1.75 (1.3, 2.4)	2.01 (1.5, 2.7)
Abdominal subcutaneous fat†, 220 mm^2	0.85 (0.6, 1.1)	0.93 (0.7, 1.2)	1.13 (0.8, 1.5)	1.01 (0.8, 1.3)

* High triglycerides was defined as serum triglycerides level of 150 mg/dl or greater or on cholesterol-lowering medication, Low HDL cholesterol was defined as HDL cholesterol level less than 40 mg/dl in men and 50 mg/dl in women or on cholesterol-lowering medication, High blood pressure was defined as blood pressure of 130/85 mm Hg or greater or on medication for hypertension, and High blood glucose was defined as serum fasting glucose level of 100 mg/dl or more or on medication for diabetes
† Per standard deviation
‡ Including non-subcutaneous fat index, age, gender, ethnicity, height, smoking status, and alcohol drinking status
§ Including abdominal subcutaneous fat, age, gender, ethnicity, height, smoking status, and alcohol drinking status
# Including non-subcutaneous fat index, abdominal subcutaneous fat, age, gender, ethnicity, height, smoking status, and alcohol drinking status

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P139

Predictors of Weight Change in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Background: The prevalence of overweight and obese adults has increased 2–3 fold in the US over the past 2 decades. We identified factors associated with weight gain in MESA. Methods: MESA is a prospective cohort study of 6814 participants age 45–85 free of cardiovascular disease (CVD) at baseline, including 4 ethnicities. Baseline data were collected from 7/00–7/02, with Exam 2 followup from 7/02–1/04 and Exam 3 1/ 04–7/05. Multiple logistic regression was used to look at predictors associated with weight gain ≥10 pounds from baseline to exam 3. Models were performed both including and excluding baseline weight. When exam 3 data were not available, exam 2 was used. Results and Conclusion: Of the 5972 participants with available data, 1414 (24%) gained ≥10 pounds. In univariate analysis, compared to Caucasians, Blacks were more likely to have significant weight gain (OR 1.3, p<0.001) and Chinese were less likely (OR 0.75, p=0.009). The multivariable adjusted characteristics associated with weight gain are listed in Table 1. There were no race-socioeconomic interactions. Results were similar when adjusted for baseline weight, except female sex was associated with weight gain (OR 1.22, p=0.008). The OR associated with baseline weight was 1.47 per SD, p<0.001. Recommended lifestyle factors, including a healthy diet and greater physical activity, were associated with protection against weight gain. Participants with hypertension and diabetes, conditions where weight loss is generally recommended, were at increased risk for weight gain. These findings emphasize the importance of developing effective public health interventions to curb the obesity epidemic, especially in those at greatest CVD risk.

BASELINE POPULATION CHARACTERISTICS INDEPENDENTLY ASSOCIATED WITH WEIGHT GAIN ≥ 10 POUNDS (ADJUSTED FOR ALL OTHER FACTORS IN THE TABLE)

Risk Factor	Odds Ratio	95% CI
Age (per 10 years)	1.11	1.03–1.19*
Male	0.96	0.83–1.10
Race (Chinese)$	0.66	0.52–0.83*
Race (Black)$	1.08	0.92–1.26
Race (Hispanic)$	0.71	0.59–0.87*
Hypertension%	1.30	1.13–1.48*
Diabetes#	1.37	1.15–1.62*
Total cholesterol (mg/dl per SD)	1.04	0.97–1.11
HDL (mg/dl per SD)	0.92	0.86–0.99*
Smoking, current	1.14	0.94–1.38
Physical activity (Moderate to vigorous in METs/min/week)&	0.92	0.87–0.98*
Healthy diet score@ (servings per SD)	0.91	0.85–0.97*
Marital status (married)	1.08	0.94–1.25
Education&	0.94	0.88–1.01
Income&	0.93	0.87–0.99*

* p-value < 0.05 $Compared to Caucasians as reference % BP >=140/90 and/or on anti-hypertensive medications # fasting glucose >=126 mg/dl and/or on diabetic medications & compared per quartile with lowest quartile as reference @ servings per day of sum of fruits, vegetables, seeds/nuts, whole grains, fish minus sum of high fat dairy, desserts, red and processed meat, and sodas.

P140

A Metabonomic Approach to Exploring the Microbiome Map of Obesity in American Population Samples: The INTERMAP Study

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Background: There are increasing numbers of theories on the contributors to obesity that go beyond the accepted increased food intake and reduced physical exercise concepts. One recently put forward is the microbial theory of obesity. The composition of the intestinal microbiome has been shown to vary significantly with obesity in both animals and humans. Metabonomic exposure studies of germ free rats to mammalian microflora have enabled the identification of the metabolic signatures for the intestinal microbiome. A similar approach was therefore used to generate urinary metabolic profiles of normal weight and obese participants for samples of the American population, including mapping microbial co-metabolites. Methods: American participants from the population based INTERMAP Study, an international study on macronutrients and blood pressure, conducted in 1996–9, men and women ages 40–59 years, 4 in-depth 24-hour dietary recalls, 2 timed 24-hour urine specimens, data on multiple possible confounders; metabolic profiling by proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy on urinary samples for 531 normal weight (BMI 18.5–24.9 kg/m^2) and 673 obese (BMI ≥ 30kg/m^2) participants. Results: Multivariate statistical analysis of the NMR data revealed differences between normal weight, obese and diabetic individuals. To enable a more targeted assessment of the relation of gut microbiome to human weight, Students t tests were performed on the 3 most prominent microbial metabolites in the human urinary spectra. Significantly (P<0.0025) lower 4-cresol sulphate, phenylacetylglutamine and hippurate were observed among obese compared with normal weight people, suggesting that colonic balance of protein putrefaction is lower in obese individuals. Conclusion: Findings lend support to a microbial role in obesity and may be relevant for public health strategies for obesity prevention and control.

P141

Body Mass Index and Risk of Intermittent Claudication

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Objective: Given that higher levels of baseline body mass index (BMI) are associated with a higher risk of CVD, we sought to further define the relationship between BMI and intermittent claudication (IC), a symptom of peripheral arterial disease (PAD). **Methods:** We used a prospective cohort study consisting of 20,917 apparently healthy U.S. male physicians participating in the Physicians' Health Study. At baseline, participants had no known PAD or other CVD. We used Cox Proportional Hazards models to calculate hazard ratios (HRs) and 95% Confidence Intervals (CIs) to evaluate the association between baseline BMI and risk of incident IC using age-adjusted and multivariable-adjusted models. Using WHO criteria, we categorized our cohort by baseline BMI into normal weight (18.5–25.0 kg/m^2), overweight (25–30 kg/m^2) and obese (≥30 kg/m^2). Our multivariable-adjusted model included baseline age, exercise, smoking, alcohol use, and parental history of early myocardial infarction. In a supplementary multivariable model, we further adjusted for three potential mediators: history of diabetes, hypertension and/or hypercholesterolemia. **Findings:** During a median follow-up of 22.0±5.1 years, there were 744 incident IC events. For each one unit higher of baseline BMI, there was an increased risk of incident IC in the age-adjusted (HR=1.07; 95% CI, 1.04 -1.09) and multivariable-adjusted models (HR=1.05, 95% CI 1.03–1.08). Further adjustment for potential mediators slightly attenuated the risk (HR=1.03, 95% CI, 1.01–1.06). Compared to those with a normal BMI, the multivariable-adjusted HRs for overweight and obese men were 1.30 (95% CI, 1.12–1.51) and 1.58 (95% CI, 1.13–2.20) (P, trend<0.01). Further adjustment attenuated the HRs to 1.21 (95% CI, 1.04–1.41) and 1.29 (95% CI, 0.93–1.81) (P, trend <0.01). Among never-smokers, the multivariable-adjusted HRs for overweight and obese men were 1.54 (95% CI, 1.18–2.01) and 2.56 (95% CI, 1.49–4.40). **Conclusions:** In a large cohort of male physicians, a higher baseline BMI was significantly associated with an increased risk of IC. The relationship was modestly attenuated by multivariable adjustment and potential mediators but remained significant, with the highest risk observed among men who had never smoked.

P142

Do the Relations Between Body Mass Index and Cardiovascular Disease Risk Factors Differ by Race?Comparisons Between the NHLBI Jackson Heart Study and Framingham Heart Study

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Background The epidemic of obesity is especially pronounced among African Americans (AA). Data from the Jackson Heart Study (JHS) and the Framingham Heart Study (FHS) were compared to assess the influence of obesity on cardiovascular disease (CVD) risk factors (RF) by race. Methods Participants in the 1st JHS exam (2002–2004) and the FHS 7th "offspring" (1998–2001) and 1st "third generation" (2002–2005) exams, aged 35–74, with BMI > 18.5 kg/m2, and free of CVD were pooled for analysis. Presence of lipid abnormalities, hypertension, or diabetes was defined based on commonly used criteria (NCEP/ATP3, JNC7, and ADA 2004). Relations of BMI to risk factor prevalence were assessed using logistic regression models adjusting for sex, age, race, smoking, and education. Tests for BMI interaction with race were performed. Results Overall, 4161 JHS (mean age 54 years, 65% women) and 5269 FHS (mean age 51 years, 54% women) participants were available for analysis. The prevalence of overweight, Stage 1, and Stage >2 obesity was 32.6%, 27.3%, and 26.7% in JHS and 39.0%, 17.5%, and 9.8% in FHS. Prevalence of all risk factors except high triglycerides was substantially higher in the JHS (p<0.0001). Increasing BMI was associated with increasing prevalence of most CVD risk factors within each race. For most risk factors, stronger relations with BMI were observed in FHS than in JHS. Conclusion Although the prevalence of obesity and most risk factors was higher in JHS compared to FHS, there were larger proportional increases in risk factor prevalence with increasing BMI in FHS than in JHS. BMI may be a better marker in European Americans for major metabolic abnormalities than in African Americans.

	Prev.			Prev.			Race
	%	OR*	P-Value	%	OR*	P-Value	Interaction
Age 35–54	**Jackson**			**Framingham**			
Diabetes	9%	1.90	<0.0001	3%	3.00	<0.0001	0.001
Hypertension	42%	1.57	<0.0001	20%	2.01	<0.0001	<0.0001
High LDL	23%	1.10	0.181	16%	1.34	<0.0001	0.006
High TG	19%	1.32	<0.0001	28%	1.79	<0.0001	<0.0001
Low LDL	37%	1.48	<0.0001	27%	1.81	<0.0001	0.001
Age 55–74	**Jackson**			**Framingham**			
Diabetes	21%	1.57	<0.0001	11%	2.19	0.000	0.001
Hypertension	74%	1.22	0.012	48%	1.45	0.000	0.029
High LDL	36%	1.01	0.929	32%	1.29	0.001	0.001
High TG	33%	1.25	0.003	45%	1.66	0.000	<0.0001
Low HDL	32%	1.38	<0.0001	31%	1.56	0.000	0.104

*Odds ratio per increase in BMI category

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P143

Waist Circumference Does Not Differentially Detect Visceral Adipose Tissue

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Background Waist circumference (WC), an easily-obtainable measure of central obesity, is a key component of the metabolic syndrome. However, the ability of WC to measure visceral adipose tissue (VAT) preferentially to abdominal subcutaneous adipose tissue (SAT) has not been assessed in a large community-based sample. **Methods** Computerized tomography and clinical anthropometric measures from 893 women (mean age 46 years, mean WC 91 cm) and 1091 men (mean age 44 years, mean WC 99 cm) in the Framingham Heart Study Third Generation cohort (examination date 2002–2005) were used for this analysis. WC was measured at the umbilical level. **Results** Mean VAT was 1134 cm^3 in women (mean SAT, 3010 cm^3) and 1992 cm^3 in men (mean SAT, 2599 cm^3). WC was more correlated with SAT than VAT in women (0.917 for SAT vs. 0.837 for VAT) and men (0.904 for SAT vs. 0.779 for VAT) with $p < 0.001$ for SAT vs. VAT comparisons. When the independent contributions of VAT and SAT to WC after adjustment for age are compared (Table), SAT has a higher independent correlation with WC (higher partial R^2) in both men and women. Additionally, in men, the change in WC is higher for a 500 cm^3 increase in SAT than a 500 cm^3 increase in VAT ($p < 0.001$). In women the change is statistically indistinguishable ($p = 0.79$). **Conclusion** Both VAT and SAT are correlated with and contribute to WC. However, SAT has a higher correlation with WC in men and women and after adjustment for age and VAT. In men, SAT also has a larger absolute effect on change in WC. This suggests that WC may be an imperfect proxy for directly measured VAT.

MULTIVARIABLE COMPARISON OF THE CONTRIBUTION OF VAT AND SAT TO WC IN MEN AND WOMEN, ADJUSTED FOR AGE

	Increase in cm of WC (95% CI)	p-value of SAT vs VAT*	Adjusted R^2
Women			
VAT (500 cm^3)	3.3 (2.9, 3.7)		0.221
SAT (500 cm^3)	3.3 (3.2, 3.5)	0.79	0.588
Men			
VAT (500 cm^3)	2.4 (2.2, 2.6)		0.438
SAT (500 cm^3)	3.3 (3.2, 3.4)	<0.0001	0.758

* F-test for comparability of standardized coefficients to measure whether the change in WC due to VAT is equal to the change due to SAT

P144

Alcohol Consumption and the Risk of Becoming Overweight or Obese in Middle-Aged and Older Women

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Background Light-to-moderate alcohol consumption is associated with a lower risk of many adverse health outcomes. However, study results on alcohol consumption and the long-term risk of becoming overweight or obese have been limited and inconsistent.***Objective*** We investigated the association of alcohol consumption with the risk of becoming overweight or obese in a prospective cohort of US women aged ≥45 years, of normal weight (body mass index (BMI) calculated from self-reported height and weight: 18.5-<25 kg/m^2), and free of cardiovascular disease, cancer, and diabetes at baseline.***Methods*** Usual alcoholic beverage consumption in the preceding year was collected on baseline questionnaire. Based on self-reported weight from annual follow-up questionnaires, we calculated BMI during cohort follow up and defined incident overweight/obesity as the occurrence of new onset BMI of ≥25 kg/m^2.***Results*** Among 19,090 initially normal weight women, a total of 7423 became overweight or obese in 10 years. After adjusting for age, race, and baseline BMI, the relative risks (RRs) [95% confidence interval] of becoming overweight or obese across increasing levels of total alcohol consumption (0, >0-<5, 5-<15, 15-<30, and ≥30 g/day) were 1.00 (reference), 0.97 [0.91–1.02], 0.90 [0.85–0.96], 0.79 [0.71–0.88], and 0.78 [0.67–0.91] respectively (p for trend: <0.0001). The inverse association remained significant after further adjusting for total energy intake, physical activity, smoking, and other lifestyle, clinical, and dietary factors (multivariate RR for total alcohol consumption of ≥30 g/day versus 0 g/day: 0.73 [0.62–0.87], p for trend: <0.0001). The association appeared to be stronger for women with lower baseline levels of BMI. Greater alcohol consumption was also significantly associated with smaller weight gain in 10 years. Heavy alcohol consumption of ≥40 g/day was not associated with the risk of becoming overweight or obese (multivariate RR: 0.80 [0.62–1.04]). *Conclusions:* Light-to-moderate alcohol consumption was associated with a lower risk of becoming overweight or obese during a period of 10 years in middle-aged and older women. The mechanisms underlying these findings remain unclear.

P145

Overweight, Obesity, and Incidence of Heart Failure

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Introduction: Overweight and obesity have been associated with left ventricular hypertrophy, increased aortic stiffness, and incidence of heart failure (HF). **Hypothesis:** We assessed the hypothesis that body mass index (BMI) and central adiposity-quantified using waist circumference, waist-hip ratio, and waist-height ratio-are associated with increased risk of HF. **Methods:** Anthropometric measures were self-reported by 37,457 women and 44,365 men without a history of HF. We used Markov chain Monte Carlo multiple imputation to address missing data. We followed participants through the Swedish inpatient and cause-of-death registers from January 1, 1998 to December 31, 2004 for incidence of HF. Relative risks (RR) were calculated using Cox proportional hazards models adjusted for age, education, smoking, alcohol consumption, physical activity, postmenopausal hormone therapy (women only), living alone (women only), marital status (men only), and family history of myocardial infarction. Fractional polynomial models were used to explore the dose-response shape of the associations and to test for nonlinearity. **Results:** Over 7 years of follow-up 522 women and 932 men developed HF. Obesity (BMI ≥ 30 kg/m^2) compared to normal weight (BMI 18.5–24.9 kg/m^2) was associated with a 60% greater risk of developing HF (95% CI 23%–107%) among women and a more than doubled risk among men (RR = 2.30, 95% CI 1.90–2.78). Measures of abdominal obesity were also associated with risk of HF in women and in men. We did not find evidence of nonlinearity in the associations between central adiposity and HF or in the association between BMI and HF among women. Among men, the risk associated with a 1-unit increase in BMI was greater at higher BMI. **Conclusions:** Both BMI and measures of abdominal adiposity appear to increase risk of HF in middle-aged and older women and men.

RELATIVE RISK, 95% CI, AND P-VALUE FOR INCIDENCE OF HF

Women	Body mass index 18.5–24.9 kg/m^2	1.00 (reference)
	Body mass index 25.0–29.9 kg/m^2	1.15 (0.94–1.40), 0.17
	Body mass index ≥ 30.0 kg/m^2	1.60 (1.23–2.07), < 0.001
	Waist circumference < 80.0 cm	1.00 (reference)
	Waist circumference 80.0–87.9 cm	1.15 (0.87–1.52), 0.32
	Waist circumference ≥ 88.0 cm	1.47 (1.16–1.87), 0.002
	Waist-hip ratio < 0.85	1.00 (reference)
	Waist-hip ratio ≥ 0.85	1.35 (1.12–1.63), 0.002
	Waist-height ratio < 0.50	1.00 (reference)
	Waist-height ratio ≥ 0.50	1.24 (1.02–1.50), 0.03
Men	Body mass index 18.5–24.9 kg/m^2	1.00 (reference)
	Body mass index 25.0–29.9 kg/m^2	1.19 (1.02–1.37), 0.02
	Body mass index ≥ 30.0 kg/m^2	2.30 (1.90–2.78), < 0.001
	Waist circumference < 94.0 cm	1.00 (reference)
	Waist circumference 94.0–101.9 cm	1.12 (0.91–1.38), 0.30
	Waist circumference ≥ 102.0 cm	1.75 (1.48–2.06), <0.001
	Waist-hip ratio < 1.00	1.00 (reference)
	Waist-hip ratio ≥ 1.00	1.39 (1.17–1.66), < 0.001
	Waist-height ratio < 0.50	1.00 (reference)
	Waist-height ratio ≥ 0.50	1.33 (1.08–1.63), 0.007

P146

The Role of CRP in Leptin Resistance in Humans: Impact on Obesity in the British Regional Heart Study

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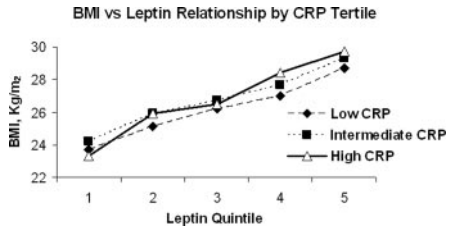
Objective: In cell culture human CRP blocks leptin signalling, and in leptin deficient mice infusion of human CRP blocks weight loss associated with leptin administration. Leptin resistance caused by CRP could have therapeutic implications. Our aim was to establish if CRP influences the relationship between leptin and obesity. **Methods**: In a cross-sectional analysis of 2113 British Regional Heart Study men (mean (SD): age 68 (5.4) years) we assessed the interaction of plasma CRP levels on the relations between leptin and several measures of obesity (mean (SD): BMI 26.5 (3.4) kg/m^2, waist circumference (W) 95.9 (9.7) cm, body fat (%BF) 34.0 (7.8) %, fat mass (FM) 27.4 (9.0) kg). We excluded men with diabetes, coronary disease, cancer, aspirin therapy, or CRP >10 mg/L. CRP and leptin were log transformed for regression analysis. **Results:** Leptin was significantly correlated with CRP (Spearman's r=0.22, p<0.0001). Leptin was more strongly correlated with measures of obesity than CRP (leptin vs CRP: BMI, 0.57 vs 0.22; W, 0.56 vs 0.26; %BF, 0.44 vs 0.22; FM, 0.52 vs 0.22, all p<0.0001). The univariate relationship between BMI and leptin was related to CRP tertile (figure). In age-adjusted linear regression models that included log leptin and log CRP predicting measures of obesity, the interaction term [log leptin x log CRP] was significantly related to BMI (p=0.04), but not to W, %BF or FM (p=0.04, 0.06, 0.13). **Conclusions**: CRP



influences the relationship between leptin and BMI, but not between leptin and other measures of obesity. CRP could have a small but significant role in leptin resistance. Validation particularly in women and in younger individuals in prospective cohorts is required.

P147

The Obesity Paradox: Interaction of Central and Peripheral Obesity on Survival Offers a New Insight

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Introduction Increasing overall obesity, as measured by body mass index (BMI), is paradoxically associated with lower mortality in certain populations (elderly, chronic heart failure,

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chronic kidney disease). We hypothesized that the observed obesity paradox may in part be better understood by measuring body fat distribution in addition to BMI. **Methods** A population-based random sample of 2042 Olmsted County, Minnesota residents, age >=45 was examined. Relative body weight was assessed by BMI, subcutaneous adipose tissue was assessed by skin fold thickness and waist-hip ratio was used as an index of central fat distribution. Relative body weight was classified into 5 groups (BMI <18.5, 18.5–24.9, 25–29.9, 30–34.9 and >=35 kg/m^2). Waist circumference and skin fold thickness quintiles were used. Hazard ratios were determined for five BMI categories and quintiles of WHR and skinfold thickness. A 5-year prospective follow-up was available for all-cause mortality. **Results** Mean age of the population at baseline was 62 years. 'Obesity paradox' was observed with a J shaped relationship between BMI and mortality (see Table). Persons with BMI between 30.0–34.9 had the lowest mortality. In contrast to BMI, skin fold thickness was associated with progressively increasing survival and WHR was associated with worsening survival. **Conclusions** It may be that the interaction of beneficial effect of subcutaneous fat with the harmful effect of a central/abdominal fat distribution on survival is responsible for the apparent obesity paradox. The mechansim(s) by which subcutaneous adipose tissue is more specifically associated with improved survival should be further evaluated.

TABLE. HAZARD RATIOS FOR OBESITY GROUPS*

	Group 1	Grup 2	Group 3	Group 4	Group 5
Overall	4.32	Referent	0.64	0.54	1.15 0.67,
Obesity	1.48,9.96		0.42,0.98	0.31,0.92	1.93 0.60
	0.01		0.04	0.02	
Peripheral	Referent	0.52	0.58	0.32	0.32
Obesity		0.32,0.84	0.35,0.92	0.17,0.55	0.16,0.56
		0.007	0.02	<0.0001	<0.0001
Central	Referent	1.87	2.04	1.74 0.89,	3.15 1.74,
Obesity		0.96,3.77	1.07,4.07	3.52 0.10	6.11
		0.06	0.03		0.0001

*The results are displayed in hazard ratio, 95% CI, p-value

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P148

Cardiovascular Risk Factors and the Metabolic Syndrome in Pediatric Nonalcoholic Fatty Liver Disease

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Background: The association between Non-Alcoholic Fatty Liver Disease (NAFLD) and Cardiovascular Risk Factors in children and adolescents remained incompletely understood. The objective of this study was to examine the association between the presence of NAFLD and multiple cardiovascular risk factors, including metabolic syndrome, among a cohort of severely obesity children and adolescents. **Methods and Results**: This study compared rates of abnormal cardiovascular risk factors in obese children with NAFLD matched with obese control subjects without NAFLD (n=300). The study tested for associations between NAFLD status and clinically abnormal levels of cardiovascular risk factor, while controlling for obesity and insulin resistance. There was no difference in the level of adiposity between cases and controls as measured by mean BMI z-score and mean waist circumference. Children and adolescents with NAFLD had a higher levels of transaminases, (ALT 87 vs. 20 U/L, P<0.001). As compared to obese subjects without NAFLD, those with also had higher levels of a many cardiovascular risk factors, including fasting glucose, insulin, lipid profiles and blood pressure. Multivariate analysis, controlling for age, sex, race/ethnicity, insulin resistance (HOMA) and BMI, showed NAFLD was associated with Hyperlipidemia (LDL ≥ 160mg/dl) OR = 6 (C.I. 1.4–26.3), Hypertension (BP ≥ 130/80) OR = 2.1 (1.2–3.5), and Hypertriglyceridemia (TG ≥ 150 mg/dl) OR =4.9 (2.5–9.4). **Conclusions**: The presence of NAFLD among severely obese youth is strongly associated with a number of cardiovascular risk factors, many of which are above clinically treatable thresholds. NAFLD is a common obesity related co-morbidity, even among youth and may also predispose young adults to premature cardiovascular morbidity and mortality.

P149

Cardiometabolic Biomarkers in Overweight and Obese Young Children: Results from a Large Survey in South-West Germany

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Background: Obesity is associated with substantial metabolic changes and subclinical inflammation. We explored associations between body mass index (BMI) and cardiometabolic biomarkers and their clustering in overweight and obese school children. Methods: A population-based cross-sectional study was carried out among 450 children aged 10 years in South-West Germany. Adiponectin, leptin, inflammatory markers, apolipoproteins (apo) AI and B, and lipoprotein-associated phospholipase A2 (Lp-PLA2) were measured. Except for adiponectin and apoAI (10th percentile), the 90th percentile was used as a cut-off point. Body weight was categorized in age- and sex-specific BMI-percentiles, overweight and obesity according to IOTF definitions. Results: In linear models, all cardiometabolic markers except apoB were statistically significantly associated with overweight. Compared with the reference category (25–75th percentile of BMI) overweight was associated with elevated concentrations of leptin (odds ratio, OR 59.88; 95% CI, 16.68–214.39), C-reactive protein (OR 6.30; 95% CI, 2.95–13.45), fibrinogen (OR 2.82; 95% CI, 1.33–6.01), and low apoAI (OR 2.62, 95% CI, 1.19–5.75). A trend for positive associations with overweight was seen for high interleukin-6, Lp-PLA2, apoB, and low adiponectin concentrations. In obese children, these associations were more pronounced for most cardiometabolic markers. The strengths of the associations clearly increased with increasing percentiles of BMI. Most importantly, in obese children 35% showed one, 20% two, 10% three, and 15% four or more clearly elevated cardiometabolic biomarkers. Conclusions: Overweight and obesity in children are associated with complex metabolic changes and a low grade inflammatory response, and might thus not only accelerate cardiovascular disease later on, but may be associated with the initiation of atherosclerosis early in life

P150

17-Year Longitudinal Changes in Body Weight and Body Mass Index Among African Americans: The Jackson Heart Study/ARIC Study Cohort

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Obesity has reached epidemic proportions. According to a 2006 BRFSS, in the US 25% were obese, 62% were overweight. Mississippi ranked #1 with an overall 31.4% obesity rate. Being morbidly obese is a critical health threat, and confers a high risk for multiple co-morbidities such as cardiovascular disease, hypertension, and diabetes. This study examines changes in body weight and BMI over a 17 year follow-up in the sub-sample (n=1618) of Atherosclerosis Risk in Communities (ARIC) cohort from Jackson, Mississippi which is also part of the Jackson Heart Study (JHS). A summary of selected characteristics by gender is shown in Table 1. For women, 46.9% at ARIC I (baseline) and 56.6% at JHS were obese, and for men, 29.8% and 36.8%, respectively. Among 331 with BMI<25 at ARIC I, 39% and 6% became overweight and obese, respectively after 17 years. Among 621 overweight at ARIC I, 32% became obese. 16% of 1370 who had no diabetes at ARIC I developed diabetes and 61% of 806 who had no hypertension developed hypertension after 17 years. A series of random-effects multilevel analysis adjusted for gender revealed that an estimated average weight at age 45 was 79.5kg with annual increment of 0.33kg. Significantly increasing weight with aging was shown regardless of risk factor status (including diabetes, hypertension and triglyceride levels). However, those with diabetes, hypertension or higher triglyceride levels (>=150mg/dL) had higher weight at age 45 and lower increasing rate than their counterparts. This was observed in both genders. For the CVD risk factor positive group, the lower annual rate change could be attributed to a higher baseline weight value or treatment. Table 1: Change of Selected Characteristics based on a 17-year Follow-up

	ARIC I	*ARIC II*	*ARIC III*	*ARIC IV*	*JHS*
Women (n=1,088)					
Mean, Age (yr)	52.4	55.3	58.3	61.3	66.1
Mean, Weight (kg)	80.9	82.2	83.3	84.4	86.0
BMI (kg/m^2) (%)					
Normal (<25)	18.3	16.0	12.8	11.7	11.7
Overweight (25–30)	34.8	34.1	34.1	32.2	30.7
Obese (>=30)	46.9	49.9	53.1	56.1	57.6
Mean, Abdominal girth (cm)	98.5	100.9	103.4	105.5	101.6
Mean, Triglyceride (mg/dL)	103.6	106.4	111.4	113.7	111.7
Diabetes (%)	13.2	19.9	20.1	23.8	27.3
Hypertension (%)	50.8	50.7	58.9	67.6	80.8
Metabolic Syndrome (%)	24.4	43.1	42.7	48.9	54.0
Men (n=530)					
Mean, Age (yr)	52.7	55.6	58.6	61.5	66.3
Mean, Weight (kg)	87.2	87.8	88.8	89.6	90.8
BMI (kg/m^2) (%)					
Normal (<25)	24.8	24.5	23.4	18.8	19.4
Overweight (25–30)	45.5	45.1	41.8	44.1	43.8
Obese (>=30)	29.8	30.5	34.8	37.1	36.8
Mean, Abdominal girth (cm)	97.0	98.5	99.9	101.3	102.0
Mean, Triglyceride (mg/dL)	117.3	118.1	117.2	116.9	111.5
Diabetes (%)	14.7	19.6	20.4	24.3	25.8
Hypertension (%)	48.3	48.2	55.3	60.1	76.1
Metabolic Syndrome (%)	22.4	29.5	30.1	34.9	36.5

Study period of ARIC I : 1987–1990, ARIC II:1990–1993, ARIC III: 1993–1996, ARIC IV: 1996–1999, JHS:2000–2004

P151

Big Men Have Increased Risk of Atrial Fibrillation Independent of Obesity

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Background: Obesity is a recognized risk factor for atrial fibrillation (AF), partly potentially due to the association between body size and atrial volume. However, other factors that determine body size could be responsible for this association. Methods: Data were derived from a random population sample of 6,903 men (mean age 51.5 years) who underwent a single midlife evaluation as part of the multifactor Swedish Primary Prevention Study in 1970 to 1973 and who were followed until 2004, for a maximum of 34.3 years. Body surface area (BSA) in youth was calculated using the Mosteller formula, entering recalled weight at age 20 (corresponding to the period of 1935 to 1945) and measured height in midlife. AF cases were ascertained through linkage with the Swedish Hospital Discharge register. Results: A total of 1254 men (18.2%) had a hospital discharge diagnosis (principal or secondary) of AF. Body surface area (BSA) at age 20 was strongly related to subsequent AF (p<0.0001), as were midlife body mass index (BMI) and midlife BSA (p<0.0001), and weight gain from age 20 to midlife. In a Cox regression model which adjusted for midlife BMI and other risk factors, hazard ratios (HR) (95% confidence intervals (CI)) for AF for the second, third and fourth quartile of BSA at age 20, compared to the lowest, was 1.42 (95% CI, 1.18 to1.69), 1.58 (95% CI, 1.32 to1.89) and 2.09 (95% CI, 1.73 to 2.53) and for increase in weight from age 20 to midlife of 5 to 15%, 16 to 35% and 35% or more, compared to no weight change, 1.13 (95% CI, 0.93 to1.37), 1.33 (95%

CI, 1.08 to 1.65), and 1.61 (95% CI, 1.18 to 2.20) ($p<0.0001$ for both). Conclusion Large body size in youth, in an era when obesity was rare, as well as weight gain from age 20 to midlife, were both related to development of AF late in life, independently of midlife BMI. Given the current trends not only for obesity but also for height, this may explain the observed increasing occurrence of AF. Further, substantial future increases in the prevalence and incidence of AF are likely.

P152

The Obesity Paradox: A Reality in Acute Coronary Syndromes Patients

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Background: Recent studies have shown a paradoxical relation between body mass index (BMI) and mortality in specific patient populations. Is this also true in acute coronary syndromes (ACS)? Aim: To investigate the association of BMI with in-hospital outcome in an ACS population. Methods: Retrospective analysis of 1603 consecutive patients hospitalized for ACS. Patients were divided into three groups according to BMI: Group A - 18.5–24.9 kg/m^2 (n=478); Group B - 25–30 kg/m^2 (n=751) and Group C - > 30kg/m^2 (n=374). Results: Obese patients were significantly younger, more likely to be male and had consistently worse baseline clinical characteristics, with a higher incidence of hypertension, dyslipidemia, diabetes mellitus (higher HA1c and fasting glucose levels, $p<0.001$), familial and previous history of CAD ($p<0.001$). They were also more previously treated with oral hypoglycemic drugs, insulin and calcium channel blockers ($p<0.001$). They presented more with third degree atrial-ventricular block and had higher TIMI score at admission, higher creatinine clearance and were more often treated with clopidogrel and IIa/IIIb inhibitors; however they had a lower incidence of heart failure. Overweigh and obese patients had a longer hospital stay ($p<0.001$). Surprisingly, group A (normal weigh) had a higher incidence of in-hospital complications and death ($p<0.001$). No differences were found regarding ACS type, myocardial necrosis markers levels and in-hospital treatment. Multivariate analysis showed that predictors of death in this population were female gender, low left ventricular ejection fraction (LVEF) and high Killip class. Conclusion: There is a significant prevalence of overweight and obesity in this ACS population. Although obesity was related to better in-hospital outcome, this was mainly due to differences in gender, LVEF and Killip class. Further studies are warranted to better explain this obesity paradox.

P153

Sex-Specific Association of Regional Body Fat with Mortality in an Older Population: The Rancho Bernardo Study

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Total mortality is known to be high in obese and overweight individuals, however the association between body fat distribution and mortality risk in elderly men and women remains controversial. Evidence suggests that peripheral fat may be atheroprotective, whereas central fat is atherogenic. This study evaluated the sex-specific association of central and peripheral fat mass with all cause and CVD mortality among 934 women and 601 men, ages 50–98 (mean 72) years. Body fat distribution was determined by whole body DEXA scan in 1997–2001, participants were followed for mortality until 2007 (mean 9 years). Overall 532 deaths occurred, 237 were attributed to CVD. Central fat mass was defined as trunk fat mass, peripheral as the sum of fat mass of the arms and legs; percents were calculated by dividing by total body mass. Mean percent central fat mass (%CFM) and peripheral fat mass (%PFM) were higher (both $p<.001$) in women (15% and 18%, respectively) than men (12% and 10%). The risk of all cause and CVD mortality was 2-fold higher for women in the lowest compared to the highest sex-specific tertile of %CFM and %PFM (separate models) before and after adjusting for age, smoking, drinking, exercise, pre-existing diseases, and number of doctor and hospital visits in the past year (Table). Mortality risk was not significantly related to regional fat mass in men. There was a significant interaction of sex by %CFM ($p=.01$), but not %PFM ($p>.10$), in models including both sexes. Exclusion of deaths that occurred during the first 2 years of follow-up, or stratification by age 72, had minimal effect on results. The significant associations in women were modestly reduced by adjustment for 4 year weight change, and were eliminated by adjustment for total body weight. These results suggest that low body fat is a risk factor for death in older women, but not older men. This association was not explained by concurrent illness, whether known or hidden, and was not specific to a particular fat region.

Women			Men		
	All Cause	CVD		All Cause	CVD
% CFM			% CFM		
<13	2.0 (1.4, 2.7)	1.7 (1.1, 2.9)	<11	1.1 (0.8, 1.5)	1.0 (0.6, 1.7)
13–16	1.1 (0.8, 1.6)	1.5 (0.9, 2.4)	11–13	0.9 (0.7, 1.3)	1.0 (0.6, 1.6)
≥17	1.0	1.0	≥14	1.0	1.0
p for trend	*<.001*	*.04*	*p for trend*	*.70*	*.97*
% PFM			% PFM		
<16	1.9 (1.3, 2.6)	1.6 (1.0, 2.7)	<10	1.3 (0.9, 1.8)	1.5 (0.9, 2.5)
17–20	1.2 (0.9, 1.7)	1.1 (0.7, 1.9)	10–11	1.0 (0.7, 1.3)	0.8 (0.4. 1.3)
≥21	1.0	1.0	≥12	1.0	1.0
p for trend	*<.001*	*.04*	*p for trend*	*.18*	*.11*

P154

Burden of Cardiovascular Disease Risk Factors in General and Abdominal Obesity: The Framingham Heart Study

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Background Obesity is associated with an increased risk for cardiovascular disease (CVD)**.** We sought to determine the prevalence, rates of treatment and control of CVD risk factors among normal weight, overweight and obese individuals in a community-based cohort. **Methods** We studied 6801 participants from the Framingham Offspring and Third Generation cohort (mean age 49 years, 54% women), free of CVD, who attended the seventh (1998–2001) or first (2002–2005) examination cycle. Age-and sex-adjusted prevalence of CVD risk factors and their rates of treatment and control were compared among normal weight (BMI 18.5-< 25 kg/m^2), overweight (BMI 25-<30 kg/m^2) and obese (BMI ≥ 30 kg/m^2) participants. **Results** The prevalence of hypertension, elevated low-density lipoprotein cholesterol (LDL-C) levels and diabetes was higher among obese participants as compared to normal weight or overweight participants (p-values <0.001). Obese participants were more likely to receive antihypertensive treatment (62.3%) than normal weight (58.7%) or overweight individuals (59.0%; p=0.002), but no differences in hypertension control were observed (36.7% [normal weight], 37.3% [overweight], and 39.4% [obese]; p=0.48). Rates of lipid-lowering treatment were higher among obese participants (39.5%) as compared to normal weight (34.2%) or overweight participants (36.4%; p=0.02), whereas control rates of elevated LDL-C levels did not differ across BMI categories (26.7% [normal weight], 26.0% [overweight], and 29.2% [obese]; p=0.11). There were no differences in diabetes treatment across BMI groups (69.2% [normal weight], 50.0% [overweight], 55.0% [obese]; p=0.54), but obese participants were less likely to have fasting blood glucose <126 mg/dL (15.7%) as compared to normal weight (30.4%) or overweight (20.7%; p=0.02) participants. **Conclusion** Despite similar or higher treatment rates of CVD risk factors among overweight and obese individuals as compared to normal weight individuals in the Framingham Heart Study, rates of control were similar for the most part. These findings emphasize the importance of prevention, treatment and control of CVD risk factors, especially among individuals with obesity.

P155

Caregiver Perceptions of Childhood Weight Status in Greater Cincinnati

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Objectives: Caregivers' accurate perception of their child's weight status and healthcare providers' ability to effectively notify caregivers about excessive weight gain are important if children at unhealthy levels are to receive adequate weight management strategies. This study determined caregivers' ability to accurately report their child's weight status. The study also explored the effect of weight status and provider interventions on caregiver perceptions and on pursuit of treatment options. Methods: Caregivers (n=633) of children aged two to 17 years were surveyed at 16 pediatric offices and asked to provide best approximations of their child's height and weight, weight treatment history, perceptions about their child's weight, and familiarity with the body mass index (BMI) and area weight treatment programs. The child's height and weight were then measured. Results: Paired t-tests revealed significant differences between caregiver reported and actual weight values (1.90 lbs. [1.27–2.53 95%CI]). Calculated BMI percentiles were underestimated in the 10–13 and 14–17 age categories ($p<.05$). BMI stratified data revealed significant underestimation of calculated compared to actual BMI percentiles in the at risk of overweight (AROW) and overweight categories. Kappa analyses revealed poor agreement between a child in the AROW or overweight BMI categories and having a history of a healthcare provider discussing (.20) or the caregiver seeking (.10) weight management services. Of 186 patients measured as AROW or overweight, 15 (8%) reported feeling their child needed treatment for weight and 34 (18%) reported that the provider told them that their child was gaining weight too fast or was overweight. Conclusions: Caregivers of children two to 17 years old in Greater Cincinnati are inaccurate in reporting their children's weight. Inaccurate calculation of BMI led to inaccurate classification of BMI-related values in older children and in children measured as AROW or overweight. Reliance by provider on caregiver concern alone may result in failure to identify children at risk. In addition, there was weak correlation between being classified in AROW or overweight categories and caregivers' perceived need for weight management services.

P156

Dyslipidemia in Extremely Overweight Adolescents Improves Following Weight Loss with Bariatric Surgery

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Background: Hyperlipidemia is a known cardiovascular risk factor in morbidly obese adults that improves following weight loss surgery. Little is known about changes in this cardiovascular risk factor following adolescent weight loss surgery in extremely overweight youth. **Purpose:** To evaluate serum lipid changes in extremely overweight adolescents before and after weight loss. **Methods**: Adolescents ≤ 19 years old who underwent laparoscopic

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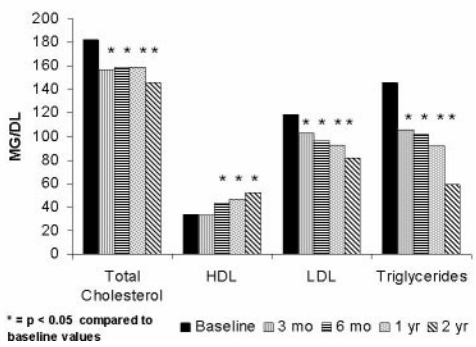
Roux-en-Y gastric bypass surgery with abnormal pre-op (baseline) lipid profiles, and lipids available at 3, 6, 12, and 24 months post-op were evaluated. Inclusion criteria were baseline dyslipidemia as indicated: HDL < 40, or LDL > 130, or triglycerides (TG) > 150. Patients were excluded if they were on anti-lipidemic medications. **Results:** 36 adolescents (avg preop weight 178 ± 23 kgs, age 17 ± 1 year) underwent bariatric surgery. Average weight loss at 2 years was 70 ± 22 kgs (n=13). See Table 1 for complete demographics. Figure 1 depicts the changes in lipids following weight loss at 3, 6, 12, & 24 months. Significant improvements were seen in total cholesterol, HDL, LDL, and triglycerides at nearly all time points. **Conclusions:** Abnormal lipid profiles in extremely overweight adolescents significantly improve following weight loss surgery. Weight loss interventions during adolescence may decrease future cardiovascular risk factors in this population.

DEMOGRAPHICS

	Baseline	3 month	6 month	1 year	2 year
Population (n)	36	22	22	24	13
Age (years)	17 ± 1 (range 13–19)	16 ± 1 (range 13–18)	17 ± 2 (range 14–19)	17 ± 1 (range 13–18)	17 ± 2 (range 13–19)
Gender	25 female 11 male	14 female 8 male	11 female 11 male	16 female 8 male	10 female 3 male
Average weight loss (kgs) from baseline to follow up (p value)	NA	- 38 ± 10 (p < 0.001)	- 50 ± 13 (p < 0.001)	-66 ± 20 (p < 0.001)	- 70 ± 22 (p < 0.001)
Change in BMI from baseline to follow up (p value)	NA	- 13 ± 3 (p < 0.001)	- 15 ± 9 (p < 0.001)	-23 ± 7 (p < 0.001)	- 25 ± 8 (p < 0.001)

Results represent mean ± standard deviations, BMI = body mass index, kgs = kilograms



P157

Exercise Capacity Is Associated with Lower Mortality Risk in Prehypertensive African Americans Compared with Caucasians

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Introduction: Epidemiologic evidence supports an inverse and strong association between fitness status, and mortality in healthy individuals. Pre-hypertensive individuals are at increased risk for cardiovascular events compared to those with normal blood pressure. However, there is no information on the association between exercise capacity and mortality in pre-hypertensive individuals. Furthermore, this relationship has not been reported in African-Americans (AA) and possible racial differences have not been explored. **Methods:** We assessed the association between peak exercise capacity (METs) and all-cause mortality in pre-hypertensive AA (n=1,850; age=54±12) and Caucasians (n=2,885; age=57±12) men at twoVeterans Affairs Medical Centers. We established four fitness categories based on the MET level achieved. Those who achieved <5 METs (n=1,077); 5–7 METs (n=1,726); 7.1 to 10 METs (n=2,203); and > 10 METs (n=1,257). **Results**: Exercise capacity was the strongest predictor of risk for mortality. The adjusted risk for AA was reduced by 18% for every 1-MET increase in exercise capacity (Hazard Ratio= 0.82; CI: 0.77–0.86; p<0.001), and 12% (Hazard Ratio= 0.88; CI: 0.85–0.90; p<0.001) for White. When compared to those who achieved <5 METs, the mortality risk in AA who achieved 5–7 METs, was 30% lower (hazard ratio= 0.70; CI: 0.55–0.88; p<0.001), 63% lower for those who achieved 7.1–10 METs (hazard ratio= 0.37; CI: 0.27–0.50; p<0.001), and 82% lower for those achieving >10 METs (Hazard Ratio= 0.18; CI: 0.10–0.32; p<0.001). In Caucasians, the mortality risk was 55% lower for those who achieved 7.1–10 METs, (hazard ratio= 0.45; CI: 0.35–0.58; p<0.001), and 66% lower for those achieving >10 METs (Hazard Ratio= 0.34; CI: 0.24–0.47; p<0.001). The risk was not lowered in those with who achieved 5–7 METs (hazard ratio= 1.0; CI: 0.8–1.2; p=0.98). **Conclusions:** Exercise capacity is a strong predictor of all-cause mortality in pre-hypertensive individuals. The relationship is stronger for AA than Caucasians with 18% reduction in mortality risk for each 1-MET increase in exercise capacity for AA and 12% for Caucasians. An overall reduction in mortality of 55% to 80% was observed for those with an exercise capacity of >7 METs compared to those who achieved <5 METs.

P158

Weight Regain Is Related to Adaptations in Physical Activity Energy Expenditure During Weight Loss

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Objective: To examine whether adaptations in physical activity energy expenditure (PAEE) (outside of intervention) and resting metabolic rate (RMR) during weight loss were associated with future weight regain in overweight/obese, older women. *Research Methods and Procedures*: Thirty-four overweight/obese (BMI=25–40 kg/m^2), postmenopausal women underwent a 20-week weight loss intervention of hypocaloric diet with or without treadmill walking (weekly caloric deficit was ~2800 kcal), with a subsequent 12-month follow-up. RMR (via indirect calorimetry), PAEE (by RT3 accelerometer) and body composition (by DXA) were measured before and after intervention. Body weight was assessed before and after intervention, and at 6- and 12-month following intervention. *Results*: The intervention resulted in decreases in body weight, lean body mass, fat mass, percent body fat, RMR, and PAEE (all p values < 0.001). Weight regain was 2.9 ± 3.3 kg (-3.1 ~ +9.2 kg) at 6-month and 5.2 ± 5.0 kg (-2.3 ~ +21.7 kg) at 12-month following intervention. The amount of weight regained after 6- and 12-month was associated with decreases in PAEE (-161.0 ± 139.6 kcal/day, -550 ~ +116 kcal/day) during the weight loss intervention (r = -0.521, p = 0.002 and r = -0.404, p = 0.018, respectively), such that women with larger declines in PAEE during weight loss experienced greater weight regain during follow-up. Weight regain was not associated with changes in RMR (-94.6 ± 121.7 kcal/day, -344 ~ +179 kcal/day). *Discussion*: This study demonstrated that both RMR and PAEE decreased during weight loss in postmenopausal women and that women with larger declines in PAEE during weight loss experienced greater weight regain during follow-up. These results suggest maintaining high levels of daily physical activity during weight loss may be important to mitigate weight regain after weight loss.

P159

Physical Activity and Incident Type 2 Diabetes in American Indians: The Strong Heart Study

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Objective: To examine the association between total physical activity (occupational plus leisure-time) and incident diabetes in American Indians. **Methods:** The study population included 1,651 participants in the Strong Heart Study who were free of diabetes, cardiovascular disease, cancer, and emphysema at baseline and participated in at least 1 follow-up exam. Total physical activity (metabolic equivalent task (MET) hrs/week) was estimated at baseline using a validated questionnaire. Incident diabetes was defined based on the 1999 WHO criteria. Discrete Cox models were used to examine the association between physical activity (in tertiles), compared to no physical activity, and incident diabetes, after adjustment for potential confounders. **Results:** During 10 years of follow-up, we identified 454 incident cases of diabetes. Compared with participants who reported no physical activity, those who reported physical activity had a lower risk of diabetes: OR=0.67 (95% CI, 0.46–0.99); OR=0.67 (95% CI, 0.45–0.99) and OR=0.67 (95% CI, 0.45–0.99) for increasing tertile of physical activity, after adjustment for age, sex, site, education, smoking, alcohol use, hours of television viewing per week and family history of diabetes. Further adjustment for BMI and other potential mediators slightly attenuated the risk estimates (Table 1). **Conclusions:** These data suggest that physical activity, compared to physical inactivity, is associated with a lower risk of incident diabetes in American Indians. However, the available data do not show differences in diabetes risk with increasing levels of physical activity. More studies are needed to address this issue.

TABLE 1. ODDS RATIOS (95% CI) OF TYPE II DIABETES ACCORDING TO TOTAL PHYSICAL ACTIVITY CATEGORY

	No Activity	<30 MET hrs/wk (median=12.1)	30–106 MET hrs/wk (median=69.0)	>106 MET hrs/wk (median=165.0)
No. cases	49	136	123	146
Total at risk	130	495	474	552
Age, Site, Sex Adj.	1.00	0.65 (0.44–0.94)	0.63 (0.43–0.93)	0.64 (0.44–0.94)
Multivariate†	1.00	0.67 (0.46–0.99)	0.67 (0.45–0.99)	0.67 (0.45–0.99)
Add. adj for BMI	1.00	0.74 (0.50–1.09)	0.74 (0.49–1.10)	0.71 (0.48–1.07)
Add. adj for mediators ‡	1.00	0.70 (0.46–1.03)	0.72 (0.47–1.08)	0.71 (0.47–1.07)

†Model includes age, site, sex, education (less than high school, high school, post-high school), cigarette smoking (never, ever, current), alcohol use (never, ever, current) television viewing (hrs/wk past year) and family history of type II diabetes. ‡Adjusts for all covariates in "multivariate†", as well as the potential mediators systolic blood pressure, diastolic blood pressure, high density lipoprotein, low density lipoprotein, plasma fibrinogen and BMI as continuous variables.

P160

The Relationship Between Physical Fitness and Body Habitus in School-Age Children: The "Partners for School Health" Program, Cleveland, Ohio

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Background: Partners for School Health (PSH) is a partnership between the American Heart Association Great Rivers Affiliate and the Cleveland Metropolitan School District (CMSD). PSH

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couples an intervention to promote healthier lifestyles with the Cooper Institute's Fitnessgram® assessments (FGAs) at 6-month intervals. FGAs include BMI, progressive aerobic cardiovascular endurance run (PACER), and measures of muscular strength and endurance [push-ups (PU), curl-ups (CU)] and flexibility [sit-and-reach (S&R)]. **Objective:** To determine the relationship between BMI, age, gender and race and ability to perform validated measures of physical fitness in urban school children. **Methods:** FGAs were conducted in 19 CMSD schools. FGA scores fell within a Healthy Fitness Zone (HFZ) or below based on age- and gender-specific standards. BMIs were grouped into <85th, 85th to <95th, or ≥95th percentile. Multiple logistic regression was used to determine adjusted odds ratios (AOR) and 95% CIs for the associations between FGAs and BMI, age, gender, and race. **Results:** Baseline FGAs were performed on 1486 children, aged 9–12 years (49% male, 59% black, 10% white, 8% hispanic, 23% 'other' race). For BMI, 24% were ≥95th and 42% were ≥85th percentile. With respect to fitness, 36% were below the HFZ for PACER, 32% for PU, 21% for CU, and 20% for S&R. As BMI increased, failure to achieve the HFZ increased for PACER (29% to 59%, $p<0.01$, χ^2 test), PU (25% to 47%, $p<0.01$), and CU (18% to 30%, $p<0.01$). There was no difference for S&R. Boys were 9 times more likely to be below the HFZ for PACER (AOR 9.5, 7.2–12.5), while girls were more likely to be below for PU (2.2, 1.7–2.8) and CU (1.4, 1.1–1.8). Increasing age increased the risk of performing below the HFZ for PACER (8.0, 4.1–15.6, age 12 vs 9), PU (2.8, 1.6–5.0), and CU (3.3, 1.8–6.1), but not for S&R. Race did not effect HFZ performance for PACER or PU, but more hispanics were below the HFZ for CU, and blacks for S&R compared to whites. **Conclusions:** In urban school children, BMI, age, and gender have significant impact on the ability to perform specific measures of physical fitness. This may be important for understanding inactivity in overweight children and for designing physical education interventions to improve overall cardiovascular risk profile.

P161

Obesity, Physical Activity, and the Development of Metabolic Syndrome

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To elucidate the impact of weight control and increases in physical activity in the prevention of metabolic syndrome (MetS), we examined the independent and joint prospective relationships between of obesity and physical activity in the development of MetS. The public use data from Atherosclerosis Risk in Communities (ARIC) study were used. ARIC is a population-based biracial cohort study of the risk factors for coronary atherosclerotic disease (CAD) in 15,792 middle-aged Americans sampled from 4 communities. MetS was defined using the revised ATP-III criteria by NHLBI and AHA. From baseline cohort, we identified, as study population, 9,359 individuals who did not have MetS and who completed the second follow-up examination in 1993–1995. At baseline the mean age was 54 (56% females and 21% African Americans). In 6 years of follow-up, 1970 individuals (25%) developed MetS. Compared to the normal weight group, the odds ratios (95% CI) of incident MetS were 2.47 (2.17 - 2.81) and 4.57 (4.01 - 5.21) for the overweight group and the obese group, respectively. Compared to individuals in the lowest quartile of leisure activity (primarily cycling and walking), the odds ratios (95% CI) of incident MetS were 0.74 (0.63 - 0.85) and 0.91 (0.81 - 1.02) in individuals in the highest and the middle quartiles of leisure activity, respectively. Adjustment of traditional CAD risk factors did not change the above pattern of associations. The joint associations of obesity, physical activity, and incident MetS are shown in Table 1. At any level of physical activity, there is graded increase in risk of incident MetS with increased levels of BMI, in contrast to a lack of graded association between physical activity and the incident MetS in all categories of BMI. Conclusion: This study highlights the need to target the obesity more than the physical activity in preventing the development of metabolic syndrome

ODD RATIOS AND 95% CI OF METS ASSOCIATED WITH BOTH BMI AND LEISURE PHYSICAL ACTIVITY

BMI Category	Lesire time physical activity	lesure time physical activity	leisure time physical activity
	TOP	Middle	Lowest
Normal	1.00	1.15 (0.90, 1.46)	1.35 (1.02, 1.77)
overweight	2.32 (1.72, 3.14)	3.34 (2.61, 4.27)	3.03 (2.29, 3.98)
Obese	5.51 (4.07, 7.47)	5.71 (4.43, 7.34)	5.52 (4.24, 7.21)

*Adjusted for age, race, sex, education level, CHD prevalence, total cholesterol and smoking

P162

Gender-Specific Association of Depression and a Haplotype in Leukotriene A4 Hydrolase Gene

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Background: Depression is an independent cardiovascular risk factor and inflammation has been implicated. Depression is twice as common in women as in men. Whether genetic variants involved in inflammation play a role in the gender difference in depression susceptibility is unclear. **Methods:** We examined the association, separately in men and women, between 12 single nucleotide polymorphisms (SNPs) in leukotriene A4 hydrolase (LTA4H) gene and depression in 1,434 Caucasian subjects (62.7±11.5 years, 30.5% female) referred for cardiovascular evaluation. Depression was defined as Patient Health Questionnaire 9 score ≥10. Single marker analysis was assessed by χ^2 test. Haplotype-specific associations were performed using likelihood ratio tests. Empirical significance levels were determined by permutation tests. Subjects who carried at least one copy of a specific haplotype were defined as haplotype carriers. Odds ratio (OR) for haplotype carrier status vs. noncarrier was calculated using logistic regression. **Results:** Depressed individuals, comprising 14.5% of the total, were more likely to be female (17.8% vs. 12.0%, $p = 0.003$), have a history of diabetes ($p<0.001$), angina ($p<0.001$), myocardial infarction (MI, $p = 0.005$) and stroke ($p<0.001$). None of the 12 SNPs was individually associated with depression. However, a six-SNP haplotype, named HapE, showed a significant protective effect on depression in women (OR of HapE carrier vs. noncarrier = 0.28, 95% CI [0.11–0.87], $p = 0.008$), but not in men (OR = 0.98, 95% CI [0.56–1.72], $p = 0.94$). HapE frequency was higher in women than in men (17.2% vs. 13.2%, $p = 0.05$). The prevalence of HapE was 6.4% among depressed women, and 19.7% among non-depressed women. Corresponding prevalence in men were 10.8% and 15.6%. After adjusting for age, body mass index, smoking, diabetes, hypertension, angina, stroke and MI, the protective effect of HapE on depression in women remained significant (OR = 0.31, 95% CI [0.10–0.89], $p = 0.03$). **Conclusion:** This is the first study to show evidence for a gender-specific association of a novel haplotype in LTA4H gene on depression. Although these results need replication in other populations, they suggest that genetic variations may underlie gender difference in depression.

P163

Kava Consumption and Coronary Artery Disease in South Asians: Is There an Association?

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Background: Kava, a root extract from the Piper Methysticum plant, is a ceremonial beverage consumed throughout the Pacific Islands. Kava consumption is associated with elevated LDL cholesterol levels and sudden cardiac death. However, the long-term effect of kava consumption on coronary artery disease (CAD) has received little attention. We investigated the association between CAD and kava consumption in Fijian South Asians. **Methods:** Subjects enrolled in the *Study To Assess Associated Risk Factors with Premature Atherosclerosis and CAD in People of South Asian Descent* (STAAR) were assessed for kava consumption, CAD status and presence of CAD risk factors. Using a logistic regression analysis, we calculated odds ratios (OR) for the presence of CAD as a function of kava consumption. Adjustments were made for age, sex, smoking history, diabetes, dyslipidemia, hypertension, socioeconomic status, fruit and vegetable intake, and regular exercise. **Results:** A complete set of data was available for 394 subjects. There were 139 (35.3%) kava consumers (KC) and 255 (64.7%) non-kava consumers (NKC). Mean ages were 55.1 ± 10.8 vs. 56.1 ± 11.5 years for KC and NKC respectively ($p = 0.5$). Compared to NKC, the KC had a higher prevalence of dyslipidemia (66% vs. 54%, $P=0.02$) and smoking history (71% vs. 25%, $P < 0.001$). There was a significantly lower prevalence of female sex in KC (8.6%) vs. NKC (47.8%), ($p < 0.001$). The prevalence of other CAD risk factors was similar for both groups ($p > 0.1$ for all). The adjusted OR for KC vs. NKC was 2.11 [95% CI, 1.21–3.68]. A strong trend towards increased CAD with increasing levels of kava consumption was observed ($p=0.047$). The OR for occasional consumption (n=97) was 2.18 [95% CI, 1.19–4.00], the OR for weekly consumption (n=35) was 2.40 [95% CI, 0.92–6.25], and the OR for daily consumption (n=5) was 3.16 [95% CI, 0.32–31.67]. **Conclusions:** This is the first study to show a positive correlation between kava consumption and prevalence of CAD. This correlation remained significant post adjustment for CAD risk factors. Further studies are necessary to elucidate the effects of long term kava usage on the pathogenesis of atherosclerosis and progression of CAD.

P164

Are Personal Perceptions of Coronary Heart Disease Risk Associated with Health Behaviors Among Postmenopausal Women?

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Background.The Coronary Risk, Individual Perception survey (CRIP) contains a 16-item scale which measures personal risk perception of CHD. The scale was previously found to discriminate between various groups with regard to their perception of personal risk. This current analysis examines whether risk perception is associated with self-reported health behaviors or an objective measure of CHD risk among participants enrolled in the Women Health Initiative (WHI). Methods. Women from the Observational Study of WHI in the New York Clinical Center were surveyed at baseline and after a one-year interval. Risk perception and health behaviors (physical activity and diet) were rated 1= strongly disagree to 6= strongly agree and scored so that higher values implied heightened perception and healthier behaviors. Summary scores for risk perception (range 16–96) and health behaviors (range 6–36) were used to examine for associations. A simple measure of CHD risk status was derived by summing up actual risk factors (age ≥ 65 years, hypertension, diabetes, dyslipidemia, or current smoker). Women with ≥3 risk factors were considered at high risk for CHD. Results. Follow-up surveys were completed for 98.3% (297/302) of women. The mean age was 69.6 yrs (±6.6), 36% were Black, 38% were White, and 26% were Hispanic. Black women (63.7%, n=65) were at higher risk for CHD, compared to White (46.4%, n=51) and Hispanic (39.7%, n=29) women ($p=0.004$). Internal consistency of the risk perception scale was good (Cronbach's $\alpha=0.83$).Compared to baseline, mean summary scores for risk perception decreased (54.6 [7.2] vs. 45.4 [11.4], respectively; $p<0.001$). Among women with >3 CHD risk factors (n=145), 42.1% (n=61) perceived themselves at low risk of CHD (kappa=0.17). In multiple regression analyses, risk perception was inversely related to health behaviors ($t=-7.5$; $p<0.001$). This suggests women with lower risk perceptions had healthier behaviors (low-fat/high-fiber diet and exercise). Conclusions. In this WHI sub-sample, risk perception was associated with health behaviors and many women at high risk of CHD perceived themselves to be at low risk. Healthcare providers should assess perceived and actual risk of CHD to improve the "risk-talk" dialogue and address any misconceptions.

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P165

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P166

A Declining Depression Level Improves Prognosis in Patients with Coronary Artery Disease

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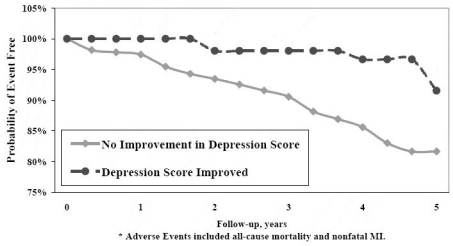
BACKGROUND: We examined whether a declining depression level over time is associated with a reduced risk of nonfatal myocardial infarction (MI) or total mortality among coronary artery disease (CAD) patients. METHODS: A prospective cohort study of 516 patients with CAD (mean age 68 years at entry, 82% males) with annual Symptom Questionnaire. Primary outcome was the composite of nonfatal MI and all-cause mortality. RESULTS During an average follow-up of 3.4 years, we documented 44 nonfatal MIs and 19 deaths. Depression scores (DS) were categorized into tertiles, fitting the intuitive classification of low, intermediate, and high levels of depression. A reduction in depression level occurs when a patient's DS changed, during follow-up, from a higher to a lower tertile (e.g. high to intermediate, high to low, or intermediate to low). A reduction in DS, regardless of cause, was associated with a decreased risk of nonfatal MI or death; the age adjusted hazard ratio was 0.2 (95% confidence interval, 0.05 - 0.85; p=0.03). In multivariate time-varying Cox model, after adjusting for age, sex, education, marital status, smoking, hypertension, diabetes mellitus, previous MI, body mass index, total cholesterol, blood pressure, heart rate, ejection fraction, and ETT duration, a reduction in DS still was associated with a decreased risk of nonfatal MI or death, the adjusted hazard ratio was 0.27 (95% confidence interval, 0.08 - 0.96; p=0.04). CONCLUSIONS A declining depression level over time is associated with a reduction in risk of MI or death among patients with CAD.



P167

Trust Is Not a Factor in Racial Disparities in Blood Pressure Control

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African Americans with hypertension (HTN) often have worse blood pressure (BP) control than whites. Among treated individuals with HTN, medication adherence may be related to trust in physicians. Trust in physicians has not been fully explored as a potential factor related to racial disparities in BP control among individuals treated for HTN. In a cross-sectional analysis, we examined baseline data from the Reasons for Geographic and Racial Differences in Stroke (REGARDS), a national cohort study of African Americans and whites aged ≥ 45. We studied 3685 participants with both treated HTN and data on trust in physicians. BP was measured during an in-home visit. Our dichotomous outcome measure was BP control defined as systolic blood pressure (SBP) ≤ 140 mm Hg or SBP ≤ 130 mm Hg for those with diabetes, renal disease, or previous myocardial infarction. The primary independent variable was trust in physicians measured on a continuous scale (0–25) using a modified version of the Primary Care Assessment Survey (PCAS) trust subscale. We used multivariable logistic regression models to determine the independent relationship of trust with BP control while adjusting for race, insurance status, comorbidities, BMI, tobacco and alcohol use, and medication adherence. The mean age of the study sample was 66.2 years (SD = 9.17), with 30.2% (n=1112) males. Of African Americans, 35.5% (n=694) had inadequate BP control, compared with 24.7% of Whites (n=430) (p<.0001). The 1944 African Americans had slightly less trust in physicians compared to the 1741 whites (PCAS score 19.9 vs. 20.5, p < 0.0001). Trust was not significantly related to BP control either before or after adjusting for demographic covariates, comorbid conditions, and health-related behaviors. African Americans continued to be less likely to have adequate BP control than whites after controlling for these covariates in the multivariable analysis (OR=0.68, 95% CI 0.58,0.80). Trust did not moderate the association between race and BP control (race*trust, p = 0.65). Among African American and white patients receiving treatment for HTN, African Americans show poorer BP control. However, trust in physicians was not related to BP control and does not seem to contribute to explaining the racial disparity in BP control.

P168

Vitality and Risk of Recurrent Cardiac Events in Acute Myocardial Infarction Survivors

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Background: Low vitality, characterized by fatigue and lack of energy, is common among survivors of acute myocardial infarction (AMI). Furthermore, low vitality has been shown to be associated with increased risk of cardiac events among individuals with and without known coronary artery disease. Whether this association holds among AMI survivors and possible mechanisms remain in question. **Objective:** To determine the association between vitality and risk of recurrent cardiac events among a population-based cohort of first AMI survivors. **Methods:** Incident AMI cases (n=1444) from Erie and Niagara (NY) county hospitals were enrolled and followed up to nine years. Vitality, measured by the SF-36 at enrollment (VIT), was categorized into four groups from high to low (≥ 80, 50–80, 20–50, ≤ 20). The primary outcome was time-to-first-event (cardiac death, recurrent MI). Hazard ratios (HR) and 95% CIs were estimated from Cox proportional hazards models with high vitality (VIT ≥ 80) as the reference. A multivariate Cox model controlled for traditional cardiovascular disease risk factors, ejection fraction and peak creatine kinase-MB at index MI, the SF-36 mental component score, and depression (CES-D). **Results:** Low vitality individuals (VIT ≤ 20) at baseline were more likely younger, female, of higher BMI, smoking, diabetic, less physically active, and to have higher CES-D scores. VIT was not strongly associated with ejection fraction (r=0.01) or peak CK-MB (r=0.01), but was strongly correlated with CES-D scores (r=-0.60). Lower vitality scores were associated with increased risk of recurrent cardiac events. Adjusted HRs (95% CI) for VIT 50–80, 20–50, and ≤ 20 (compared to ≥ 80) were 1.28 (0.85, 1.90), 1.62 (1.04, 2.54), and 3.10 (1.63, 5.89), respectively (p_{trend} = 0.002). The association persisted in both early (≤ 2 years) and late (> 2 years) follow-up periods, and for recurrent MI and cardiac death individually. **Conclusion:** Low vitality was associated with increased risk of recurrent cardiac events among first AMI survivors after controlling for traditional risk factors, markers of index MI severity, and psychological confounders. Future studies should investigate physiologic and psychologic links with vitality as possible targets of intervention after AMI.

P169

Fatness and Fitness: How Do They Affect Health-Related Quality of Life in People with Diabetes?

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Background Disease complications reduce health-related quality of life (HRQOL) in people with type 2 diabetes mellitus. Less is known about the association of modifiable risk factors such as obesity and fitness with HRQOL. **Objective** We hypothesized that decreased total body fatness and increased levels of fitness would be associated with higher HRQOL and attenuate the adverse effect of diabetes. **Design** Cross-sectional study using baseline data from subjects recruited for two exercise training studies. **Participants** One study enrolled subjects with and the other without diabetes. All subjects had mild hypertension, a sedentary lifestyle and were without other medical conditions that precluded exercise. **Methods** Aerobic fitness was assessed as maximal oxygen uptake (VO_2max) during treadmill testing, total body fatness by dual-energy x-ray absorptiometry (percent body fat) and HRQOL by the Medical Outcomes Study SF-36. We used multivariate linear regression analyses to test the association of HRQOL outcomes with diabetes, fitness and fatness. **Results** There were 121 non-diabetics and 71 diabetics. Diabetics were younger (p<0.01), more likely to be men (p<0.01), non-white (p<0.01) and meet criteria for metabolic syndrome (p=0.03). Diabetics had significantly lower mean scores for general health perceptions (GHP) and physical component score (PCS). In a multivariate regression analysis, diabetes (p<0.01) and lower VO_2max (p=0.02) but not percent body fat, were associated with reduced GHP. The effect size was greatest for diabetes (effect size= - 3) even after accounting for fitness, fatness and other clinical variables. In a second multivariate analysis higher percent body fat (p=0.02) and having diabetes (p=0.04), but not VO_2max, were associated with reduced PCS. The largest effect size was for percent body fat (effect size= - 2.4). **Conclusions** Lower levels of fatness and improved fitness reduced the negative association of diabetes with HRQOL. These data suggest that patients with diabetes that make lifestyle changes focused on physical activity and weight reduction may be able to improve their HRQOL.

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P170

Perceived Risk of Developing Heart Disease Among Hypertensive Patients in Primary Care

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Background: Perceptions of heart disease (HD) risk among hypertensive patients seen in primary care are poorly characterized. **Methods:** In a cross sectional study of hypertensive patients in 30 Maryland primary care practices, we asked patients, "How likely do you think it is that you will develop heart disease or heart failure in the next 10 years?" Using multivariable logistic regression, we assessed independent predictors of low perceived risk including patients' demographics, comorbidity, behaviors, health literacy, and religious beliefs. We also compared patients' perceptions to their risks estimated with the Framingham risk equation. **Results:** Among 198 patients, most were >60 years old (57%), female (63%), non-White (65%), had not attended college (71%), had income <$35,000 (59%), and had ≥ 9th grade health literacy (65%). Over one-third had diabetes (41%), had controlled hypertension (57%) or LDL cholesterol (57%), and were obese (89%) or current smokers (22%). Most felt religion is at least somewhat important (95%) and prayed several times weekly (88%). Overall 13%, 27%, 30%, and 31% rated themselves "not", "slightly," "moderately" or "very" likely to develop HD. Compared to participants with incomes >$35,000, those with incomes <$35,000 were more likely to rate themselves "not" likely to develop HD ((adjusted percent (AP) 95% confidence interval (CI): 43(12–80) versus 4 (reference), p<0.01). Participants with diabetes and praying at least several times weekly were less likely than those without diabetes or praying less than once weekly to rate themselves "not" likely to develop HD (AP (95% CI): 4(1–12) versus 13(reference) and 3(1–10) versus 22 (reference), both p<0.01). Non-Whites who felt religion is very important were more likely than Whites who felt religion is less than very important to rate themselves "not" likely to develop HD (AP (95% CI): 25 (10–48) versus 7(reference), p<0.01). Among those rating themselves 'not' likely the median (range) Framingham risk score was 10% (6–16%). **Conclusions:** Many hypertensive patients believe they are at low risk for HD, despite contrary clinical evidence. Targeted education of individuals with inappropriately low perceptions of risk could enhance compliance with therapies to improve outcomes.

P171

Influence of Caregiving on Lifestyle and Psychosocial Risk Factors Among Family Members of Patients Hospitalized with Cardiovascular Disease

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Background: Few data have evaluated the relationship between caregiving and cardiovascular disease (CVD) risk. The purpose of this study was to determine the prevalence and predictors of caregiver strain and to evaluate the association between caregiving and CVD lifestyle and psychosocial risk factors among family members and/or cohabitants of patients hospitalized with CVD. **Methods**: Participants in the NHLBI **F**amily **I**ntervention **T**rial for **Heart** Health (**F.I.T. Heart**) who completed a 6-month follow-up as of September 2007 were included in this analysis (n=210; mean age 49±14 years, 67% female, 30% non-white). At 6 months, standardized information was collected regarding lifestyle and caregiver strain (high caregiver strain =≥7). In a subsample (n=70), additional psychosocial information was obtained at 6 months. **Results**: The prevalence of serving as a CVD patient's primary caregiver was 39% at 6 months; 11% of participants reported caring for the patient most of the time, 32% some of the time or occasionally, and 17% none of the time. Caregivers (primary/most) were more likely to be women (63% vs 27%, p<0.01), married/living with someone (p<0.01), >50 years old (p<0.01), have ≤high school education (p=0.03), unemployed (p=0.05) and be smokers (p=0.01) than non-caregivers (some/occasional/none). Adherence to prevention guidelines was poorer among caregivers vs non-caregivers including a greater intake of saturated fat (p=0.049) and a higher waist circumference (p=0.03) in a multivariable model adjusted for confounders at baseline. Mean caregiver strain scores were significantly higher among those with depressive symptoms (p<0.01) and low social support (p<0.01) at 6 months in a multivariable model adjusted for sex, marital status, and baseline levels of depression and social support. **Conclusions**: Caregivers of cardiac patients may be at increased risk themselves for CVD morbidity and mortality compared to non-caregivers due to suboptimal lifestyle and psychosocial risk factors. These data suggest that hospitalization for CVD may be a unique opportunity to identify caregivers of cardiac patients that may benefit from interventions to lower CVD risk.

P172

Self-Rated Health Is Significantly Associated with B-Type Natriuretic Peptide Levels in Men and Is Associated with C-Reactive Protein Levels in Women Among 17,571 Japanese Adults

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Background: Poor self-rated health (SRH) is independently associated with increased total and cardiovascular mortality. Elevated serum high-sensitive C-reactive protein (hsCRP) levels and elevated plasma B-type natriuretic peptide (BNP) levels are strong predictors for cardiovascular mortality and morbidity. Therefore, poor SRH may be associated with higher levels of these biomarkers. Methods: A total of 17,571 participants aged 40 to 69 years (5,569 men and 12,002 women) who underwent annual health check-ups from 2002 and 2004 in a Japanese general population were enrolled. Plasma levels of BNP (pg/mL) and serum levels of high-sensitive CRP (mg/L) were determined. SRH was assessed by using a questionnaire that consisted of a five point scale about health. Persons who selected good or fairy good were defined as good health. Other persons were defined as poor health. A logistic regression model was used to examine the association between SRH and levels of biomarkers (logarithm-transformed BNP and hsCRP) after adjusting for age, body mass index, systolic blood pressure, LDL- and HDL-cholesterol levels, HbA_{1c} levels, Habits (drinking, smoking and exercise), and past history of myocardial infarction or stroke. Results: Proportions of men and women who reported good health were 78.7% (4,383 of 5,569) and 75.7% (9,090 of 12,002), respectively. Multivariate analysis revealed that poor SRH was significantly associated with high BNP levels in men, while it was significantly associated with high hsCRP levels in women (see table). Conclusions: These findings suggest that SRH is independently associated with levels of CRP and BNP among Japanese adults, and sex difference may exist in this association.

MULTIVARIATE ADJUSTED ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR POOR SELF-RATED HEALTH

	Men	(n = 5,569)	Women	(n = 12,002)
	OR	95% CI	OR	95%CI
ln hsCRP	1.01	0.95–1.08	1.10	1.06–1.15
ln BNP	1.08	1.02–1.14	1.00	0.96–1.04

OR, odds ratio; CI, confidence interval

P173

Antidepressants and Anxiolytics Improve Prognosis in Patients with Coronary Artery Disease

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BACKGROUND: We examined whether the use of antidepressants or anxiolytics was associated with a reduced risk of nonfatal myocardial infarction (MI) or total mortality among coronary artery disease (CAD) patients. METHODS: A prospective cohort study of 693 patients with CAD (mean age 67 years at entry, 85% males, 41% with history of MI), using annual clinical and psychometric questionnaires. Primary outcome was the composite of nonfatal MI or all-cause mortality. RESULTS: During an average follow-up of 4.6 years, the annualized incidence of non-fatal MI, cardiac mortality, and total mortality was 2.2%, 0.8%, and 1.4%, respectively for a combined event rate of 3.2 events per 100 person-years (pyrs) (104 total events). 131 subjects (19% of 693) used antidepressants or anxiolytics sometime during the follow-up. Their event rate was 2.2 events per 100 pys. 562 subjects (81% of 693) did not use antidepressants or anxiolytics. Their event rate was significantly higher - 4.1 events per 100 pys (p=0.04). 69% (91 out of 131) of patients on psychiatric drugs experienced significant improvement of their anxiety or depression level (by 1 standard deviation or more on the Kellner scale) in contrast with 53% (299 out of 562) of patients who were not on psychiatric drugs (p=0.001). In multivariate Cox model, after adjusting for age and sex, the use of antidepressants or anxiolytics was associated with a decreased risk of nonfatal MI or death, the adjusted hazard ratio was 0.57 (95% confidence interval [C.I.], 0.33 - 0.96; p=0.04). To control for baseline anxiety and depression level, we focused on 352 subjects that had elevated level of anxiety or depression at study entry. Among them, 86 subjects (24% of 352) used antidepressants or anxiolytics to treat their depression or anxiety. In multivariate Cox model, after adjusting for age and sex, as well as changes in anxiety and depression scores, the use of antidepressants or anxiolytics was associated with a decreased risk of nonfatal MI or death, the adjusted hazard ratio was 0.43 (95% C.I., 0.20 - 0.92; p=0.03). CONCLUSIONS: Use of antidepressants or anxiolytics is associated with a reduction in risk of MI or death among patients with CAD, and the observed benefit might not be solely attributable to improvement of anxiety or depression.

P174

Teens 'n Screens: The Influence of Neighborhood Social Environment on Patterns of Television, Video, Computer, and Internet Use in Adolescents

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We describe patterns of TV/video, computer/internet, and total screentime in adolescents through secondary school, and examine the influence of neighborhood social environment (NSE) on screentime trajectories. Data were derived from the Nicotine Dependence In Teens Study, a cohort of grade 7 students from 10 Montreal schools established in 1999 and followed for 5 years. Students completed questionnaires 4 times/year in class. Average hours/week of TV/video, computer/internet use, and total screentime were computed based on self-report. Neighborhoods were defined by census district. NSE was based on 2001 Census data and included % of university graduates, grade 9 education, low-income, and single-parent households. Indicators of NSE varied substantially across neighborhoods and were tertiled, using the most favorable tertile as the reference. TV/video, computer/internet, and total screentime trajectories were identified using latent class growth analysis. Influence of NSE on trajectory class was investigated using logistic regression. Complete data were available for 731/1129 adolescents in 217 Montreal neighborhoods (46% boys; 57% with 1 or both parents university educated). The best fitting models identified 3 trajectory classes: high, average and low consumers, for each of TV/video, computer/internet use, and total screentime. Forty percent of girls and 31% of boys were in the high TV/video class; 49% of boys and 37% of girls were in the high computer/internet class. Estimated total screentime over 5 years was ≥40 and ≥32 hours/week for boys and girls in the high consumer groups, respectively. For all indicators of NSE, living in the least favorable tertile increased the odds of being in the high screentime group up to 5-fold among girls, after adjusting for parental education. For boys, living in neighborhoods with lower educational attainment increased odds of being in the high screentime group 2- to 3-fold. NSE influenced TV/video similarly, but was weaker for computer/internet. NSE influences screentime patterns and notably TV/video in adolescents,

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potentially increasing neighborhood disparities in health outcomes. Adolescents in disadvantaged neighborhoods may face constraints in pursuing healthy alternatives to TV/video.

P175

Omega-6 and *Trans* Fatty Acids in Blood Cell Membranes from Acute Coronary Syndrome Patients and Controls

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Introduction: The relationship between blood cell membrane fatty acids (FAs) and risk for acute coronary syndromes (ACSs) is unclear. Previous studies have shown ACS patients to have significantly lower amounts of the long-chain omega-3 FAs, but the relations between risk and amounts of other FAs thought to influence risk for coronary heart disease (CHD), such as the omega-6 and *trans* FAs, are also of interest. **Hypothesis:** We hypothesized that low levels of linoleic acid (LA) and high levels of arachidonic acid (AA) and the *trans* isomers of oleic acid (OA) and LA are associated with ACS. **Methods:** We analyzed the FA composition of blood cell membranes from 768 ACS patients and 768 age-, sex- and race-matched controls. Omega-6 and *trans* OA and LA associations with ACS case status were assessed using multivariable conditional logistic regression models adjusting for matching variables and lipid levels (LDL, HDL, log-triglycerides), body mass index, diabetes, hypertension, family history of coronary artery disease, personal history of myocardial infarction, alcohol consumption, smoking, statin, aspirin, anti-platelet drug use, and blood cell content of EPA+DHA. **Results:** Regarding omega-6 FAs, blood cell membrane LA content was 13% lower in those with ACS than controls ($p<0.0001$) whereas AA content was 3.6% higher in cases ($p<0.001$). In ACS cases vs. controls, blood cell content of the major *trans* isomers of OA was 13.3% ($p<0.0001$) higher, and the content of *trans-trans* isomers of LA was 6.3% higher ($p=0.003$). In multivariable analyses, a 1-standard deviation (SD) increase in LA was associated with an odds ratio (OR) for case status of 0.30 (95% CI, 0.24–0.38). The relationship of AA to ACS was U-shaped and statistically significant ($p<0.001$). For *trans* FAs, the OR for a 1-SD increase in *trans* OA was 1.24 (95% CI; 1.06 to 1.44) and for *trans-trans* LA 1.1 (95% CI; 0.93–1.29). All associations were independent of membrane omega-3 FA content. **Conclusions:** Odds for ACS case status was primarily associated with reduced LA and increased *trans* oleic acid content of blood cell membranes. These findings confirm past studies indicating that higher LA and lower *trans* fat levels in membranes are associated with reduced risk for cardiac events.

P176

A Prospective Study of Impaired Fasting Glucose and Undiagnosed Diabetes to the Risk of Stroke in Asymptomatic Men

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Objective: Although clinical diabetes is a strong risk factor for cardiovascular disease (CVD), whether fasting plasma glucose (FPG) levels are related to stroke remains unclear. We examined the association between FPG and fatal, nonfatal, and total stroke events in a large cohort of asymptomatic men. **Methods**: Participants were 43,933 men (mean±SD age 44.3±9.9 yrs) who were free of known CVD at baseline, and whose FPG levels were assessed at a central clinical laboratory during a preventive medical examination at the Cooper Clinic, Dallas, TX between 1971 and 2003. Patients with diagnosed diabetes or low FPG (<80 mg/dL) were excluded from the present analysis. Mortality follow-up was through December 31, 2003 using the National Death Index. Nonfatal stroke events were ascertained from mail-back surveys and defined as a history of physician diagnosed stroke. Total stroke included fatal and nonfatal stroke. Cox regression models were used to quantify the pattern and magnitude of association between stroke events and FPG levels. **Results**: There were 595 total stroke events (156 fatal and 456 nonfatal strokes) during 702,928 man-yrs of exposure. Age adjusted fatal, nonfatal, and total stroke event rates per 10,000 man-yr across normal FPG (80–109 mg/dL), impaired fasting glucose (IFG, 110–125 mg/dL), and undiagnosed diabetes (≥126 mg/dL) were 2.1, 3.4, and 4.0 (trend P =0.002), 10.3, 11.8 and 18.0 (trend P =0.008), and 8.2, 9.6 and 12.4 (trend P =0.008), respectively. After further adjusting for body mass index (BM)); smoking; alcohol intake; family history of CVD; and personal history of hypertension, or hypercholesterolemia, the inverse association between FPG and fatal, nonfatal or total stroke events remained significant (trend P <0.05 each). For FPG levels ≥110 mg/dL, each 10 mg/dL increment FPG was associated with a 7% higher risk of total stroke events (P =0.02) after adjustment for age, BMI, smoking, alcohol intake, hypertension or hypercholesterolemia, and family history of CVD. **Conclusions:** Hyperglycemia ≥ 110 mg/dL (IFG and diabetes) was associated with higher risk of fatal, nonfatal, or total stroke events in asymptomatic men. Prevention and control of hyperglycemia may play an important role in stroke prevention strategies.

P177

Hypertension, Left Ventricular Mass, and Geometry Among Hispanic Subgroups: The Multi-Ethnic Study of Atherosclerosis

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Hispanics are the largest and fastest growing ethnic minority in the United States. We examined the prevalence of hypertension, left ventricular hypertrophy (LVH), and LV geometric patterns within Hispanic subgroups and compared with non-Hispanic whites in the Multi-Ethnic Study of Atherosclerosis. **Methods**: Study participants had no clinical cardiovascular (CV) disease and had completed cardiac magnetic resonance imaging. Hispanics were categorized into subgroups based on self-reported ancestry. Hypertension was defined as systolic blood pressure greater than 140 mmHg, diastolic blood pressure greater than 90 mmHg or current use of antihypertensive medications. LVH (defined as the highest quartile of LV mass indexed to height$^{2.7}$), and LV geometry (classified according to the presence/absence of LVH and abnormal/normal LV mass/LV end-diastolic volume ratio) were measured. **Results:** Among Hispanic participants, 329 were Caribbean-Hispanic, 574 were Mexican-American, and 161 were Central/South American, and 41 were missing ancestry information. Caribbean-Hispanics were more likely to be hypertensive than non-Hispanic whites after adjustment for age, lipids, education, physical activity, body mass index, smoking, diabetes, gender, and presence of the metabolic syndrome (OR 1.7 [95% CI 1.2–2.3]), whereas Mexican-Americans and Central/South Americans did not differ significantly from non-Hispanic whites (OR 0.8 [95% CI 0.7–1.1]; OR 1.3 [95% CI 0.9–1.9], respectively). All Hispanic subgroups had a higher prevalence of LVH than non-Hispanic whites (Caribbean-Hispanics: OR 2.9 [95% CI 2.0–3.5]; Mexican-Americans: OR 2.7 [95% CI 2.2–3.4]; Central/South Americans: OR 1.7 [95% CI 1.1–2.5]) after adjustment for the above confounders plus systolic blood pressure, and a higher prevalence of concentric hypertrophy (6.7%, 8.2%, 6.2%, respectively) compared to non-Hispanic whites (3.8%; P<0.0001). **Conclusion**: Caribbean-Hispanics had higher prevalence of hypertension, LVH and abnormal LV geometry compared to non-Hispanic whites. A higher prevalence of LVH was observed among Mexican-Americans despite a lower prevalence of hypertension. Subgroup differences need to be appreciated when evaluating CV risk among Hispanics.

P178

Black Race and Hypertension Are Strong Predictors of Premature Heart Failure: The Cardia Study

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Background: Heart failure (HF) is a devastating illness that usually presents in the elderly. The epidemiology of HF at younger ages is not well understood. **Methods**: We used data from the Coronary Artery Risk Development In young Adults (CARDIA) cohort of 5,115 healthy black and white men and women age 18–30 at baseline. Incident events were defined as an adjudicated hospitalization or death due to HF. We examined blood pressure and other potential antecedents at Year 0, 5, and 10 (including echocardiographic measures at Year 5), using Cox models and forward selection procedures ($p<0.05$). **Results:** In 20 years of follow-up, 28 incident HF events were observed. With one exception, all of these occurred among black participants (Table 1), age at onset 39±6 years). Among blacks with follow-up after Year 10, blood pressure elevations at Years 0, 5, and 10 were independently associated with subsequent HF, and prevalence of hypertension increased progressively among those who later developed HF (Table 2). Depressed systolic function on echocardiogram at Year 5 (percent fractional shortening) was also an independent predictor of future HF (adjusted HR per SD=0.6, 95% CI 0.4–0.9). **Conclusions:** Among young and middle age adults, HF occurs almost exclusively among blacks and is not rare. Elevated blood pressure and depressed systolic function are early antecedents that may be targets for screening and interventions aimed at HF prevention.

TABLE 1. INCIDENCE FOR HEART FAILURE OVER 20 YEARS

	# events	Incidence (95% CI)
Black women	16/1480	1.1% (0.6–1.7)
Black men	11/1157	1.0% (0.5–1.7)
White women	1/1305	0.08% (0.002–0.4)
White men	0/1171	0% (0.0–0.3)

TABLE 2. ANTECEDENTS OF HEART FAILURE (HF) AMONG BLACK CARDIA PARTICIPANTS

	Year 0			Year 5			Year 10		
	Mean (SD)			Mean (SD)			Mean (SD)		
	HF	No HF	Adjusted HR*	HF	No HF	Adjusted HR*	HF	No HF	Adjusted HR*
Diastolic blood pressure (DBP)	78.4 (12.7)	68.7 (10.0)	1.9 (1.2–3.1)	83.9 (18.2)	70.3 (10.3)	†	90.9 (16.9)	74.0 (10.5)	†
Systolic blood pressure (SBP)	120.5 (10.8)	111.3 (10.9)	†	126.9 (20.2)	109.6 (11.67)	1.6 (1.3–2.0)	137.1 (22.5)	112.7 (13.3)	2.6 (1.8–2.9)
Percentage of blacks with hypertension (SBP≥140 or DBP ≥90 mmHg or on BP meds)	23%	3%		33%	5%		68%	11%	

*Hazard ratio per SD; †not retained in forward selection

P179

Alcohol Consumption and Mortality Among Men with Prior Myocardial Infarction

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Background: Moderate alcohol consumption is associated with lower risk of coronary heart disease among healthy populations. However, data on alcohol consumption patterns after first myocardial infarction (MI) and risk of death have been limited, and there are no prospective studies with alcohol consumption measures before and after confirmed MI. **Methods:** We conducted a prospective cohort study among U.S. male health professionals who had survived

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a first myocardial infarction from 1986 to 2004. Of the 1879 men with confirmed incident nonfatal MI, 317 deaths were documented through the end of follow-up in 2004. Participants were free of cardiovascular disease (CVD), stroke, or cancer at baseline in 1986. We calculated average alcohol consumption beginning from the time period immediately before the first MI and subsequently updated post-MI intake every 4 years as part of the usual biennial questionnaire cycles. Cox proportional hazards analyses were used to estimate the hazard ratios (HR) and 95% confidence intervals (CI), and multivariable models adjusted for age, smoking, ethnicity, CVD risk factors, and detailed information on MI treatment and severity from medical records or discharge summaries. **Results:** Compared to nondrinkers, the multivariable-adjusted hazard ratios for total mortality were 0.66 (95% CI 0.50–0.87) for 0.1–9.9 grams/day, 0.60 (95% CI 0.43–0.84) for 10.0–29.9 grams/day, and 0.70 (95% CI 0.44–1.10) for ≥30 grams/day (p for trend=0.05). For cardiovascular mortality, the adjusted hazard ratios were 0.66 (95% CI 0.44–0.99) for 0.1–9.9 grams/day, 0.52 (95% CI 0.32–0.83) for 10.0–29.9 grams/day, and 0.69 (95% CI 0.37–1.30) for ≥30 grams/day (p for trend=0.07). When stratified by site of initial MI (anterior versus other), the hazard ratios were similar in direction, but less strongly inversely associated with mortality among men with anterior MIs. **Conclusion:** Our findings indicate that moderate alcohol consumption after myocardial infarction may be protective against total and cardiovascular mortality among men. The inverse association may be strongest among men with a non-anterior initial myocardial infarction.

P180

Association of Parental Hypertension with Circulating Concentrations of Select Biomarkers in Nonhypertensive Offspring: The Framingham Heart Study

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Background: Although it is established that children of hypertensive parents are at increased risk of developing hypertension (HTN), data are limited about circulating concentrations of putative biomarkers (that may play a role in the development of high blood pressure) in non-hypertensive offspring of hypertensive parents. **Methods and Results:**We compared concentrations of 5 different biomarkers (urinary albumin-to-creatinine ratio; circulating C-reactive protein [CRP], renin, aldosterone, and plasminogen activator inhibitor type 1) in non-hypertensive Framingham offspring with none (n=239), one (n=487) or both hypertensive parents (n=331). Parental hypertension was defined as onset before age 60 years, based on longitudinal observations on the original Framingham cohort participants. Serum CRP concentrations were higher in non-hypertensive offspring with one (median: 1.7; Q1-Q3: 0.8–3.6 mg/L) or both parents who were hypertensive (median: 1.8; Q1-Q3: 0.7–3.6 mg/L), compared to offspring without parental HTN (median: 1.4; Q1-Q3: 0.7–3.2 mg/L). In multivariable analyses adjusting for age, sex, body mass index and systolic and diastolic blood pressure at baseline, parental HTN was associated with a higher serum CRP concentration in offspring (15% increase per parent with HTN; [95% CI, 5% to 25% increase], p=0.002) The levels of the other 4 biomarkers evaluated did not significantly differ between offspring with and without hypertensive parents (P for trend >0.05 for all). **Conclusions:** Serum CRP concentrations are higher in non-hypertensive offspring of hypertensive parents. These data are consistent with the notion that inflammation may mediate in part familial influences on HTN risk.

P181

Myeloperoxidase Predicts Cardiovascular Mortality in Patients with Coronary Artery Disease

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Background: Reactive oxygen species mediate the signalling of inflammatory pathways throughout all stages of atherosclerosis, from endothelial dysfunction to plaque rupture. Activated leukocytes within atherosclerotic lesions produce reactive oxygen species, causing local and systemic oxidative injury; however, contributions of oxidative stress to the clinical features of atherosclerosis have not yet been clearly established. Biomarkers of oxidative stress associated with presence of coronary artery disease (CAD) include myeloperoxidase (MPO), nitrotyrosine (N-tyr), and oxidized LDL (oxLDL). Although these markers have been found within atherosclerotic plaques - where they directly contribute to atherogenesis - their relative abilities for predicting outcomes in stable CAD have not yet been determined. Study Design: We tested the hypothesis that oxidative stress biomarkers MPO, N-tyr, and oxLDL, predict cardiovascular mortality in patients with CAD. Plasma levels of these biomarkers were measured using commercial enzyme-linked immunoassays in a cohort of 1117 patients with angiographic evidence of CAD. After a mean follow-up time of 8.5 years, 233 deaths were observed, of which 109 were cardiovascular disease (CVD)-deaths. The relative value of plasma biomarkers for prediction of CVD mortality was determined using Cox proportional hazards models with adjustment for: age, sex, smoking status, hypertension, diabetes, BMI, LDL-cholesterol, total:HDL-cholesterol, hsCRP, and family history of CAD. Interpretation: Patients whose plasma MPO levels were in the highest tertile had an increased risk of CVD mortality [HR(95%CI):2.04(1.02–4.10) p=0.04]. Non-significant trends were observed between elevated N-tyr and oxLDL and CAD, and between N-tyr and risk of CVD-death. Individuals with 2 biomarkers in the highest tertile had a 2-fold higher risk of CVD-death [2.03(1.03–4.41) p=0.04], and patients with 3 biomarkers in the highest tertile had a 3-fold higher risk [2.97(1.06–8.34) p=0.04]. While oxidative stress biomarkers associate with an elevated risk of CVD mortality, further studies are warranted to establish the clinical prognostic value of these biomarkers.

P182

Pericardial and Intra-Thoracic Fat Volumes Correlate with Circulating C-Reactive Protein, Monocyte Chemoattractant Protein-1, and Urine Isoprostanes: The Framingham Heart Study

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Background: Regional distribution of body fat is an important correlate of cardiovascular disease and its risk factors. Regional fat depots have differing systemic effects as well as local effects on contiguous tissues. We sought to assess whether levels of systemic inflammatory markers correlate with pericardial and intra-thoracic fat. **Methods:** Participants of the Framingham Offspring Study (n=997; 53% women; mean age 60 ± 9 years) underwent multi-detector CT scans to measure volumes of pericardial (within the pericardial sac) and intra-thoracic (within the thorax but excluding pericardial) fat, and provided fasting blood and urine samples to measure levels of twelve markers of inflammation (C-reactive protein [CRP]; interleukin-6; CD40 ligand; fibrinogen; intracellular adhesion molecule-1; lipoprotein-associated phospholipase A2; monocyte chemo-attractant protein-1 [MCP-1]; myeloperoxidase; osteoprotegerin; P-selectin; tumor necrosis factor receptor 2; and urine isoprostanes). Multivariable linear regression models with backward elimination were used to determine the magnitude of fat volume attributable to increasing log-transformed inflammatory marker levels, adjusting for age, sex, smoking, alcohol, aspirin, menopausal status, and hormone replacement therapy. Subsequent models additionally adjusted for BMI, waist circumference (WC), visceral adipose tissue (VAT) volume, blood pressure, lipids, diabetes, and prevalent cardiovascular disease. **Results:** The mean (± SD) pericardial and intra-thoracic fat volumes were 124 (± 49) cm^3 and 115 (± 61) cm^3, respectively. For intra-thoracic fat, backward linear regression models adjusting for the covariates demonstrated significant positive associations with CRP (p<0.0001), urine isoprostanes (p=0.0003), and MCP-1 (p=0.03). For pericardial fat, full multivariable adjustment revealed positive associations with CRP (p=0.002) and urine isoprostanes (p=0.03). **Conclusions:** CRP, MCP-1, and urine isoprostane levels are positively correlated with intra-thoracic and pericardial fat volumes. These associations persist even after accounting for total adiposity, suggesting that pericardial and intra-thoracic fat may be unique pathogenic fat depots.

P183

The Inverse Correlation Between Serum Glutathione Peroxidase 3 Activity and Cardiovascular Mortality in the Minnesota Heart Survey

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Background: It is widely held that serum lipid hydroperoxides activate macrophages which then invade the vessel wall and initiate atherosclerosis. Since serum glutathione peroxidase 3 (GPx3) reduces these hydroperoxides, it should decrease macrophage activation thereby reducing the level of vessel injury. Therefore there should be an inverse correlation between the GPx3 activity and cardiovascular (CVD) mortality. To our knowledge, no previous prospective studies have tested this hypothesis. Methods: In a nested case-control study of participants in the Minnesota Heart Survey we assayed GPx3 activity in 137 CVD deaths and 249 controls who were identified after 8 to 12 years of follow up. Controls were age-sex frequency matched with cases. Participants were randomly drawn from the Minneapolis/St. Paul metropolitan area and were predominantly white and aged 26 to 85 years. CVD mortality was based on death certificates. We estimated odds ratios in logistic regression models adjusted for age, sex, baseline year, body mass index, smoking history, alcohol intake, physical activity, total serum cholesterol, HDL cholesterol (HDLc), systolic blood pressure and non-fasting blood glucose. Results: The adjusted odds ratios (95% confidence intervals) for CVD mortality for increasing quartiles of GPx3 activity were 1.00, 0.90 [0.48 to 1.68], 0.77 [0.40 to 1.49], and 0.42 [0.21 to 0.86] (P for trend = 0.02). This inverse correlation was exclusively confined to those with below median HDLc (38 mg/dl for men; 48 mg/dl for women, p for interaction = 0.006). In the subset of those with low HDLc the odds ratios for increasing quartiles of GPx3 activity were 1.00, 0.82 [0.36 to 1.88], 0.60 [0.23 to 1.59], and 0.17 [0.06 to 0.47] (P for trend < 0.001). On the other hand, increasing levels of GPx3 activity for those with high HDLc were not associated with decreased CVD mortality (P for trend = 0.82). Conclusions: We find that in this cohort of individuals from the general population high GPx3 activity was independently associated with lower CVD mortality in individuals with low HDLc. Since GPx3 reduces lipid hydroperoxides, these results also support a hypothesis for a role of oxidized lipids in the initiation of atherosclerosis possibly through their activation of macrophages.

P184

Total Tissue Factor Pathway Inhibitor Level and Prevalence of Subclinical Atherosclerosis: The Multi-Ethnic Study of Atherosclerosis (MESA)

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Introduction. Tissue factor pathway inhibitor (TFPI) is an integral membrane protein that down-regulates tissue factor-factor VIIa and factor Xa coagulation complexes. Because it is a membrane protein, higher circulating levels of the shed form might reflect endothelial damage.

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Hypothesis. We hypothesized that higher total TFPI was associated with subclinical atherosclerosis, independent of cardiovascular disease risk factors. **Methods.** MESA is a cohort study of 6814 men and women without clinical CVD, aged 45–84, from four ethnic groups (Caucasian, African American, Hispanic, Chinese). Cross-sectional associations of total TFPI with CVD risk factors and measures of subclinical atherosclerosis were analyzed in a random sample of 1000 participants. Atherosclerosis measures included coronary artery calcium (CAC) score, common and internal carotid intima-media thickness (IMT) and ankle-brachial index (ABI). **Results.** TFPI was higher with older age, higher LDL cholesterol, current smoking and diabetes, but did not differ by ethnicity or other vascular risk factors. In unadjusted relative risk regression, higher TFPI was associated with each subclinical disease measure. Adjusted for age, gender, and LDL cholesterol, the only risk factors contributing to the models, TFPI in the 4th compared to 1st quartile was associated with a 1.2-fold (95% CI 1.0–1.4) increased risk of detectable CAC, a 1.3-fold increased risk of CAC >400 Agatston units (95% CI 1.1–1.6), a 1.6-fold (95% CI 1.1–2.5) increased risk of internal carotid IMT >80th percentile, but not with common carotid IMT, ABI <0.9 or CAC score in analysis limited to those with detectable CAC. The findings were consistent across ethnic groups. **Conclusion.** In this diverse population, higher TFPI was associated with increased risk of prevalent CAC and elevated internal carotid IMT, independent of other factors. Higher TFPI in people with subclinical CVD may be due to endothelial cell damage and vascular inflammation. TFPI is a good candidate biomarker for further study on progression of atherosclerosis.

P185

Association of Inflammatory Biomarkers with Decline in Cystatin C-Based Estimated Glomerular Filtration Rate in the Elderly: The Cardiovascular Health Study

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Background: Prior cross-sectional studies have demonstrated a consistent and linear association between circulating markers of inflammation and cystatin C, a marker of kidney function, but the direction of the association is unclear. The objective of this study is to determine whether elevated markers of inflammation are independently associated with kidney function decline. **Methods:** This study included 4,128 subjects from the Cardiovascular Health Study. Cystatin C was measured at baseline, year 3, and year 7; eligible subjects had at least two measures. Cystatin C-based estimated glomerular filtration rate (eGFR) was estimated using the equation GFR = 76.7 x (cystatin C)$^{-1.18}$. As in prior studies, rapid kidney function decline was defined as an annual cystatin C-based eGFR loss of 3 mL/min/1.73m^2. Measurements at the baseline visit included levels of five inflammatory biomarkers: C-reactive protein (CRP), interleukin 6 (IL-6), intercellular adhesion molecule 1 (ICAM-1), white blood cell count, and serum albumin. **Results:** In multivariate logistic regression models, CRP, IL-6, ICAM-1, and white blood cell levels had no significant associations with kidney function decline. In contrast, lower serum albumin levels were associated with significantly greater odds of rapid kidney function decline (Table). Similar results were observed when eGFR slope was analyzed as a linear outcome. **Conclusion:** Among five inflammatory markers, only serum albumin levels were associated with kidney function decline, as measured by cystatin-C based eGFR. Table. Associations of inflammatory biomarkers with rapid kidney function decline (cystatin C-based eGFR) using logistic regression

Biomarker	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
CRP (per SD = 7.74 mg/L)	1.03 (0.96, 1.10)	1.05 (0.98, 1.13)
IL-6 (per SD = 1.82 pg/mL)	1.04 (0.97, 1.11)	1.07 (0.99, 1.16)
ICAM-1 (per SD = 85.59 ng/mL)	0.98 (0.87, 1.10)	1.11 (0.97, 1.27)
WBC (per SD = 2.02 cells/μL)	1.03 (0.96, 1.10)	1.06 (0.98, 1.14)
Albumin (per SD = -0.29 g/dL)	1.15 (1.06, 1.23)†	1.17 (1.08, 1.26)†

* adjusted for baseline cystatin C-based eGFR, age, gender, race, hypertension, diabetes, smoking, LDL, HDL, prevalent CHD, and prevalent CHF † $p<0.05$

P186

Holter-Based T-Wave Alternans Identifies Community-Dwelling Older Adults at Increased Risk for Sudden Cardiac Death: Results from the Cardiovascular Health Study

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Abstract: Background: Microvolt T-wave alternans (TWA) measured from treadmill testing detects abnormalities in ventricular repolarization that identify patients at increased risk of sudden death (SCD). TWA can be measured from 24-hour Holter recordings using a time domain method called modified moving average (MMA). Whether Holter TWA predicts SCD is unknown. Methods**:** The Cardiovascular Health Study (CHS) is an NIH-sponsored population-based study of risk factors for cardiovascular disease and stroke in adults aged >=65 years old. Of the 1649 with 24-hour Holter recordings in the CHS, 49 had SCD during follow up. SCD occurred 7.7±3.6 (range 0.2–13) years after the Holter recording. Cases were matched 2:1 with N=96 controls alive at the time of death of the case and without SCD, based on age, gender, history of MI and diabetes. Subjects were 74±5 yrs, 98M, 47F. MMA TWA analysis was performed using a MARS system (GE Healthcare Milwaukee, WI) running software version 7.1.1. which provides a histogram of TWA values and the associated ECG strips. The 3 highest values for TWA from artifact-free periods were identified and averaged for each channel (TWA1 and TWA2). The cutpoint that maximized the separation between those who did and did not have SCD was determined using Cox regression analyses. Results: TWA1 was 44±21μV for SCD vs. 38±13 μV for controls, p= 0.029. TWA2 was 39±28 μV for SCD vs. 32±13 μV for controls, p=0.034. Higher TWA1 was significantly associated with SCD (RR=1.03, 95%CI=1.01–1.04, p=0.002). Similarly, higher TWA2 also predicted SCD (RR=1.02, 95% CI=1.006–1.03, p=0.004). The best cutpoint for prediction of SCD from TWA1 was >46 μV. TWA1 above this cutpoint identified 37 patients (17 SCD) with a nearly two fold risk of sudden death of [RR=1.9 (95% CI= 1.0–3.4, p=0.034)]. The channel 2 cutpoint was >37 μV which identified 35 people (17 SCD) with a relative risk of sudden death of 2.2 (95% CI=1.2–4.1, p=0.010). The 17 participants with TWA above the cutpoint on both channels had an even higher risk of SCD (RR=3.1, 95% CI=1.4–6.8, p=0.004). Conclusions: Higher TWA measured using MMA during 24-hour Holter recordings may identify older adults at increased risk of SCD long before the event occurs.

P187

Secondhand Smoke Exposure and Endothelial Progenitor Cell Depletion in Children

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Background: Many forms of cardiovascular disease (CVD) in adults are initiated and progress silently during childhood. The vascular endothelium plays a key role in promoting cardiovascular health; it maintains vascular tone and hemostasis, and is replenished by circulating endothelial progenitor cells (EPCs). EPCs are believed to reflect the integrity of the coronary vasculature. Circulating levels of EPCs may be a biological marker for vascular function, and decreases have been noted in adult patients with coronary artery disease and in adult smokers. One quarter of children in the US are exposed to secondhand smoke (SHS), but little is known about the effect of SHS on the cardiovascular system during childhood. **Hypothesis:** Circulating EPCs are measureable in toddlers and teens, and SHS is related to EPC reductions in children. **Methods:** Children ages 2–5 (n=57) and 9–14 (n=68) with varying levels of SHS exposure were studied. SHS exposure was measured by the number of adult smokers a child was exposed to in a 24 hour period. EPC levels were measured by flow cytometry (determined by AC133+/CD34+/CD45- cells; FACSCalibur flow cytometer). Unstained cells served as controls. **Results:** Both age groups studied had reliably measurable EPC numbers. In adolescents (ages 9–14), a statistically significant negative relationship was found between SHS exposure and circulating EPCs, when expressed as total number/mcl blood or as percentage of leukocytes ($p < .05$). This relationship was also observed in the toddler group (ages 2–5) but with a statistically steeper slope ($p < .05$). **Conclusion:** This data demonstrates that EPCs are measurable in toddlers and adolescents and that circulating EPC prevalence is negatively affected by SHS exposure in otherwise healthy children. These data also suggest that effects of SHS on EPCs may be more pronounced in the youngest ages when compared to adolescents, and that imprinting of smoking-related cardiovascular disease may occur very early in life.

P188

Early Growth, Weight Gain Over the Life Course, and Low-Grade Inflammation in Young Adulthood: Northern Finland 1966 Birth Cohort Study

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Background: Low-grade inflammation might mediate associations between poor early life growth, excessive weight gain and subsequent risk of cardiovascular disease in adulthood. Our aim was to investigate relationships between fetal growth, weight over the life course and low-grade inflammation measured by serum high sensitivity C-reactive protein (CRP) levels at 31 years. Methods: Study sample consisted of prospective population-based Northern Finland 1966 Birth Cohort of 5840 participants attending a clinical examination at 31 years, including measurement of CRP. Weight and height were assessed at birth, 12 months, 14 and 31 years of age. Results: C-reactive protein levels at 31 years were 16% (95% CI 8, 23%) higher per 1kg lower birth weight, 21% (95% CI 2, 37%) higher per 10cm lower birth length and 24 % (95% CI 10, 36%) higher per 1 kg/m3 lower ponderal index, after adjustment for potential confounders. Participants with highest tertile body mass index (BMI) at 31 years and lowest tertile birth weight had the highest average CRP levels. Per unit increase in BMI from 14 to 31 years was associated with 16% (95% CI 14, 17%) higher CRP levels; the association was larger for those in the top BMI tertile at age 14 years. Conclusions: Systemic low-grade inflammation may lie on the causal pathway that relates impaired fetal growth and weight gain from childhood to adulthood to adverse adult cardiovascular health. Lifestyle changes from early life might be an important step in reducing cardiovascular risk in adults.

P189

Association of Markers of Inflammation and Hemostasis with the Risk of Sudden Cardiac Death: Atherosclerosis Risk in Communities (ARIC) Study

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OBJECTIVE: This study examines the hypothesis that chronic inflammation is associated with a higher risk of sudden cardiac death as compared to the risk of non-fatal myocardial

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infarction. METHODS: Sudden cardiac death and non-fatal MI events were identified in the ARIC cohort during follow-up from 1987 through 2001. Sudden cardiac death was defined as death adjudicated by a physician panel to be a sudden, pulseless condition without a known non-cardiac cause. Non-fatal MI was defined as incident definite or probable myocardial infarction that did not result in a fatal outcome within 28 days. Markers of inflammation and hemostasis were determined at baseline using standard procedures. Cox proportional hazard regression and multinomial logistic regression were used to estimate associations. RESULTS: Levels of markers of inflammation (albumin and white blood cell count) and hemostasis (fibrinogen, von Willebrand factor, factor VIIIc) were elevated (except for albumin, which was reduced) in cases of sudden cardiac death (n=304) and non-fatal MI (n=930) relative to the respective noncases. In analysis adjusted for the presence of cardiovascular risk factors, diabetes and glucose, gradients of association of fibrinogen, albumin, and white blood cell count, examined over tertiles of distribution and per one SD change, were similar for both endpoints. Associations of the von Willebrand factor (vWF) and factor VIIIc, however, were stronger for sudden cardiac death relative to non-fatal MI (3rd versus 1st tertile hazard ratios: vWF: sudden cardiac death 2.29 (95% CI 1.66, 3.18), non-fatal MI 1.33 (95% CI 1.12, 1.56); factor VIIIc: sudden cardiac death 2.44 (95% CI 1.77, 3.37, non-fatal MI 1.33 (95% CI 1.13, 1.56)). Those associations remained when analysis was limited to never smokers only. CONCLUSION: Greater von Willebrand factor and factor VIIIc are associated with an increased risk of sudden cardiac death as compared non-fatal MI, suggesting that these markers may be particularly important in the etiology of sudden cardiac death.

P190

Tumor Necrosis Factor α and Mortality in Heart Failure in the Community

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Background: Inflammation plays a key role in the pathogenesis of heart failure (HF). The inflammatory cytokine tumor necrosis factor-α (TNFα) has been reported to be elevated in trial patients with severe systolic dysfunction and associated with mortality. Whether this is the case for HF with preserved ejection fraction (EF) is not known. Further, community data on this matter are lacking. **Objective**: To prospectively determine the distribution and correlates of serum TNFα, its association with mortality, and benefit in risk assessment according to EF in a community population with HF. **Methods:** Olmsted County residents with HF were prospectively recruited from July 2004 to March 2007. Clinical characteristics, echocardiography, and TNFα, were measured. Subjects were classified into quartiles of TNFα levels. **Results:** Among 486 participants (mean age 76.7 $\pm$ 13.0 yrs, 49% male, 55% EF$\geq$50%), median TNFα was 2.1pg/mL, (IQR 1.5–3.1pg/mL), and elevated levels ($>$ assay upper limit of normal of 2.8pg/mL) were present in 143 (29%). Higher TNFα was associated with decreased creatinine clearance, current non-smoking status, anemia, and greater comorbidity across the four quartiles ($p_{trend}<0.05$ for all). No association between TNFα and sex, BMI, or NYHA class was detected. Mean follow-up was 17 months. Survival decreased with increase in TNFα ($p=0.016$), with 1-year mortality rates of 16%, 18%, 23%, and 32 % from lowest to highest quartile, respectively. After adjustment for age, sex, and EF, the hazard ratios for death were 1.24, 1.37, and 1.90 from lowest to highest quartile, respectively ($p_{trend}=0.007$), using the lowest quartile as the referent. There was no interaction between TNF and EF. TNFα also contributed to risk assessment as indicated by the increases in the area under the receiver operating characteristics curves obtained in all models examined ($p<0.05$ for all). **Conclusions:** TNFα was elevated in 29% of community HF patients and was associated with renal insufficiency, non-smoking status, anemia, and greater comorbidity. Elevated TNFα is independently associated with mortality irrespective of EF and provides a significant incremental increase in risk assessment above established risk indicators.

P191

Body Iron Stores Are Not Associated with Risk of Coronary Heart Disease in US Men and Women

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Background: Iron overload can generate the production of hydroxyl radicals and promote ischemic myocardial damages in animal models. Nevertheless, epidemiologic studies have shown conflicting results concerning the association between body iron stores and risk of coronary heart disease (CHD). Objective: To assess the hypothesis that higher body iron stores as assessed by plasma ferritin levels are associated with an elevated risk of CHD in U.S. men and women. Design: We identified and confirmed 245 incident non-fatal myocardial infarction or fatal CHD cases and randomly selected 487 controls matched on age, smoking and fasting status among women that provided blood samples in the Nurses' Health Study during up to nine years of follow-up. Among the Physicians' Health Study participants who provided blood samples, 521 cases and 495 controls matched on age and smoking status were selected during up to 18 years of follow-up. We examined plasma ferritin levels with the use of a sandwich immunoassay method among these participants. Results: Among the controls in the Nurse' Health Study in which relatively complete information on diet was available, plasma ferritin levels were significantly correlated with energy-adjusted intake of total iron [Spearman correlation coefficient (r) = 0.12], heme iron (r = 0.12), or red meat (r = 0.15). In both cohorts, plasma ferritin levels were weakly associated with plasma levels of C-reactive protein (r = 0.03 for women and 0.06 for men). After multivariate adjustment for established and potential confounders, plasma ferritin levels were not significantly associated with the risk of developing CHD in either cohort. The relative risks comparing risk of CHD among men and women in the highest quartile to that in the lowest quartile of plasma ferritin levels were 0.95 (95% CI: 0.66, 1.39) and 0.90 (95% CI: 0.54, 1.51), respectively. The pooled relative risk contrasting extreme quartiles was 0.94 (95% CI: 0.69, 1.27; P for trend = 0.49). These associations were not modified by age or smoking status in either sex, or by postmenopausal status in women. Conclusions: Our data do not support the hypothesis that body iron stores are associated with an increased risk of CHD among healthy U.S. men and women.

P192

Lipoprotein-Associated Phospholipase A2 in Heart Failure: Impact on Mortality Risk Assessment in the Community

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Background: Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a useful prognostic marker in patients with coronary artery disease, but little is known of its role in heart failure (HF). We evaluated the association of Lp-PLA2 with death after HF and examined its incremental value for risk assessment over established risk factors. **Methods and Results:** Residents of Olmsted County, MN, diagnosed with HF between September 2003 and April 2007 (n=646; mean age 76 [SD 13] years; 51% women) were prospectively enrolled and followed. Lp-PLA2 levels were measured at baseline and evaluated along with various risk indicators. Lp-PLA2 was positively associated with male gender and LDL cholesterol and inversely associated with statin use and diabetes. During follow up (mean=18 months), 213 deaths occurred. Lp-PLA2 was moderately associated with mortality (hazard ratio [HR]=1.42; 95% confidence interval [CI]: 1.01–1.99, for highest [$\geq$280 ng/mL] vs. lowest [$\leq$220 ng/mL] tertile, adjusted for age, sex, and comorbidities). However, the latter relationship was modified by age ($P_{interaction}=0.009$), with a strong association in younger patients (fully adjusted HR=2.84; 95% CI: 1.54–5.23, for age$\leq$80 years) and none in older ones (fully adjusted HR=0.86; 95% CI: 0.54–1.38, for age$>$80 years). For patients aged 80 years or less (n=354), Lp-PLA2 markedly increased the areas under the receiver operating characteristic (ROC) curves over established predictors (Table). **Conclusions:** In this community-based cohort of HF, Lp-PLA2 was strongly and independently associated with mortality and had a major impact on risk prediction over traditional risk factors in those who were younger.

Variables Included in the Model	Area Under the ROC Curve: Without Lp-PLA2	With Lp-PLA2 Added	P
None	0.5	0.600	0.003
Age, sex, and comorbidity	0.625	0.674	0.005
+ hypertension, diabetes, current smoking, hyperlipidemia, and statin use	0.656	0.706	0.002
+ ejection fraction, NYHA class, and C-reactive protein	0.704	0.731	0.04

P193

Coagulation Factors II, V, IX, X, XI, XII, Plasminogen and α-2 Antiplasmin and Risk of Coronary Heart Disease: A Case-Cohort Study in ARIC

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BACKGROUND Previous prospective studies reported associations of several hemostatic factors, such as fibrinogen, coagulation factors VII and VIII, von Willebrand factor, tissue plasminogen activator antigen or plasminogen activator inhibitor-1, with coronary heart disease (CHD), but few studies have examined other hemostatic factors. We performed a case-cohort study of the associations of coagulation factors II, V, IX, X, XI, XII, plasminogen and α-2 antiplasmin with CHD. Our a priori hypothesis was that these factors would be positively associated with incident CHD. **METHODS** An ARIC case-cohort sample consisted of 412 black or white CHD or stroke cases and a cohort random sample (CRS) of n=412, matched to the cases by sex, race and age group. Subjects were aged 47–68 at exam 2 of ARIC (1990–92) and initially free of CHD and stroke. In the present study, we included the 368 CHD cases and the entire CRS. The hazard ratio and 95% confidence interval (HR [95%CI]) for CHD were calculated according to quartiles of each coagulation/fibrinolytic factor using sample weighting via Barlow's methods. Trends tests were conducted using continuous variables. **RESULTS** After adjustment for age, sex and race, coagulation factors IX, XI and α-2 antiplasmin were associated positively with risk of CHD (HR for highest vs lowest quartile was 1.38 [0.92–2.06], p for trend =0.009 for factor IX, 2.05 [1.34–3.16], p for trend =0.002 for factor XI, and 1.45 [0.93–2.25] for α-2 antiplasmin, p for trend =0.01). However, these hemostatic factors were correlated with classical risk factors, so that after adjustment their associations with CHD were attenuated and no longer statistically significant. No associations were observed for factor II, V, X, XII or plasminogen. **CONCLUSIONS** The associations of factor IX, XI and α-2 antiplasmin with incident CHD were not strong and were accounted for by confounding with classical risk factors.

P194

The Influence of an Imprecise Gold Standard on Estimating Kidney Function

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Background: Kidney function based on estimated glomerular filtration rate (eGFR) from serum creatinine (cr) or cystatin C (cys) has been studied as a cardiovascular risk factor. We evaluated

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the accuracy of different GFR estimates while quantifying the imprecision in the gold standard measured GFR (mGFR). **Methods:** We selected participants from the African American Study in Kidney Disease and Hypertension (AASK) and Modification in Diet in Renal Disease (MDRD) Study with at least 2 baseline mGFR values as well as serum cr and cys measurements. GFR was measured using urinary clearance of ^{121}I-iothalamate. We evaluated the performance of cys and scr in predicting a single mGFR, the average of 2 mGFRs, and the average of 3 mGFRs. The models were then modified to predict mGFRs before and after excluding discrepant GFRs (% difference > 25%). Accuracy was measured as the percentage of estimates within 30% (p30) of the gold standard. **Results:** The average of eGFR from cys and eGFR from the MDRD Study equation performed better (p30=91.7%) than cys or MDRD alone (p30=83.5%, p30=87.9%). The model using the average of eGFR from cys and eGFR from MDRD equation to predict mGFR after the exclusion of discrepant mGFRs (p30=93.5%) performed as well as the mGFR at another visit (p30=93.6%) separated by an average of 62 days. The table compares the performance of each model. **Conclusions:** Estimating GFR with multiple markers may result in as much precision as a single gold standard measurement. Using data from multiple visits provides a promising approach for overcoming a gold standard with limited precision.

ACCURACY OF MODELS FOR ESTIMATING GFR FROM 121-IOTHALAMATE CLEARANCE

	P30 from single mGFR		P30 from avg of 2 mGFRs		P30 from avg of 3 mGFRs	
Estimate	Before (n=1995)	After (n=1746)	Before (n=1995)	After (n=1746)	Before (n=1268)	After (n=973)
#1 Cystatin C	83.5%	84.7%	85.9%	86.3%	86.8%	87.2%
#2 MDRD Study Equation	87.9%	88.9%	88.3%	89.5%	90.0%	92.0%
Average of Estimate #1 and Estimate #2	91.7%	93.5%	93.5%	94.2%	94.2%	95.9%
Measured GFR at another visit	93.6%	–	93.2%	94.2%	–	–

Exclusion Criteria = % difference > 25%

P195

Sensitive C-Reactive Protein and the Risk of Type 2 Diabetes Mellitus: A Prospective Study in Finland

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Objectives: C-reactive protein (CRP) is an acute phase protein and sensitive marker of inflammation. Increased CRP is associated with increased cardiovascular disease (CVD) risk in prospective studies. The aim of the present study is to assess, whether sensitive CRP predicts also the development of type 2 diabetes mellitus. Methods: The study cohort includes 6299 men and 6562 women aged 35 to 74 years, free of diagnosed diabetes at baseline, who participated in a CVD risk factor survey in 1997 or 2002 in Finland. CRP was analyzed using an immunoturbidometric method. The study cohort was followed until the end of 2006 through computerized record linkage. Hazard ratio (HR) of diabetes was assessed for sex specific CRP quartiles using Cox proportional hazard models. Results: During the follow-up 242 men and 122 women developed incident diabetes. Among men the age-adjusted HR of diabetes increased from the lowest to the highest CRP quartile as follows: 1.0, 1.61, 3.69 and 4.74 (p for the trend <0.001) and in women: 1.0, 1.43, 4.71 and 13.0 ($p<0.001$). After further adjustment for education, physical activity, smoking, dietary variables, alcohol and coffee drinking, systolic blood pressure and waist-to-hip ratio the HRs were 1.0, 1.37, 2.55 and 2.65 ($p<0.001$) in men and 1.0, 1.51, 3.69 and 7.46 ($p<0.001$) in women. The HRs remained significant also after exclusion of subjects with coronary heart disease, stroke and cancer at baseline. CPR had a stronger association with diabetes in women than in men (p for interaction: $\chi2=4.57$, 1df, $p=0.033$), but the association did not differ between age groups, by smoking status, level of obesity, or alcohol drinking habit. Conclusions: CRP is a significant predictor of type 2 diabetes in the general population. It can be used as an additional risk marker for screening high-risk people.

P196

Withdrawn

P197

High Plasma Tissue Factor Level Is an Independent Risk Marker of Recurrent Cardiovascular Events in Postinfarction Patients

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Proinflammatory and procoagulant factors play a critical role in the thrombotic complications of atherosclerotic coronary artery disease. Exposure of tissue factor (TF) in vulnerable plaques is believed to initiate intravascular thrombus formation while circulating TF is hypothesized to participate in the propagation and formation of an occlusive thrombus. To determine whether elevated plasma TF is associated with an increased risk of recurrent coronary events, we measured plasma TF levels in a subset of 136 participants in the **Thrombo**genic Factors and Recurrent Coronary Events (**THROMBO**) **study using** a well characterized ELISA developed in our laboratory. In a nested case comparison study, 70 cases with recurrent cardiovascular (CV) events within 18 months (fatal or nonfatal CV event or unstable angina pectoris) were m:n matched for decade of age, sex and diabetes status with 66 non-cases without recurrent events who had at least 18 months of event-free follow-up. Evaluation of the TF ELISA showed an average plasma TF of 27.0 pg/mL (SD 12.9) among 15 healthy controls, and 26.9 pg/mL (SD 3.94, n=6) using pooled plasma controls, with an interassay coefficient of variability of 14.7%. When adjusted only for the matching variables, TF was significantly associated with recurrent CV events whether modeled as a continuous variable (OR 1.03, 95% CI 1.01–1.05, p=0.007) or dichotomized at its 75th percentile of 62 (OR 4.9, 95% CI 1.7–13.6, p=0.003). Adjusted for other covariates via multivariable conditional logistic regression, TF remained a significant predictor of recurrent events. The only covariates that were significant in addition to continuous TF were prior angina pectoris among diabetics (OR 12.0, 95% CI 2.5–57.3, p=0.002), but not among non-diabetics (OR 1.3, 95% CI 0.5–3.3, p=0.533), and white race (OR 0.26, 95% CI 0.09–0.72, p=0.009). All biomarkers (lipid, inflammatory and hemostatic factors dichotomized at their 75th percentile) were insignificant. Similar results were obtained when dichotomizing TF. These results suggest that elevated plasma TF is an independent risk marker of recurrent CV events in stable post-infarction patients.

P198

Contribution of Novel Biomarkers to Incident Stable Angina and Acute Coronary Syndrome in Asymptomatic Men: The Prime Study

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Background: the histopathological observations that inflammation and acute thrombosis are more closely associated with acute coronary syndrome (ACS) than stable angina (SA) have not been yet explored on an epidemiological basis. Our aim was thus to compare the association of some novel biomarkers with incident SA and ACS in the population **Methods**: We used data from the PRIME Study, a prospective cohort of 9758 asymptomatic middle-aged men recruited in Belfast (Northern Ireland), Strasbourg, Lille and Toulouse (France) between 1991 and 1993. A nested case-control study has been performed after the completion of 5 years of follow-up, using the baseline plasma sample of 292 incident coronary events and 580 matched controls (2 controls by case). Association of each biomarker with SA and ACS was estimated in separate conditional logistic regression analysis contrasting the fourth against the first quartile of every biomarker. Odds ratios (OR) were thereafter compared using a z-test. **Results**: After 5 years of follow-up, 114 incident SA and 178 ACS (40 cases of unstable angina and 138 fatal and non-fatal myocardial infarctions) were validated (adjudication medical committee). After adjustment for traditional risk factors, higher circulating levels of hs-CRP, ICAM1, interleukin 6 and interleukin 18 were associated with both SA and ACS but the differences were not statistically significant (all p-values>0.05). Elevated levels of fibrinogen, von Willebrand factor and possibly higher level of D-Dimers and lower level of Tissue Factor Pathway Inhibitor were associated with ACS only, but the difference was statistically significant for von Willebrand factor specifically ($OR_{4th\ against\ 1st\ quartile}=3.21$ (1.65–6.23) vs. 0.85 (0.37–1.94) ; $p_{z\text{-}test}=0.01$). Association of von Willebrand factor with ACS persisted after additional adjustment for hs-CRP and IL-6 (OR: 2.84 (1.38–5.85), suggesting that mechanisms other than inflammation may be also involved. **Conclusion**: the present data suggest that stable angina and acute coronary syndrome may not share all the same risk factors. In particular, higher level of von Willebrand factor may be more predictive of incident ACS than SA in initially asymptomatic men.

P199

Lifestyle and Clinical Characteristics Associated with Lipoprotein-Associated Phospholipase A2 Activity in Women

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Lipoprotein-associated phospholipase A_2 (Lp-PLA_2) is a pro-inflammatory enzyme that has consistently been shown to be associated with elevated risk of coronary heart disease. Although there is substantial variability in Lp-PLA_2 activity in free living healthy adult populations, no study to date has examined lifestyle and clinical characteristics which contribute to differences in circulating levels. We measured Lp-PLA_2 using a colorimetric activity assay in 858 female participants of the Nurses' Health Study who provided a blood sample in 1990 and were controls in a nested case-control study of myocardial infarction. Women were between the ages of 43 and 70 at the time of blood draw and were free of cancer and cardiovascular disease. Lifestyle variables included body mass index, smoking status, physical activity, aspirin use, and alcohol intake. Clinical characteristics included hypercholesterolemia, hypertension, diabetes, cholesterol-lowering medication use, and post-menopausal hormone use. Multivariable linear regression models were constructed with Lp-PLA_2 activity as the dependent variable and age, fasting status at blood draw, and the above mentioned participant characteristics as independent variables. In the fully adjusted model, hypercholesterolemia (β = 15.9nmol/mL/min increase in Lp-PLA_2, $p < 0.0001$), current smoking (β = 12.0, $p < 0.0001$), and being overweight or obese (β = 3.9, $p = 0.04$) were associated with significantly elevated Lp-PLA_2 activity. Lp-PLA_2 activity was significantly lower in those who currently used post-menopausal hormones (β = -5.0, $p < 0.0001$). Other characteristics listed above were not significantly associated with Lp-PLA_2 activity. The present study identified smoking, overweight or obesity, and hypercholesterolemia as characteristics that were associated with increased Lp-PLA_2, whereas post-menopausal hormone use was inversely associated with Lp-PLA_2. These represent potentially modifiable characteristics that can help favorably alter Lp-PLA_2 levels. In addition, since several of these characteristics are well established risk factors for CHD, their association with Lp-PLA_2 may suggest a plausible biological pathway between these characteristics and CHD.

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P200

Association of Monocyte and Platelet Markers with Peripheral Arterial Disease: ARIC Carotid MRI Study

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Peripheral artery disease (PAD), characterized by an ankle-brachial index <0.9, is an important manifestation of systemic atherosclerosis. PAD is associated with elevated risk of thrombotic and inflammatory complications, including CHD and stroke events. Circulating monocytes and tissue macrophages are a major source of inflammatory cytokines, and platelet hyper-reactivity contributes to thrombosis. We performed a cross-sectional epidemiologic study of blood cells from 219 PAD cases and 1655 non-cases from the ARIC Carotid MRI Study, and used flow cytometry, a novel tool for epidemiologic studies, to measure platelet receptors GP IIb, and GP IIIa, platelet activation markers P-selectin and CD40L, platelet-monocyte complexes (PMC), and monocyte expression of CD14, toll-like receptors -2 and -4 (TLR-2, TLR-4), P-selectin glycoprotein ligand-1, and myeloperoxidase (MPO). Traditional risk factors were associated with PAD in the expected direction: PAD cases were older, more often African-American, smokers, had high blood pressure, diabetes, elevated BMI and CRP, and had lower HDL-C. After adjusting for age, gender, race and field center, platelet CD40L median fluorescence intensity (MFI) (12.19 vs 12.47, $p=0.005$), and MPO MFI (94.56 vs 104.57, $p=0.0001$) remained significantly lower, and monocyte TLR-4 (%) (65.46 vs 64.53, $p=0.013$) higher, in PAD cases than noncases. CD40L correlated with platelet P-selectin ($R=0.44$). The lower expression of platelet activation markers in PAD patients may indicate persisting platelet activation and degranulation, resulting in a depleted platelet population in circulation. More interestingly, monocyte TLR-4 was higher and intracellular MPO level was significantly lower in PAD cases than non-cases, indicating monocyte activation and significant reduction of monocyte MPO content. Most likely, monocytes release MPO upon activation, which binds to vessel wall, and by its oxidative properties contributes to peripheral arterial disease. Our study results indicate that both platelet and monocyte activation play a significant role in pathogenesis of PAD.

P201

Correlates of N-Terminal Prohormone Brain Natriuretic Peptides in African Americans Without Heart Failure: The African-American Study of Kidney Disease and Hypertension (AASK)

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End stage renal disease is strongly associated with the development of heart failure, though it remains unclear whether moderate kidney disease also imparts an increased risk. N-terminal prohormone brain natriuretic peptide (NT-proBNP) reflects cardiac stress and is used as a diagnostic biomarker of heart failure. Previous studies suggest that anemia and lower kidney function are associated with higher levels of NT-proBNP among individuals with heart failure. Few other factors have been studied and data from those without heart failure and from African-Americans are limited. The current investigation explores cross-sectional correlates of NT-proBNP in a population of African-Americans with chronic kidney disease. The AASK trial enrolled non-diabetic African Americans with hypertensive kidney disease (glomerular filtration rate [GFR] $= 20-65$ ml/min/1.73m^2) and no evidence of clinical heart failure. NT-proBNP was measured using a sandwich chemiluminescence immunoassay (CV=2.9%) in 982 AASK participants. In unadjusted analyses, hematocrit ($r=-0.05$; $p<0.001$), GFR ($r=-0.21$; $p<0.001$) and body mass index (BMI; $r=-.05$; $p=0.09$) were inversely correlated with log NT-proBNP levels. Systolic blood pressure ($r=0.19$; $p<0.001$) and log urinary protein:creatinine ratio ($r=0.19$; $p<0.001$) were positively correlated with log NT-proBNP levels. After adjustment, lower hematocrit and GFR, and higher systolic blood pressure and protein:creatinine ratio remained associated with higher NT-proBNP. Adjusted* linear regression coefficients for change in log BNP associated with 1 SD change in covariate Lower hematocrit and lower GFR may indicate volume expansion in chronic kidney disease. Urinary protein excretion is a marker of endothelial dysfunction. These results suggest that these processes in CKD are associated with concomitant cardiac stress and may play a role in the development of heart failure.

	SD	Adjusted* Coefficient (95% CI)
Hematocrit	4.92	-0.15 (-0.24, -0.06)
Glomerular filtration rate	13.62	-0.37 (-0.45, -0.28)
Log protein:creatinine ratio	1.53	0.23 (0.14, 0.32)
Systolic blood pressure	23.93	0.30 (0.19, 0.41)
Body mass index	6.60	-0.04 (-0.12, 0.04)

*Adjusted for covariates listed and age, HDL and non-HDL cholesterol, diastolic blood pressure, prior heart disease, electrocardiographic evidence of LVH and duration of hypertension.

P202

Low Heart Rate Variability Is Associated with Incident Coronary Artery Disease in Siblings of Patients with Premature Coronary Artery Disease

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Background: Autonomic dysfunction in terms of decreased heart rate variability (HRV) predicts incident coronary artery disease (CAD) over the short term; this association is not well studied in apparently healthy at-risk populations over the long term. We prospectively examined the association of HRV and incidence of CAD in healthy siblings of persons with premature CAD. **Methods**: We performed Fourier analysis on 24-hour ambulatory ECG recordings in healthy young siblings (30–59 years, $N = 328$) of patients with premature CAD < 60 years. The normalized fraction of total spectral power at high frequencies (HF, 0.125–0.5Hz, marker of vagal activity), low frequencies (LF, 0.05 - 0.125Hz, marker of sympathetic activity), and summary variables (HF+LF, sum of sympatho-vagal function, and LF/HF ratio, sympatho-vagal balance) were calculated as indices of HRV. Incident first CAD events (sudden cardiac death, myocardial infarction, unstable angina, or coronary revascularization) over 10-year follow-up were analyzed using Cox regression, adjusting for age, sex, smoking, diabetes, hypertension, total and HDL cholesterol. Interaction of HRV with diabetes, which may cause autonomic neuropathy, was assessed. **Results**: A total of 37 CAD events occurred during the follow-up period. The table shows that there was a significantly higher adjusted risk of incident CAD with lower baseline levels of normalized LF and HF. These associations were qualitatively retained and jointly significant when both LF and HF were covariates. The sum HF+LF was also significantly associated with CAD risk, but the ratio LF/HF was not. Baseline diabetes did not modify the CAD risk association for LF ($p = 0.25$) or HF ($p = 0.45$). **Conclusion**: In apparently healthy siblings of patients with premature CAD there is increased CAD risk associated with both impaired sympathetic and vagal control. Instead of counterbalancing one another, the vagal and sympathetic impairments are additive to long-term risk.

ASSOCIATION OF HEART RATE AND VARIABILITY WITH INCIDENT CAD

	Heart Rate (beats/min)	LF (fraction of total power)	HF (fraction of total power)	LF adjusted for HF (fraction of total power)	HF adjusted for LF (fraction of total power)	LF+HF (fraction of total power)	LF/HF (ratio)
Relative Hazard (per 1 SD of lower rate or HRV measure)	1.10	1.42	1.60	1.33	1.45	1.74	0.77
p-value (Wald test)	0.58	0.03	0.05	0.04*	0.01	0.11	

*Because of the high correlation between HF and LF (Pearson $r = 0.41$), Wald tests for each variable in the combined model was non-significant, omnibus chi-squared test performed.

P203

Different Relationship Between Cystatin C Levels Predicts Progression of Coronary Atherosclerosis in People with and Without Type 1 Diabetes

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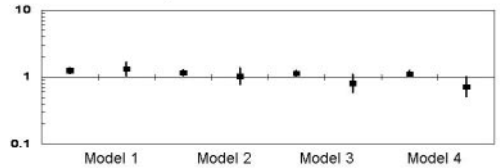
Elevated cystatin C, a marker of renal dysfunction, predicts progression of coronary atherosclerosis (CA) in adults with type 1 diabetes (T1D) in the Coronary Artery Calcification in Type 1 Diabetes (CACTI) Study. In contrast, studies have reported a vasculo-protective role for cystatin C. We investigated cystatin C's relationship to CA progression in people with and without T1D. Coronary artery calcification (CAC) was measured twice (Imatron C-150), over 2.4 ± 0.4 yrs ($n=1123$, 45% male, age 37 ± 9 yr, 45% T1D, duration 23 ± 9 yr). CA progression ($n=195$) was defined as either CAC progression (>2.5 increase in square root calcium volume score) or incident CAD. Cystatin C's relationship to CA progression was determined univariately, in stepwise multiple logistic regression stratified by T1D and then combined with a cystatin C*T1D interaction term. Cystatin C was higher in T1D than non-T1D subjects (0.85 ± 0.39 mg/L v 0.78 ± 0.10, $p<0.0001$). Univariately, cystatin C (per 0.1 mg/L) was related to CA progression in T1D (OR=1.26, 95% CI: 1.15–1.38, $p<0.0001$) and non-T1D subjects (OR=1.33, 95% CI: 1.04–1.70, $p=0.02$). In stratified multiple logistic regression, elevated cystatin C (indicating worsening renal function) predicts CA progression in T1D subjects (OR=1.11, 95% CI: 1.00–1.22, $p=0.048$); conversely, in non-T1D subjects, increasing cystatin C predicts lower CA progression (OR=0.63, 95% CI: 0.43–0.93, $p=0.02$; $p=0.006$ for cystatin C*T1D interaction). A non-stratified model (Fig 1) revealed similar results. Our data suggest a complex relationship between cystatin C and CA requiring further study prior to routine use of cystatin C as a bio-marker of renal function and predictor of CA.

Association between Cystatin C and CA Progression in Non-Stratified Models with a Cystatin C*T1D Interaction Term Included



Model	T1D	Non-T1D	Cystatin C*T1D
	OR (95%CI), p-value	OR (95%CI), p-value	p-value
Cystatin C, T1D status	1.26 (1.15-1.38) <0.0001	1.33 (1.04-1.69) 0.029	0.70
Above + age, baseline CAC, sex	1.16 (1.06-1.28) 0.002	1.03 (0.78-1.38) 0.82	0.44
Above + BMI, SBP, HDL	1.14 (1.04-1.27) 0.007	0.81 (0.59-1.10) 0.17	0.03
Above + BMI*T1D, SBP*T1D	1.13 (1.03-1.26) 0.01	0.73 (0.52-1.02) 0.067	0.01

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P204

Ambient Particulate Matter Air Pollution (PM) and Myocardial Ischemia: The Environmental Epidemiology of Arrhythmogenesis in the Women's Health Initiative (EEAWHI)

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Background The mechanisms by which PM increases coronary heart disease (CHD) mortality remain unclear. We therefore examined the association between PM and myocardial ischemia, an important factor in arrhythmogenesis. **Methods** We conducted our examination in EEAWHI, an ancillary study of Women's Health Initiative clinical trial participants. We focused on first-recorded, high-quality, resting, standard 12-lead ECGs among 57908 participants with residential addresses in the contiguous U.S. who were examined at 49 sites from 1999–2003. We used Minnesota Code criteria to identify ST segment (ST) and T wave (T) abnormalities associated with myocardial ischemia. We also estimated T amplitude (μV). We used data from EPA Air Quality System monitors and national-scale, log-normal kriging to spatially interpolate daily mean, residence-specific concentrations of PM $<$ 2.5 μm in diameter ($PM_{2.5}$, $\mu g/m^3$) at geocoded addresses of participants during the study period. Analyses excluded 2379 women with QRS $>$ 120 ms. **Results** Overall, 6% of women (aged 52–90 yr; 83% non-Hispanic White) had ST and 16% had T abnormalities. Lead-specific T amplitude was normally distributed (range of means = -14 to 348 μV). Mean (SD) $PM_{2.5}$ averaged over the preceding 0–2 days was 14 (7) $\mu g/m^3$. We used logistic and linear regression models adjusted for demographic, clinical, temporal and climatic factors to estimate strength of association and test for interactions. A 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 3% (95%CI = -3%, 10%) increase in the odds of ST abnormality and 5% (0%, 9%) increase in the odds of T abnormality. Corresponding decreases in T amplitude were observed in all ECG leads except V1, reaching a minimum of -2 (-5, 0) μV in lead V3. Effects were slightly stronger among users v. non-users of β-blockers: 10% (1%, 20%) v. 3% (-1%, 8%) increases in the odds of T abnormality (p = 0.198) and -8 (-15, -1) v. -2 (-4, 1) μV decreases in T amplitude (p = 0.076), but in general, there was little suggestion of effect measure modification by CHD or its major risk factors. **Conclusions** Acute exposure to $PM_{2.5}$ is associated with ECG evidence of myocardial ischemia among postmenopausal women. The principal manifestations include subclinical, but potentially arrhythmogenic decreases in T wave amplitude.

P205

Pesticides and Myocardial Infarction Incidence and Mortality Among Male Pesticide Applicators in the Agricultural Health Study

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Background: Acute organophosphate and carbamate pesticide poisonings have been shown to result in adverse cardiac outcomes. Low-level pesticide exposure has not been assessed as a potential risk factor for myocardial infarction (MI). Methods: Using data from the Agricultural Health Study, we analyzed self-reported lifetime use of pesticides from enrollment (1993–1997) and self-reported doctor-diagnosed incident myocardial infarction diagnoses from follow-up interviews (1999–2003) among male pesticide applicators to assess non-fatal MI incidence. We also analyzed mortality through 2004. Using proportional hazard models we estimated the association between lifetime use patterns of 50 pesticides and myocardial infarction incidence and mortality. Results: We observed 665 nonfatal self-reported MI incidents among the 27,231 participants who completed the follow-up interview and 452 MI deaths among the 55,569 men enrolled in the study. We saw associations between MI incidence and mortality and commonly associated risk factors, including age, BMI, and history of smoking. However, we saw no evidence of an association between MI and ever having used pesticides, individually or by class (e.g., organophosphate hazard rate ratio (HRR) = 0.88, 95% confidence interval (CI) = 0.69, 1.12, carbamate HRR = 1.11, 95% CI = 0.92, 1.35, organochlorine HRR = 1.19, 95% CI = 0.99, 1.44). Additionally, there was no evidence of a dose response with any measure of pesticide exposure. The study has 80% power to detect hazard rate ratios as low as 1.24 and 1.57 for pesticides with exposure prevalence of 50% and 5%, respectively. Conclusions: In a population with low risk for MI, we see no increased risk of MI incidence or mortality associated with the occupational use of pesticides.

P206

Future Coronary Heart Disease Attributable to Passive Smoking in China

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BACKGROUND: Passive cigarette smoking leads to increased risk for CHD and noncoronary diseases. Of 313 million Chinese nonsmokers, 69% are women, and many are exposed to passive smoking. We simulated the CHD and nonCHD effects of eliminating passive smoking in China over 2010–2030. **METHODS:** The CHD Policy Model-China is a computer simulation of the future epidemic of CHD in China. Self-reported prevalence of passive smoking in Chinese adults was obtained from the 2000–2001 nationally representative International Collaborative Study of Cardiovascular Disease in Asia. Passive smoke exposure was assumed to carry a 1.26 higher relative risk for myocardial infarction or arrest. First, we simulated CHD and nonCHD outcomes over 2010–30 assuming persistence of current levels of active and passive smoking. Second, holding active smoking constant, we simulated incremental changes with eliminating passive smoking. **RESULTS:** Prevalence of passive smoke exposure was 63, 55, 52, and 35% among non-smoking Chinese women aged 35–44, 45–54, 55–64, and 65–84 years. Prevalence in non-smoking men was 33, 34, 32, and 23%. We predicted 16.3 million total deaths will be attributable to passive smoking in China over 2010–30, and almost 80% of these will be in women (Table). With elimination of passive smoking, CHD outcomes were reduced most in adults $<$65 years old. Overall mortality reductions led to increases in the population at risk for CHD. Absolute CHD incidence consequently increased in persons $\geq$65 years old. **CONCLUSIONS:** Elimination of passive smoking in China would reduce CHD and noncoronary deaths, especially among women. Tobacco control efforts in China should target passive and active cigarette smoking.

TABLE. PREDICTED CORONARY AND NONCORONARY OUTCOMES ATTRIBUTABLE TO PASSIVE SMOKING OVER THE YEARS 2010–2030 IN CHINESE MEN AND WOMEN AGED 35–64 OR ≥65 YEARS OLD, THE CHD POLICY MODEL-CHINA

	Men		Women	
	35–64	≥ 65	35–64	≥ 65
Predictions assuming	6,448,120,000	1,581,475,000	6,176,184,000	1,698,577,000
no change in current	10,323,000	10,245,000	7,513,000	9,040,000
passive smoking	14,929,000	15,304,000	10,021,000	13,918,000
Person-years, 2010–30	3,803,000	8,074,000	2,108,000	6,197,000
New CHD cases Total	39,095,000	73,459,000	23,609,000	62,906,000
CHD events CHD deaths				
Non-CHD deaths				
Incremental changes	+1,013,000	+14,052,000	+32,624,000	+64,540,000
with elimination of	-109,000	+48,000	-118,000	+368,000
passive smoking	-227,803	-25,000	-249,000	+178,000
Person-years, 2010–30	-91,000	-99,000	-107,000	-148,000
New CHD cases Total	-1,529,000	-1,632,000	-6,015,000	-6,716,000
CHD events CHD deaths				
Non-CHD deaths				

P207

Transcription Factor 7-Like 2 Polymorphism and Context-Specific Lifetime Risk of Type 2 Diabetes in African-American and Caucasian Adults: The Atherosclerosis Risk in Communities (ARIC) Study

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Genetic variants in the transcription factor 7-like 2 gene (TCF7L2) have been consistently associated with type 2 diabetes mellitus (T2DM). However, large population-based studies of African-Americans are lacking. Moreover, few studies have assessed the metabolic context of TCF7L2 effects on T2DM. Understanding the putative effect of genetic susceptibility variants in the metabolic context of T2DM is of substantial public health relevance. Therefore, we investigated the association of the TCF7L2 rs7903146 polymorphism with prevalent T2DM, and its metabolic-specific effects in 3,813 African-American and 10,732 Caucasian middle-aged adults in the ARIC cohort. T2DM was defined by a fasting or nonfasting glucose concentration, self-reported physician diagnosis, or pharmacological treatment. The T risk allele was more prevalent in diabetics compared to non-diabetics at baseline (33 vs. 29%, in African-Americans; 35 vs. 29%, in Caucasians). Individuals heterozygote (CT) and homozygote (TT) for the risk allele had higher cumulative lifetime risks (95%CI) of T2DM by age 55 years vs. wild-type (CC) individuals in African-Americans [21.8% (19.8–24.0%) and 25.6% (21.0–30.7%) vs. 18.2% (16.5–20.1%)] and also Caucasians [10.2% (9.3–11.1%) and 12.0% (10.1–14.2%) vs. 7.5% (6.8–8.2%)]. The relationship between the T allele and prevalent T2DM was additively modified by obesity, hypertension, and low HDL. Individuals with one or two T alleles had the highest cumulative risk of T2DM if they were obese, had hypertension and low HDL, followed by individuals with any two, those with any one, and those with none of the traits. For example, individuals with three abnormal metabolic traits and the CC, CT, or TT genotype had significantly higher age-, gender- and center-adjusted odds (95% CI) of T2DM relative to those with the CC genotype and none of the traits (referent) in African-Americans [10.6 (6.3–17.7), 16.2 (9.6–27.3), and 18.4 (7.3–46.5)] and also Caucasians [11.9 (8.3–16.9), 17.0 (11.8–24.4), and 19.5 (10.2–37.0)]. Our study demonstrates the importance of this susceptibility variant among African-Americans and suggests an important additive interaction with known metabolic risk factors in increasing the susceptibility to T2DM conveyed by TCF7L2.

P208

Common Variant in the Lipoprotein Lipase Gene and Risk of Coronary Heart Disease Among Women and Men: Potential Interaction with Obesity

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Background: High lipoprotein lipase (LPL) activity is associated with lower plasma triglyceride levels. The S447X variant has been suggested to be of greater significance among individuals where the lipid transport system is under stress, such as in obesity. **Objective:** To investigate the association between the LPL S447X variant and risk of coronary heart disease (CHD), and to address if obesity was a modifier of this association. **Methods and Results:** The S447X

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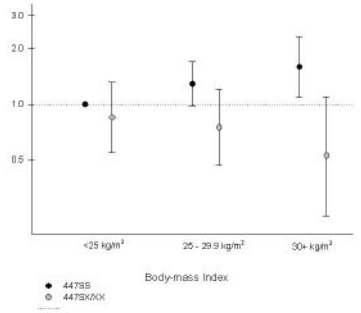
polymorphism was genotyped in two parallel nested case-control studies of incident CHD in the Nurses' Health and Health Professionals Follow-up Studies where 246 and 259 cases, respectively, were matched to controls (1:2) on age and smoking. LPL S447X genotype was associated with a lower risk of CHD in both study populations in a co-dominant fashion. Due to few 447X homozygotes (MAF: 0.12), we contrasted carriers vs. non-carriers. In the pooled study sample, the odds ratio (OR) for CHD among 447X carriers was 0.54 (95% confidence interval [95% CI], 0.34–0.86), compared to non-carriers. This association was modified by obesity (p for interaction: 0.01). Compared to non-carriers, who were lean (body-mass index [BMI] <25 kg/m^2), the OR for CHD among obese individuals (BMI ≥ 30 kg/m^2) was 1.59 (95% CI, 1.09–2.32) in non-carriers and 0.53 (95% CI, 0.25–1.10) in 447X carriers (see figure). Compared to non-carriers, the 447X-carriers had lower plasma triglyceride ($p<0.001$), and this was also observed among those with highest BMI. **Conclusions:** The LPL S447X variant was associated with lower plasma triglycerides and a lower risk of CHD. Carriers of this common variant did not have elevated risk of CHD typically associated with obesity.

Figure. Joint effects of the S447X LPL genotype and body-mass index on the risk of CHD in the pooled Nurses' Health and Health Professionals Follow-Up Studies.



P209

LDL Receptor Haplotypes and Coronary Heart Disease in African-American Participants in the Atherosclerosis Risk in Communities Study

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Mutations of the LDL receptor (LDLR) cause Familial Hypercholesterolemia and premature atherosclerosis. We have previously showed that LDLR variants affect circulating lipid values in the Atherosclerosis in Communities (ARIC) study. In this study, we evaluated the association of LDLR genetic variants and incident CHD. Two single nucleotide polymorphisms in the 3' regulatory region of LDLR [rs1433099 (C44857T) and rs2738466 (A44964G)] were genotyped in White and African American ARIC participants. LDLR haplotypes were estimated using the phase reconstruction method (PHASE 2.1). We excluded individuals with prevalent CHD and those using anti-lipid drugs. In each race strata, the associations between LDLR haplotypes and CHD events (hospitalized, fatal, or EKG diagnoses of myocardial infarct, or coronary revascularization procedures) obtained through December 2004 were estimated using Cox proportional hazard models adjusting for age, sex, hypertension, diabetes, BMI and smoking. Two common haplotypes were observed: CA and TA. The CA haplotype occurred at frequencies of 50% and 22%, for 1 and 2 copies, respectively, among Whites, and 41% and 9%, for 1 and 2 copies, respectively, among African American participants. TA haplotype frequencies for 1 and 2 copies were 8% and 39%, respectively for Whites, and 50% and 28%, respectively for African American individuals. Mean follow-up was 15 years, with 1298 CHD events among 9698 White individuals, and 380 CHD events among 3438 African American individuals. Carrying 1 or 2 copies of the LDLR CA haplotype was associated with fewer CHD events (hazard ratio [HR] 0.76, 95% confidence interval [CI] 0.62, 0.93) compared to those that did not carry any copies of the haplotype, and each additional copy of the LDLR TA haplotype was significantly associated with more CHD events (HR 1.20, 95% CI 1.04, 1.39) among African American but not White individuals. Additional ajustment for baseline HDL and LDL did not substantially change these findings. Further research adjusting for changes in lipid values across time, to test if the association is independent of lipid levels, is needed. These results suggest that genetic variants in the promoter of the LDLR may influence CHD in African American individuals.

P210

Novel Association of Hepatic Nuclear Factor 4α (HNF4α) Variants with Triglycerides in a Population of African Descent: The Tobago Family Health Study

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Background: Individuals of African heritage have less atherogenic lipoprotein profile than Caucasians, characterized by lower levels of triglycerides (TG) and higher levels of HDL-C, although the mechanisms for these differences remain unclear. Importantly, these ethnic differences, especially in TG levels, are independent of obesity and several other risk factors, and appear to be consistent across different populations of African heritage. **Methods:** To examine the potential genetic contributions to fasting, serum levels of TG, we systematically screened 15 positional and biological candidate genes, which have been associated with lipoproteins in non-African populations or were identified as candidate genes for lipoproteins in animal studies. 384 tag and potentially functional single nucleotide polymorphisms (SNPs) were genotyped in the NHLBI supported RS&G's Genotyping Lab at Johns Hopkins University, using the Illumina GoldenGate assay among 432 Afro-Caribbeans (mean age=42yrs) from 7 multi-generational pedigrees (median family size 51 individuals, 3535 relative pairs). **Results:** After adjusting for age, gender, BMI, current smoking and alcohol intake, physical activity, parity, menopausal status, intake of oral contraceptives and lipid-lowering drugs, 30 SNPs in 6 genes showed nominal associations with TG ($P<0.05$). The strongest associations, which remained significant after adjustment for the number of genes tested ($P<0.003$), was observed for 4 SNPs in the HNF4α gene (Table), a transcription factor which regulates hepatic expression of a number of genes associated with lipoprotein metabolism. Each of four SNPs accounted for ~2–4% of the total phenotypic variability in TG. **Conclusion:** Our findings show for the first time that common HNF4α variants are strongly associated with lower triglyceride levels in a population of African descent.

TABLE. GENOTYPIC ADJUSTED TRIGLYCERIDE MEANS (± SE) FOR 4 SNPS IN THE HNF4A GENE

HNF4α SNP rs#	1/1	1/2	2/2	Minor Allele Frequency	P-value for Trend
rs3746575	89.3±5.3(N=115)	100.1±4.2(N=178)	121.3±7.5(N=49)	0.40	0.0006
rs1028583	91.5±5.2(N=154)	98.2±4.4(N=153)	119.0±4.4(N=35)	0.33	0.001
rs3212198	91.0±4.9(N=119)	99.8±4.5(N=172)	118.9±7.2(N=51)	0.40	0.0019
rs6073435	93.2±4.7(N=138)	98.2±4.5(N=156)	126.0±8.1(N=48)	0.37	0.0024

P211

Genome-Wide Linkage Scan for Plasma High-Density Lipoprotein Cholesterol and Triglyceride Among American Indian Populations: The Strong Heart Family Study

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Recent studies have implicated chromosomal regions linked to variation in plasma high density lipoprotein cholesterol (HDL-C) and triglyceride (TG) levels, although the results have been inconsistent and previous studies of American Indian populations have been lacking. In an attempt to localize quantitative trait loci (QTLs) influencing HDL-C and TG, we conducted genome-wide linkage scans of HDL-C and TG in participants of the Strong Heart Family Study. A total of 3484 men and women aged 18 years or older, in >32 extended families at three centers (Arizona, Oklahoma, and North and South Dakotas) were phenotyped for HDL-C and TG concentrations and other risk factors. Quantitative genetic analyses were implemented using a variance component approach and the computer program SOLAR. With adjustment for age, sex and field center, we detected a QTL influencing HDL-C on chromosome 6, nearest marker D6S289 at 6p22.3 (LOD = 4.4) in the Arizona sample. This region of chromosome 6 harbors the ELOVL2 gene, which also displays significant association with HDL-C in the Diabetes Genetic Initiative genome wide association (GWAS) data. We also detected a QTL influencing TG on chromosome 15 nearest marker D15S153 at 15q22.31 (LOD = 4.5 in the overall sample and LOD = 3.8 in the sample from the North and South Dakotas). This region on chromosome 15 harbors the LIPC gene which also displays significant association with TG in the Diabetes Genetic Initiative GWAS data. After further adjustment for waist circumference, smoking status, alcohol intake, estrogen use (for women), lipid-lowering treatment, diabetes status, and impaired fasting glucose, we found a QTL influencing TG on chromosome 10, nearest marker D10S217 at 10q26.2 (LOD = 3.7) in the Arizona population. The replication of QTLs for HDL-C and TG and the implication of ELOVL2 and LIPC in these regions suggest that chromosomes 6p and 15q warrant further investigation with intensive fine mapping for gene discovery. This work brings us closer to the identification of the functional genes that influence variability in these major CVD risk factors and thus a better understanding of the multiple factors that control concentrations of HDL-C and triglycerides in the blood.

P212

Common Variation in Cytochrome P450 Epoxygenase Genes (CYP2J2, CYP2C8, and CYP2C9) and Risk of Incident Nonfatal Myocardial Infarction and Ischemic Stroke

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The biologically active epoxyeicosatrienoic acids have protective vascular effects. CYP2J2, CYP2C8 and CYP2C9 are known to be a source of epoxyeicosatrienoic acids in cardiac tissues. A CYP2J2 promoter polymorphism has been associated with cardiovascular disease in some, but not all studies. We conducted a population-based, case-control study to determine whether common genetic variation in the CYP2J2, CYP2C8, and CYP2C9 genes was associated with the risk of incident, non-fatal myocardial infarction and ischemic stroke. We used publicly available single nucleotide polymorphism (SNP) discovery data from a mixed race panel of 90 individuals to select

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30 tagSNPs that were genotyped in 856 myocardial infarction cases, 368 ischemic stroke cases and 2688 controls identified between 1995 and 2002. Haplotypes were inferred using Phase. We used logistic regression to examine the association between both SNPs and haplotypes and events and adjusted models for age, sex, race, and year of identification. A Wald test of all haplotype terms assessed the global hypothesis that no haplotype had an association with the outcome that was significantly different from one. Globally, variation in CYP2J2 was associated with myocardial infarction risk (p=0.027). Two intronic CYP2J2 tag-SNPS, rs10889160 and rs11572325, were associated with an increased risk of myocardial infarction [OR: 1.24, 95% CI: 1.07 to 1.43, p=0.004 and OR: 1.27, 95% CI: 1.08 to 1.51, p=0.006, respectively]. An additional copy of a CYP2J2 haplotype which included the minor alleles of the significant SNPs was associated with an increased risk of myocardial infarction [OR: 1.39, 95% CI: 1.05 to 1.85]. The confidence interval for the CYP2J2 SNP in the strongest linkage disequilibrium (r^2=0.85) with the putative functional promoter polymorphism included values compatible with unity [OR: 1.17, 95% CI: 0.95–1.43]. There was no evidence of an association between variation in CYP2J2 and ischemic stroke and there was no association between variation in CYP2C8 or CYP2C9 and myocardial infarction or stroke. Our findings corroborate those of other studies reporting an association between variation in CYP2J2 and myocardial infarction, but which specific functional variant or variants may be important is unclear.

P213

Candidate Genes from Distinct Molecular Pathways and Obesity: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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BACKGROUND: The genetic and environmental factors accounting for the variability of obesity in the general population remain unclear. Appetite regulatory neural network and adipocyte homeostasis molecular pathways are critical to feeding behaviors and long-term weight maintenance. In the present study, associations between weight (WT) and 4 genes (leptin (LEP), leptin receptor (LEPR), neuropeptide Y (NPY) and peptide YY (PYY)) from these pathways were examined. METHODS: The study included participants in the CARDIA Study. Participants were 18–30 years old upon recruitment (1985–86). WT was determined at baseline and at years 2, 5, 7, 10, 15, and 20. Genotyping was conducted using tag SNPs (7 for LEP, 16 for LEPR, 9 for NPY and 5 for PYY) that characterize the common pattern of genetic variation in these genes. Race-specific linear regression models were used to examine associations of the various SNPs with WT measurements, controlling for sex and age. The overall association based on the 7 repeated WT measurements was tested with GEE. False discovery rate (q) was used to adjust for multiple testing. RESULTS: Among Whites, WT increased significantly over the 20-year period (mean increase 29.0 and 26.1 lbs, for men and women, respectively). A larger increase in WT was seen in Blacks (36.6 and 40.0 lbs, for men and women, respectively). In Blacks, 6 SNPs across the LEP and LEPR genes demonstrated associations with WT using the data from the 6 examinations (all nominal p-values <0.05; 4 q-values <0.05; 2 q-values between 0.05 and 0.1). In the LEP gene, two SNPs, rs17151919 and rs4731427 were associated with a higher average WT over the 6 examinations of 6.9 and 4.9 lbs, respectively, for each additional copy of the variant allele in Blacks. The genetic associations with WT tended to increase with time - each copy of the rs17151919 variant allele was associated with a higher WT of 5.8 lbs at baseline and 10.6 lbs at year 20. In Whites, 2 SNPs in the LEP gene tended to be associated with WT (q-value 0.09, 0.16). There was little evidence that variation in NPY and PYY were associated with WT in Blacks or Whites. CONCLUSIONS: After accounting for multiple testing, several SNPs in LEP and LEPR were associated with WT in young adults. The associations were more prominent in Blacks than Whites.

P214

Apolipoprotein B Genetic Variants and High-Density Lipoprotein Cholesterol Postprandial Response: The Genetics of Lipid-Lowering Drugs and Diet Network Study

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Objectives. Apolipoprotein B (APOB) plays a role in plasma lipoprotein metabolism. APOB containing, very low-density lipoproteins (VLDL) and high-density lipoproteins (HDL) exchange lipid components through the action of cholesterol ester transfer protein. Thus, genetic variation at the APOB locus may influence inter-individual variation in HDL-C after a dietary fat challenge. Methods. Participants (N=916) from the Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study are included in this analysis. We examined individual associations between five single nucleotide polymorphisms (SNPs) in the APOB gene (M516, A618V, T2515T, P2739L, and E4181K) and HDL-C response to fenofibrate (160 mg/day for 3 weeks) and two postprandial lipid challenges (before and after fenofibrate). We used a growth curve model, adjusted for cardiovascular disease related covariates to characterize lipid changes across time points and tested the association of these changes with the APOB SNPs employing a mixed model where the family effect was considered a random effect. Results. Before fenofibrate treatment, individual SNP analysis demonstrated no significant associations with HDL-C concentrations. After fenofibrate treatment, the change in HDL-C concentration between 0–3.5 hours after the postprandial challenge was associated with APOB E4181K (p=0.0029). The presence of the C allele increased HDL-C plasma lipids, and the HDL-C response by genotype did not differ by gender. Conclusions. Genetic variation in the APOB locus influences HDL-C plasma levels during a postprandial lipid challenge after treatment with fenofibrate.

P215

Interleukin-18 Gene Polymorphisms and Incident Coronary Heart Disease in Middle-Aged Men and Women: Results from the MONICA/KORA Augsburg Case-Cohort Study, 1984–2002

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Background: Interleukin-18 (IL-18), a member of the IL-1 cytokine superfamily, plays an important role in both innate and acquired immune responses and has been suggested to be involved in the development of atherosclerotic plaque instability. However, prospective studies examining the association between levels of IL-18 and incident coronary heart disease (CHD) yielded inconsistent results. It was the aim of the present study to examine whether single nucleotide polymorphisms (SNPs) in the corresponding gene modulate IL-18 serum concentration and whether these polymorphisms are associated with the risk to develop CHD. Methods: A case-cohort study was conducted in initially healthy, middle-aged men and women based on data from the MONICA/KORA Augsburg studies collected between 1984 and 2002 (mean follow-up time 10.2 years). For the selection of tagging SNPs, the International HapMap Project was used. The final set comprised four SNPs (rs5744222 C>A, rs1946518 C>A, rs2043055 T>C and rs3882891 A>C) which were genotyped in 339 cases with incident CHD and 1,816 non-cases by the Sequenom MALDI-TOF MS System. Results: As previously shown, two (rs5744222 and rs2043055) of the four examined SNPs were significantly associated with IL-18 serum concentrations. For the rs5744222 SNP mean IL-18 serum concentrations were lowest in carriers of the rare A/A genotype (p-value for trend: <0.001) while for the rs2043055 SNP concentrations were highest for carriers of the rare C/C genotype (p for trend: <0.001). None of the examined SNPs was significantly associated with incident CHD when men and women were analyzed together. However, female C/C carriers of the rs2043055 SNP had an elevated risk of CHD after multivariable adjustment [HR (95% CI): 3.19 (1.46–6.96)]. Conclusions: These data support the hypothesis that SNPs within the IL-18 gene modulate IL-18 serum concentrations, and they suggest that rs2043055 might play a causal role in the etiology of CHD in women.

P216

Hormone Therapy and Risk of Venous Thromboembolism Among Postmenopausal Women: Impact of Cytochrome P450 3A5 Genetic Polymorphism. The Esther Study

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Background. Oral estrogen use increases the risk of venous thromboembolism (VTE). Transdermal estrogen may be safe with respect to thrombotic risk. Expression of the human cytochrome P450 3A5 (CYP3A5) is implicated in the hepatic catabolism of steroidal hormones, especially estrogen. Subjects with the CYP3A5*1/*1 and CYP3A5*1/*3 genotypes express the enzyme. Therefore, we investigated the impact of the CYP3A5 genetic polymorphism on the association between hormone therapy by route of estrogen administration and VTE risk. **Methods**. We performed a multicenter case-control study of VTE among postmenopausal women who were enrolled in 1999 through 2006 at 8 clinical centers and in the general population, in France. CYP3A5 genotype was successfully evaluated in 193 consecutive cases with a first documented episode of idiopathic VTE and in 534 controls. Relative risks were estimated by odds ratios (OR) and 95% confidence intervals (CI). **Results**. The allele frequency of CYP3A5*1 was 9% and 10% among cases and controls, respectively (OR=0.9; 95% CI: 0.6–1.5). Oral but not transdermal estrogen increased VTE risk compared with non-users (OR=3.8; 95% CI: 2.3–6.5 and OR=1.1; 95% CI: 0.7–1.7, respectively). Compared with non-users, OR for VTE in current users of oral estrogen was 3.1 (95% CI: 1.7–5.4) among patient without CYP3A5*1 allele and 22.1 (95% CI: 3.7–133.2) among patients who expressed the enzyme (test for interaction of CYP3A5*1 allele and oral estrogen on VTE risk was significant, p=0.04). By contrast, there was no significant interaction of CYP3A5*1 allele and transdermal estrogen use on VTE risk. **Conclusion**. Women with CYP3A5*1 allele using oral estrogen can define a subgroup at high VTE risk. If confirmed, these findings could benefit women in the management of their menopausal symptoms with respect to the VTE risk associated with oral estrogen.

P217

Admixture Mapping Identifies a Locus on Chromosome 1q to Be Associated with White Blood Cell Count in African Americans: The Atherosclerosis Risk in Communities (ARIC) Study

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White blood cell (WBC) count is associated with multiple cardiovascular risk factors and infection. African Americans (AA) have lower WBC count than European Americans (5.7 and 6.3 x1,000 cell/mm^3 respectively in ARIC). A recent study suggests that this ethnic difference in WBC count may be genetically determined (Nalls M, AJHG in press). Therefore, we performed

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a genome-wide admixture scan using 1,402 markers that are highly informative for African versus European ancestry to identify a genomic region(s) that may partially account for the ethnic difference in WBC count. Data from 3,377 AA ARIC participants were included for the present analyses. The genome-wide analysis was performed using a case-control approach: cases had WBC count < 3.9 and controls > 7.4 x1,000 cell/mm^3, corresponding to the 15th and 85th percentile. A Bayesian method was used to test for association between genetic ancestry in each chromosomal region and case-control status. A general linear model with 3 genotypic means was used to test for association between marker and WBC and cell subtype counts. A locus on chromosome 1q was strongly associated with WBC count (LOD > 70). The strongest signal came from a marker known to affect the expression of the Duffy blood group antigen (rs2814778, minor allele frequency 17%). AA ARIC participants with both copies of the common West African allele at rs2814778 had significantly lower WBC count than their counterparts with either 1 or 2 copies of the minor allele ($p<0.0001$; Table). The difference in WBC count between the two homozygous groups was $\sim$ 1 standard deviation, and this variant explained about 19% of the population variation in WBC count. Rs2814778 was also significantly associated with neutrophil and monocyte counts (Table). Using admixture mapping, we identified a locus on chromosome 1 that was significantly associated with WBC count in African Americans. Additional studies are needed to determine the nature of the association and clinical implications.

MEAN (STANDARD DEVIATION) WBC AND CELL SUBTYPE COUNTS (X1,000 CELL/MM3) IN 3,377 AA ARIC PARTIC

Genotype	AA	AB	BB
N(%)	2,354 (70%)	880 (26%)	143 (4%)
WBC*	5.1 (1.5)	6.9 (2.0)	7.0 (1.9)
Neutropphils*	2.3 (1.1)	3.9 (1.5)	3.9 (1.5)
Monocytes*	0.32 (0.19)	0.38 (0.19)	0.38 (0.20)
Lymphocytes	2.1 (0.7)	2.2 (0.7)	2.3 (0.9)
Eosinophils	0.15 (0.15)	0.19 (0.20)	0.17 (0.12)
Basophils	0.03 (0.04)	0.04 (0.05)	0.04 (0.05)

* $p < 0.0001$

P218

Visfatin: A Genetic Link Between Insulin Sensitivity and Free Fatty Acids

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Adipose tissue is no longer considered a simple depot for triglyceride storage. On the contrary, adipose tissue secretes adipokines into the circulation that can influence insulin sensitivity in distant sites as well as in adipose tissue itself. Adipokines have increasingly been implicated as mediators of obesity-related insulin resistance and the increased risk of type 2 diabetes associated with obesity. Many adipokines also have inflammatory and/or prothrombotic effects, possibly linking obesity to cardiovascular disease. Visfatin, also known as pre-B cell colony-enhancing factor (PBEF1), is highly enriched in visceral fat of mice and humans; circulating visfatin levels are increased in obesity and correlate with visceral adiposity. However, its importance in human obesity and insulin resistance remains unknown and controversial. In this study, we sought to determine whether visfatin is a genetic determinant of metabolic traits. We genotyped 5 single nucleotide polymorphisms (SNPs) in PBEF1 in 975 Mexican Americans from 190 families. These SNPs were selected using HapMap data to tag the majority of the variation in the gene. Insulin sensitivity (SI) was obtained from hyperinsulinemic euglycemic clamps done in 370 genotyped offspring. Association analyses were conducted using generalized estimating equations (GEE1) to account for familial correlation, adjusting for age, sex, and BMI. Two linked SNPs were associated simultaneously with improved insulin sensitivity and lower free fatty acid (FFA) levels (see Table). A third SNP was also associated with lower FFA. Haplotype analysis did not provide additional information. These results implicate visfatin as an inherited factor mediating the relationship between FFA and insulin sensitivity. Considering its high expression in visceral fat, visfatin may regulate lipolysis and/or FFA release from adipose tissue; in turn, these FFA enter the circulation and impact on whole-body insulin sensitivity.

VISFATIN SNP ASSOCIATION WITH SI AND FFA (DOMINANT MODEL)

SNP-trait	Major allele homozygotes	Minor allele carriers	P value
rs10953502-SI	1.92 (1.40)	2.25 (1.54)	0.0056
rs10953502-FFA	708 (313)	655 (298)	0.035
rs3801272-SI	1.92 (1.38)	2.25 (1.61)	0.0036
rs3801272-FFA	706 (307)	639 (312)	0.02
rs1319313	699 (314)	644 (308)	0.048

Data are median (interquartile range). FFA are in umol/L. rs10953502 and rs3801272 are in linkage disequilibrium (r2=0.8)

P219

The Protective Effect of KCNMB1 E65K Against Hypertension Is Restricted to Blood Pressure Treatment

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Genetic polymorphisms that influence smooth muscle cell contraction and relaxation may affect the response to anti-hypertensive therapy. The β subunit of the large conductance calcium-activated potassium channel contains a non-synonymous polymorphism (E65K, minor allele frequency (MAF) $\sim$10%) noted previously to be associated with reduced diastolic blood pressure (BP). We tested whether E65K is associated with BP in the Heart SCORE (n=1,075) and Framingham Heart Study (FHS) (n=1,519) cohorts without CVD. In Heart SCORE Caucasians (n=687), ANCOVA (dominant model) revealed an association between E65K and lower systolic (E = wild type, K = substitution) (adjusted-mean mmHg ($\pm$SD) for E: 133.7 ($\pm$7.3), K 130.6 ($\pm$8.4), p=0.02) and diastolic BP (E 79.7 ($\pm$2.6), K 77.6 ($\pm$3.1), p=0.02). In logistic regression, Caucasian K-carriers were at lower risk for elevated systolic (OR=0.55, 95%CI: 0.33–0.91) and diastolic (OR=0.47, 95%CI: 0.28–0.79) BP. Importantly, the protective effect of E65K was primarily evident among subjects receiving anti-hypertensive therapy. In the FHS, the K-carriers were less likely to have higher blood pressure and hypertension, although these results did not reach significance. In pooled Caucasian Heart SCORE and FHS subjects we found that older (age $>$ median 58 years), treated hypertensive K-carriers had lower systolic, diastolic and pulse pressure (p=0.003, 0.0002, 0.09, respectively). Of note, KCNMB1 contains a second non-synonymous polymorphism (V110L, MAF $\sim$10%), which we also genotyped in the FHS cohort. Haplotype analysis found low linkage-dysequilibrium with E65K (D'=1.0, R^2=0.01). The rare alleles within the haplotype were noted to be out-of-phase, with the frequency of the K-L haplotype exceedingly low ($<$0.01%); suggesting that V110L would unlikely confound the effect of E65K on blood pressure. In summary, Caucasians wild-type E65K carriers are less responsive to anti-hypertensive treatment than subjects harboring the K-allele. The presence of both V110L and E65K substitutions were mutually exclusive, and haplotype analysis does not elucidate these findings. This association can now be tested further in pharmacogenomic studies, which may identify preferred treatment options for carriers of the E65K polymorphism.

P220

Associations Between Genetic Variation in Tumor Necrosis Factor Receptors 1 and 2 and Insulin Resistance: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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BACKGROUND: Members of the tumor necrosis factor receptor superfamily, including receptors 1 and 2 (TNFRSF1A, TNFRSF1B), have been shown to influence the regulation of insulin signaling pathways and may be involved in the development of insulin resistance (IR). Identifying genetic risk factors for the development of IR may help identify individuals at increased risk of developing diabetes and CVD. Using longitudinal data from CARDIA, we examined the association between IR and common patterns of variation in the TNFRSF1A and TNFRSF1B genes in non-diabetic African Americans (AA, n=1,598) and European Americans (EA, n=1,952), aged 18–30 at baseline. METHODS: IR was measured by the homeostasis model assessment (HOMA) ((fasting insulin X fasting glucose)/22.5) using data from five exams (baseline (1985–86) and years 7, 10, 15, and 20). SNPs with a minor allele frequency $\geq$ 5% were identified by resequencing 24 AA and 23 EA individuals (http://pga.gs.washington.edu). From those identified, 11 tagSNPs for TNFRSF1A and 28 for TNFRSF1B were chosen using linkage disequilibrium-based criteria. Haplotypes were estimated using Phase (v. 2.1). Race- and sex-specific GEE linear models were used to examine the associations between tagSNPs/haplotypes and IR. Models were adjusted for age, center and percent African ancestry. RESULTS: The T allele for TNFRSF1A 10186 was associated with increased HOMA scores and insulin levels in the AA population compared to CC homozygotes (Table 1). In women this association was statistically significant. No evidence for other associations was found for the AA population, and no associations between IR and TNFRSF1A were found in the EA population. Haplotype results were consistent with SNP analyses. No associations with IR were found for TNFRS1FB. CONCLUSIONS: These findings suggest that TNFRSF1A 10186, which alters the amino acid residue at position 75 from PRO to LEU, is associated with increased insulin levels in young, non-diabetic AA women.

TABLE 1: RESULTS OF GEE ANALYSIS OF TNFRSF1A 10186 IN AFRICAN AMERICAN SUBJECTS (RS4149637; MAF 0.081)

	Percent Change for Carriers of T Allele* (95% CI)	
	Men [n=665]	Women [n=933]
HOMA Score	8.2 (-1.0, 18.2)	15.2 (6.8, 24.3)
Fasting Plasma Glucose	0.1 (-1.5, 1.7)	0.5 (-1.0, 1.9)
Fasting Plasma Insulin	8.1 (-0.1, 17.0)	14.6 (6.8, 23.0)

*as compared to CC homozygotes

P221

Effect of Macrophage Migration Inhibitory Factor Gene Variants and Serum Concentrations on Risk for Coronary Heart Disease: Results from the MONICA/KORA Augsburg Study, 1984–2002

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Background: Macrophage migration inhibitory factor (MIF), a central mediator of innate immunity, has been reported to contribute to the development of cardiovascular disease. MIF is expressed in atherosclerotic lesions in humans, and gene deletion and antibody inhibition

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studies in animal models indicated that MIF may be cause rather than consequence of atherosclerosis. We sought to assess the triangular association between macrophage migration inhibitory factor (MIF) genotypes, circulating MIF levels and risk for incident coronary heart disease (CHD) in the large, prospective, population-based MONICA/KORA case-cohort study (Augsburg, southern Germany). Methods: MIF genotypes (rs755622, rs2070766, rs2070767 and rs1007888), haplotypes and serum concentrations were determined in 363 individuals with incident CHD and 1,908 individuals without CHD during follow-up (mean follow-up time 10.3 years). Results: Circulating MIF concentrations were not associated with the risk for CHD. In women, carriers of the minor alleles rs755622C and rs2070766G had a higher risk for incident CHD, and a haplotype that contained these two minor alleles was significantly associated with increased risk for CHD (HR 2.44, 95%CI 1.30–4.59). Conclusion: The lack of association between serum levels and incident CHD indicates that MIF may not be a novel biomarker for CHD risk. However, the association of a haplotype containing the rs755622C allele, which has been reported before to increase the susceptibility for various other proinflammatory conditions, points towards a role for MIF in local vascular inflammation and atherogenesis.

P222

Genetic Variation in Fcγ Receptor IIa and Risk of Coronary Heart Disease: Negative Results from 2 Large Independent Populations

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Background. The potential active role of the immunglobulin receptor FcγRIIa in atherosclerosis is still a matter of controversy, although it is expressed on various cells involved in atherogenesis, and CRP, a major inflammatory mediator has been reported to bind to FcγRIIa. Furthermore, a functional polymorphism in the FcγRIIa receptor has been described causing an amino acid exchange from Arg to His. In particular, it was shown that binding of CRP to FcγRIIa is strongly decreased in 494A homocygotes implying that this genotype may thus be less susceptible to coronary heart disease (CHD). We therefore evaluated the potential association between the allelic status of FcγRIIa and risk of CHD in two large independent populations. Methods. FcγRIIa-R/H131 polymorphisms were determined in a population of 527 patients with a history of myocardial infarction and 527 age- and gender-matched controls drawn from a population-based MONICA- Augsburg survey. In the LURIC study, 2,227 patients with angiographically proven CHD, defined as having at least one stenosis $\geq$50%, were compared with 1032 individuals with luminal narrowing $<$50%. Results. Distributions of FcγRIIa genotypes were not different between cases and controls in both populations (p=0.86 and p=0.67). In addition, genotype frequencies of the FcγRIIa gene did not show a significant departure from the Hardy-Weinberg equilibrium. FcγRIIa R(-131)$\rightarrow$H genotype was not independently associated with lower risk of CHD after multivariable adjustments, neither in the MONICA population (odds ratio (OR) 1.08; 95% confidence interval (CI) 0.81 to 1.44), nor in the LURIC study (OR 0.96; 95% CI 0.81 to 1.14). Conclusions. Our results do not confirm an independent relationship between FcγRIIa genotypes and lower risk of CHD in these populations.

P223

Novel Quantitative Trait Loci Identified for Triglyceride Response to Fat Challenge in the Goldn Study

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Background: Elevated triglycerides are associated with increased risk of CHD and are relatively responsive to immediate diet, as well as long-term exercise and lipid-lowering drug treatment. Post-prandial lipemia (PPL), characterized by hypertriglyceridemia, shows considerable inter-individual variability and investigation of its genetic architecture may provide clues to the mechanisms affecting CHD risk. Methods and results: Families participating in the NHLBI Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study (n=1036 subjects) were included. Each participant was asked to suspend for three weeks the use of lipid-lowering drugs, if applicable, and was given a high-fat milkshake (83% fat and 700 kcal/m^2). Triglyceride (TG) concentrations, as well as large VLDL particles and chylomicrons (CHY) were measured by standard methods and NMR at 0, 3.5 and 6 hr after the fat load. Growth curve models were used to obtain estimates of uptake (0–3.5hrs) and clearance (3.5–6hrs), taking into account the effects of age, sex, BMI, diabetes, alcohol, and carbohydrate and fat intake. Heritabilities ranged from 32–54% for uptake and 23–45% for clearance. Linkage analysis was carried out using a variance components model. There was remarkable similarity in the lod surfaces for the intake and uptake phenotypes at all locations with lods above 2, suggesting that the underlying QTLs influence the PPL dynamic as a whole. The strongest signals were found on chromosome 3 (lod=3.47, p=0.000064) and 4 for TG (lod=2.71, p=0.00041), and 9 for CHY (lod=3.16, p=0.00014). These peaks occurred at least 10 cM from the locations of any of the 20 candidate genes we considered known to affect lipid metabolism, suggesting alternative genes underlying response to fat load. Conclusion: These unique data allow investigation of the genetic architecture underlying response to a fat load, which provides new clues to the genes and pathways influencing lipid metabolism and inter-individual variability in this dimension. Three potential QTLs were identified, which will be followed up with bioinformatic analysis and linkage disequilibrium mapping.

P224

Cholesterol Ester Transfer Protein Polymorphisms Are Associated with CETP Expression, Lipoproteins, and Subclinical Atherosclerosis in the Multi-Ethnic Study of Atherosclerosis

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Introduction: Cholesterol Ester Transfer Protein (CETP) is a key regulator of reverse cholesterol transport. Study of CETP single nucleotide polymorphisms (SNPs) may explain variations in CETP expression, lipoprotein profiles, and atherosclerosis, and provide insight regarding pharmacologic CETP inhibition. **Methods**: From the Multi-Ethnic Study of Atherosclerosis (MESA), 2,847 subjects were selected for a candidate gene study - approximately 700 subjects from each race/ethnic group: African American, Caucasian, Chinese, and Hispanic. Seven CETP haplotype-tagging SNPs were studied using the Illumina GoldenGate assay. The following phenotypes were evaluated: CETP mass and activity, lipoprotein concentrations, lipoprotein particle number and size (by NMR), CT coronary artery calcium (CAC), and carotid artery intimal medial thickness. Genotype-phenotype associations were examined using binomial and linear regression assuming additive inheritance, adjusted for age, race and gender. To account for multiple tests among correlated phenotypes and genotypes, the false discovery rate (q-value) was computed for each comparison. **Results**: In the combined sample, minor alleles of rs3764261 (minor allele frequency (MAF) = 0.29) and rs708272 (Taq1B, MAF = 0.39) were associated with lower CETP mass and CETP activity, a higher concentration of HDL-C, and larger HDL particle size ($p<1 \times 10^{-8}$, $q<0.0001$ for all), as well as more HDL particles ($p = 0.009$, $q = 0.03$). In addition, the same alleles were associated with fewer LDL particles and larger LDL particle size ($p<0.005$, $q<0.03$ for both), although the LDL-C concentrations did not differ. Consistent with this protective lipid profile, there was a lower prevalence of CAC (Agatston score > 0) with the minor rs3764261 allele (CC = 50% vs. CA = 47% vs. AA = 44%, $p = 0.04$, $q = 0.1$). Within race/ethnicity and gender strata, nearly all of the CETP and lipoprotein trends remained statistically significant. Similar, but less consistent and weaker associations were observed with the other CETP SNPs as well. **Conclusion**: Minor alleles of two common SNPs in the CETP gene, rs3764261 and rs708272, are associated with lower CETP expression, a protective lipoprotein profile and a lower prevalence of coronary artery calcification.

P225

Adiponectin Gene (ADIPOQ) Polymorphisms Are Associated with Coronary Artery Calcium Phenotypes in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Background: Circulating adiponectin is thought to play a protective role in atherosclerotic plaque formation and low levels have been associated with coronary heart disease (CHD). Single nucleotide polymorphisms (SNPs) of ADIPOQ have been associated with CHD and circulating adiponectin levels. Little research exists on the association of ADIPOQ with subclinical cardiovascular disease (CVD) measures. Objective: We investigated associations of ADIPOQ polymorphisms with CAC phenotypes to further understand of the role of ADIPOQ in the atherosclerotic process. Methods: We used data from the baseline visit of 2847 Caucasian, African-American, Hispanic and Chinese adults aged 45–84 enrolled in MESA. Twelve ADIPOQ SNPs were genotyped and CAC was measured by computed tomography scan. Since CAC prevalence was $>$10% in all ethnic groups, its associations were assessed using log binomial regression. Linear regression was used for mean arterial CAC mass models, adding 1 then log transforming. Separate regressions were performed for each ethnic group. Analyses were stratified by age tertiles when there were significant interactions of age and SNP. P-values $\leq$ alpha of 0.05/12=0.0042 were considered statistically significant. Results: All SNPs were in Hardy-Weinberg equilibrium within ethnic groups. Among Chinese, the GG genotype of rs822396 was associated with greater CAC prevalence (RR 1.66, 95% CI (1.24, 2.22), p=0.0006) compared to the AA genotype. Among Hispanics aged 56–66, the AA genotype of rs11711353 was marginally associated with greater of CAC prevalence (RR 1.67, 95% CI (1.17, 2.41), p=0.0053) as compared to those with the GG genotype. African Americans aged $>$ 67 with the GG genotype of rs1063538 had 212.3% (95% CI (49.9, 553.2), p=0.0025) greater mean arterial CAC mass as compared to those with the AG genotype. Conclusions: ADIPOQ polymorphisms rs822396, rs11711353, rs1063538 were significantly associated with coronary artery calcium phenotypes in non-Caucasian ethnic groups. Further investigation is needed to ascertain whether these particular SNPs are associated with circulating adiponectin or are functional SNPs of ADIPOQ.

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P226

Variations in the UCP-3 Gene Are Associated with Specific Obesity Phenotypes

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Objective: Uncoupling protein 3 (UCP-3) uncouples oxidative metabolism from ATP synthesis, resulting in the production of heat instead of energy storage. Single nucleotide polymorphisms (SNPs) in UCP-3 might result in a reduced function or expression of UCP-3 and therefore lead to an increased capacity to store energy as fat. **Research Methods and Procedures**: We conducted a population-based, cross-sectional study among 400 Dutch men between 40 and 80 years, in whom we genotyped and analysed seven SNPs in UCP-3. BMI, WHR, ultrasonographically assessed amount of visceral and peripheral fat, and Total fat mass assessed with DEXA were used as obesity phenotypes. Linear regression analyses were performed to examine the independent effects of these SNPs on obesity phenotypes. **Results**: A significant association with BMI was found for three SNPs; rs647126, rs1685356 and rs2075577. Subjects homozygous for the minor allele of rs647126 had an average increase in BMI of 1.11 kg/m2 (95% CI: 0.09;2.14, P = 0.033). The same tendency was seen for the other two SNPs (rs1685356 and rs2075577). Subjects homozygous for the minor allele of rs1685356 as well as subjects homozygous for the minor allele of rs2075577 had a significantly increased BMI (1.22 kg/m2, 95% CI: 0.23;2.22, P = 0.016, and 1.23 kg/m2, 95% CI: 0.20;2.25, P = 0.019 respectively). Furthermore, a significant association between rs1685354 and visceral fat mass was observed. A significant decrease in visceral fat mass was seen in subjects heterozygous for this SNP (-0.52 cm, 95% CI: -0.99;-0.05, P = 0.030). Subjects homozygous for the minor allele also had a decreased visceral fat mass, but this did not reach statistical significance (-0.51 cm, 95% CI: -1.61;0.60, P = 0.368). **Discussion**: Our results suggest that SNPs in the UCP-3 gene are associated with specific obesity phenotypes.

P227

The Role of Shared Genes in the Relationship Between Stature and Subclinical Coronary Artery Atherosclerosis

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Short stature is associated with increased coronary heart disease (CHD) risk. Although mechanisms underlying this are unknown, possible explanations include environmental exposures in early life that may impact growth and CHD and shared genes (pleiotropy) for growth and CHD. Evidence for pleiotropy, however, has been inconsistent. We examined the relationship between adult height and coronary artery calcification (CAC), a measure of subclinical coronary atherosclerosis, which is heritable (heritability (h^2) >40%), in 877 (46% men) asymptomatic white adults (625 families) from the Epidemiology of Coronary Artery Calcification Study. Genetic (pleiotropic) and environmental correlations between adult height and log transformed CAC score were estimated. Mean (± standard deviation) age was 62.9(±8.6) years; mean height was 168.3(±9.3) centimeters (cm); 69.7% had detectable CAC; and mean CAC score was 222.0(±503.6). After accounting for age and sex, estimated height h^2 was 82%±9% (P<0.001); age and sex accounted for 63% and genetic factors for 30% of total height variation. After adjusting for age and sex, height was statistically significantly inversely associated with log CAC score (P=0.006); for every one-cm increase in height, there was a 3.3% relative decrease in CAC score. This relationship was similar after further adjusting for fasting glucose, systolic blood pressure, pack-years of smoking, low-density lipoprotein cholesterol, waist circumference and family history of CHD (P=0.011). After adjusting for age and sex, the environmental correlation between height and log CAC score was 0.61±0.34 and was statistically significantly different than zero (P=0.03); the genetic correlation was -0.35±0.11 and was statistically significantly different than zero (P=0.001) and minus one (P<0.001). Adult height was inversely associated with subclinical coronary artery atherosclerosis with evidence for shared environmental factors. Both height and CAC score are, in part, genetically determined traits, and both shared and unique genes likely influence these traits. Genetic and environmental determinants of adult height may provide insights regarding the role of genes and gene-by-environment interactions in CHD.

P228

ABO Genotype and Risk of Nonfatal Venous and Arterial Thrombosis

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Background: ABO genotype has been associated with risk of venous thrombosis (VT), with the A^1 allele conferring highest risk. Others have reported associations of blood groups A and B with myocardial infarction (MI). For ischemic stroke (IS), it has been suggested that the A^1 allele is associated with higher risk. Objective: To examine the association of ABO genotype with VT, MI, and IS. Methods: We used data from 3 interconnected population-based case-control studies of VT, MI, and IS. Included in the study were incident non-fatal MI (n=909) and IS (n=415) cases that occurred among hypertensive adults and post-menopausal women and incident non-fatal VT cases (n=349) among post-menopausal women. Controls were frequency matched to cases on age, sex, hypertension status, and year of identification. ABO genotypes (O^1, O^2, A^1, A^2, and B) were determined using single nucleotide polymorphisms. Subjects were grouped by diplotype according to the presence of O, A^1, A^2, and B alleles (see Table). Logistic regression was used to test the association of diplotypes carrying the A^1, A^2, and B alleles (reference = O) with risk of MI, IS, and VT separately. Results: Compared with O group, the A^1 allele was associated with an 80% increase in risk of VT (OR 1.80 [95% CI: 1.37–2.36]). The B allele was associated with a 60% increase in VT (OR 1.59 [1.04–2.41]) and IS (OR 1.60 [1.16–2.22]). The A^2 allele was associated with a 25% decrease in MI risk (OR 0.75 [0.57–0.98]). Discussion: Our analyses confirm reports of an increased risk in VT among carriers of the A^1 allele and identify other risk alleles for VT, MI and IS that will need replication. Risk alleles for ABO genotypes may differ for these thrombosis outcomes.

Table:	VTE	MI	Stroke
diplotype group	OR (95% CI)	OR (95% CI)	OR (95% CI)
O1O1/O1O2	ref	ref	ref
A1A1/A1A2/A1O1/A1O2/A1B	1.80 (1.37–2.36)	1.06 (0.90–1.26)	1.05 (0.82–1.33)
A2O1/A2O2/A2A2/A2B	1.24 (0.82–1.87)	0.75 (0.57–0.98)	0.90 (0.63–1.30)
BB/BO1/BO2	1.59 (1.04–2.41)	1.13 (0.87–1.47)	1.60 (1.16–2.22)

P229

Fatty Acid Translocase/CD36 Gene Variants May Modulate Left Ventricular Function

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Introduction: Long-chain fatty acids (LCFA) are an essential energy source for the heart. Fatty acid translocase (CD36) confers tissue-specific expression entrained to substrate availability. Evidence from animal models suggests that CD36 affects contractile function. This study characterized the role played by CD36 SNPs in modulating LV systolic function. **Methods:** CD36 (GeneID: 948) SNPs were genotyped in 192 African Americans (age 49±12 yrs, 70% F, 56% HTN, 24% DM) with normal LV ejection fraction (LVEF >50%). TagSNPs were selected based on the HapMap Yoruban data with a reported minor allele frequency ≥ 5% (53 tagSNPs) and genotyped using Sequenom® technology. Echo indices included tissue-Doppler imaging-derived systolic (Sm) mitral annular velocity (a load-independent measure of LV contractile function). Stepwise regression models including potential confounding covariates (age, sex, HTN, DM, LV mass indexed to $height^{2.7}$, BMI) were performed to test association with each SNP alone and then in a model including all significant SNPs. PHASE was used to infer haplotypes; linkage disequilibrium (LD) substructure was evaluated by Haploview. False Discovery Rate (FDR) was used to adjust for multiple comparisons. **Results:** The proportion of subjects with LVH was 21%. Five SNPs were significant for Sm in stepwise models: rs17266080 (p=0.01), rs3211911 (p=0.007), rs3211931 (p=0.02), rs3211960 (p=0.05), and rs7755 (p=0.001). When these SNPs were simultaneously entered into the stepwise model, 2 remained significant: rs7755 (r^2=.044, p=.004; located in 3'UTR) and rs3211911 (r^2=.019, p=.05; located in intron 7). Study of the LD substructure of the 2 SNPs yielded 3 haplotypes with frequencies ≥ 5%. When each haplotype was tested against all others, the TA haplotype was associated with increased Sm (p=.0008, haplotype frequency 22%) and the GG haplotype was associated with decreased Sm (p=.006, haplotype frequency 5%). After adjustment by FDR, the TA haplotype and rs7755 SNP remained significant (both p = .04). **Conclusions:** Findings of association between CD36 SNPs and Sm, an index of subclinical LV systolic function, implicates a potential role for this important candidate gene in modulating LV function by affecting myocardial metabolism.

P230

Apolipoprotein B Genetic Variants and Response to Fenofibrate: The Genetics of Lipid-Lowering Drugs and Diet Network Study

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Objectives. Hypertriglyceridemia is associated with a high level of triglyceride (TG)-rich very low-density lipoproteins (VLDL), and apolipoprotein B (APOB) is essential for VLDL formation. Fenofibrate reduces TG levels, but demonstrates considerable individual variability in effectiveness. Thus, genetic variation at the APOB locus may account for some of the inter-individual differences observed in lipid response to fenofibrate treatment. Methods. Participants (N=739) from the Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study that completed a three week intervention with fenofibrate 160 mg daily are included in this analysis. We examined individual associations between five single nucleotide polymorphisms (SNPs) in the APOB gene (M516, A618V, T2515T, P2739L, and E4181K) and TG response to fenofibrate. We used a growth curve model, adjusted for cardiovascular disease related covariates to characterize lipid changes across time points and tested the association of these changes with the APOB SNPs using a mixed model including the family effect as random. Results. TG change with fenofibrate treatment was associated with two APOB SNPs, P2739L and T2515T (p=0.0075 and 0.0047, respectively). Fenofibrate treatment lowered TG by 72.3 mg/dL among those with the TT genotype of APOB P2739L, compared to 47.1 mg/dL with the CC genotype. For APOB T2515T, the heterozygous genotype was associated with greater TG lowering (54.9 mg/dL) than either homozygous genotype (40.7 mg/dL for AA genotype and 47.7 mg/dL for GG genotype). Conclusions. Genetic variation in the APOB locus predicts TG response to fenofibrate treatment.

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P231

Mutations in the HFE Gene and Cardiovascular Disease Risk: An Individual Patient Data Meta-Analysis of 53,880 Subjects

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Background: A link between increased iron load and risk of coronary heart disease (CHD) has long been postulated. Extensive research has been conducted on the association between mutations in the gene coding for hemochromatosis (HFE), an iron-overload disease, and cardiovascular disease risk. To date, results have been rather uncertain, which can largely be attributed to the small size and resulting limited statistical power of most of the studies. The results of an Individual Patient Data (IPD) meta-analysis of eleven observational studies are reported. Methods: Individual patient data were obtained from published and unpublished studies that had information available on both the C282Y and H63D mutations in relation to CHD risk. Individual records were provided on each of the 53,880 participants in eleven studies. In total 10,514 patients with coronary events were documented, of whom 5,724 had an acute myocardial infarction. The crude association between HFE genotypes and coronary events was examined by logistic regression analysis. Adjustments for potential confounders including age, gender, smoking, hypertension, hypercholesterolemia and type 2 diabetes were made. Results: After full adjustment the odds ratio for CHD was 1.12 (95% CI: 0.92–1.37) for subjects with the compound heterozygous (C282Y/H63D) genotype relative to those with the wild-type/wild-type genotype. The odds ratios for C282Y/C282Y, C282Y/wild-type, H63D/H63D and H63D/wild-type were 0.78 (95% CI: 0.49–1.26), 0.98 (95% CI: 0.90–1.07), 1.16 (95% CI: 0.97–1.38) and 1.07 (95% CI: 1.00–1.14), respectively. Conclusions: The results of this large IPD meta-analysis do not support the view that HFE gene mutations are associated with an increased risk of CHD or acute myocardial infarction.

P232

Matrix Metalloproteinase 2 Genetic Variation Influences Measures of Fibrous Cap Thickness: The Atherosclerosis Risk in Communities (ARIC) Study

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Objective: Genetic variation in the matrix metalloproteinase 2 (MMP2) gene promoter alters transcriptional activity and has been consistently associated with CHD, presumably through atherosclerotic destruction and remodeling. We tested this hypothesis by examining the association of MMP2 promoter variation with multiple plaque characteristics measured by gadolinium-enhanced MRI. **Methods:** Participants (N~1,700) of the biracial ARIC cohort were recruited to participate in the Carotid MRI Study in 2004–2005 based on results of their last ultrasound examination. Using a stratified sampling plan, two groups were recruited: ~900 participants with thick carotid artery walls and 800 participants randomly sampled from the remainder of the cohort. MRI studies were performed on a 1.5T scanner equipped with a bilateral 4-element phased array carotid coil. **Results:** Fifty-one percent of participants were female, 78% white, 22% African American, and the mean age was 70 years. Multiple plaque characteristics, including carotid artery wall thickness, lipid core and fibrous cap measures, were evaluated for associations with MMP2 genetic variation (Table 1). MMP2 variant genotypes (CT+TT) were significantly associated with higher cap thickness measures, but not with wall thickness or lipid core measures. Individuals with the CC genotype had approximately 0.1 mm thinner cap thickness compared to those carrying a T allele (p=0.01). **Conclusions:** Genetic variation within the MMP2 promoter region was associated with cap thickness and therefore may influence the role of MMP2 in plaque vulnerability.

TABLE 1. ADJUSTED MEANS AND PERCENTAGES FOR CAROTID ARTERY WALL THICKNESS, LIPID CORE AND CAP MEASURES BY MMP2 RS243865 GENOTYPE

	N	CC	N	CT + TT	P*
Carotid Artery Wall Thickness Measures					
Total Wall Volume (mm^3)	1065	4.166	580	4.190	0.8
Max Wall Thickness (mm, segment)	1065	2.161	580	2.135	0.7
Percent with Lipid Core		23.1%		22.8%	0.9
Lipid Core Measures**					
Total Lipid Core Volume (mm^3)	285	0.730	164	0.682	0.7
Mean Lipid Core Area (mm^2)	285	0.081	164	0.073	0.4
Cap Measures					
Mean Minimum Cap Thickness (mm, 2 adjacent)	280	0.454	164	0.540	0.01
Mean Cap Thickness (mm, 2 adjacent)	280	0.641	164	0.748	0.01

*P-value for test of differences in means and percentages (adjusted for age, race and sex); **Includes only those participants with presence of a lipid core in two adjacent slices Table of Contents ● Report ● Detailed and/or summarized report

P233

Evidence of Genetic Regulation of Circulating Free Fatty Acid Levels in Alaskan Eskimos

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Obesity, particularly upper body or abdominal obesity is a major risk factor for several complex diseases such as cardiovascular disease, type 2 diabetes and metabolic syndrome. Increased abdominal obesity or adiposity is associated with an increased release of free fatty acids (FFAs) into the circulation, which in turn increases insulin resistance in muscle and liver, and induces dyslipidemia and endothelial dysfunction. The main aim of this study was to investigate genetic factors influencing the variation in circulating FFAs in Alaskan Eskimos participating in the Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) study. For this analysis, data were available for 761 individuals (over 35 years of age). Quantitative genetic analyses were conducted using a variance components decomposition approach implemented in the software package SOLAR. Quantitative genetic analysis showed that all fatty acids were significantly heritable ($p < 0.001$), with heritabilities ranging from 0.33 to 0.66. A genome-wide scan conducted to identify chromosomal regions affecting the variation in serum FFAs detected a 20cM region on chromosome 8 (p12- p21) that had a quantitative trait locus (QTL) for monounsaturated fatty acids (MUFAs) (logarithm of odds score (LOD) = 3.6, $p < 0.00001$). The same region had a QTL for polyunsaturated fatty acids (PUFAs) (LOD = 2.4, $p < 0.001$). Interestingly, this region has two important candidate genes, beta-3 adrenergic receptor (ADRB3) and lipoprotein lipase (LPL), both of which have important roles in fatty acid metabolism. Other QTLs identified were on chromosomes 6 for PUFAs (LOD = 2.9, $p < 0.0005$), 2 for saturated fatty acids (SFAs) (LOD = 1.4, $p < 0.05$), and 10 for total FFAs (LOD = 2.5, $p < 0.001$). These results indicate that there is strong genetic influence on the variation in circulating free fatty acid levels. In addition, the major QTL localized on chromosome 8 accounted for 42% and 27 % of the total variation in MUFAs and PUFAs, respectively, and thus, seems to be a major susceptibility locus for serum unsaturated fatty acid levels.

P234

Identification of a Pleiotropic Locus on Chromosome 7q for a Composite Left Ventricular Wall Thickness Factor and Body Mass Index: The Hypertension Genetic Epidemiology Network Study

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Left ventricular (LV) hypertrophy is an important predictor of cardiovascular morbidity and mortality. The growth of LV mass is considered to be a compensatory process to maintain end-systolic wall stress and cardiac output in response to physiological and pathological stimuli such as body growth, obesity, and hypertension. Therefore, LV mass and wall thickness are closely associated with measures of body size and blood pressure. Additionally, there are significant correlations between LV mass and function, suggesting the contribution of common physiologic mechanisms including pleiotropic genes. We conducted a genome-wide scan for a composite phenotype reflecting LV mass and function, termed LV wall thickness factor, as part of the HyperGEN Study. Doppler echocardiography was performed in 434 African-American families (913 hypertensive siblings and 431 offspring) and 284 Caucasian families (589 hypertensive siblings and 530 offspring), respectively. A composite factor, which correlated strongly with LV diastolic interventricular septal thickness (IVSD) and posterior wall thickness (PWTD) and moderately with stress-corrected midwall shortening (MWS), was derived from a factor analysis model. Prior to the factor analysis, each of the component traits was adjusted for age, age^2, and gender in race- and generation-specific linear regression models. Factor score for this composite factor was analyzed in multipoint variance components linkage model implemented in SOLAR with 387 anonymous autosomal markers. In Caucasians, we observed a maximum LOD score of 3.12 at 160 cM on chromosome 7 between markers D7S2195 and GATA189C06. The peak LODs of the 3 component traits clustered at the same region as the composite factor: 2.51 for PWTD, 1.83 for IVSD, and 0.44 for MWS. Adjusting the factor score for BMI, but not SBP, substantially reduced the peak LOD at this region (LOD=1.92). Bivariate linkage analysis of the composite factor with BMI yielded improved LOD (1df LOD = 3.42 at 158 cM) compared to the univariate LODs (LOD = 0.82 for BMI at156 cM). There were no LOD scores ≥ 1.9 for this factor in African Americans. In conclusion, our study suggests that this region on chromosome 7 contains pleiotropic genes influencing both LV wall thickness and BMI in Caucasians.

P235

Genetic Influences on Heart Rate Variability at Rest and in Response to Stress

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Objective: To examine the genetic and/or environmental sources of individual differences and their dependency on ethnicity or sex in heart rate variability (HRV) at rest and in response to

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a series of acute behavioral stressors. **Methods:** Data were available from 234 European American and 174 African American twin pairs including monozygotic and dizygotic of same- as well as opposite-sex (mean age: 17.8± 3.2; range: 11.9- 32.9). HRV indexed by root mean square of successive differences (RMSSD) of normal R-R intervals and high-frequency power (HF) was measured at rest and during a videogame challenge, a virtual reality car driving simulation and a social stressor interview. A bivariate analysis of the resting and the average stress levels across the 3 tasks was used. The heritability of HRV reactivity to stress as a change score was also calculated from the bivariate model. **Results:** Model fitting showed no ethnic or sex differences for all measures, with heritabilities of 0.47 (95%CI: 0.35–0.57) and 0.56 (0.46–0.64) for RMSSD and 0.42 (0.30–0.53) and 0.56 (0.46–0.64) for HF at rest and during stress. The bivariate analysis also indicated that up to 80% and 70% of the heritabilities of RMSSD and HF during stress could be attributed to shared genes with their resting levels. The specific heritabilities due to novel genetic effects emerging during stress were 0.11 (0.03–0.19) for RMSSD and 0.17 (0.05–0.26) for HF. The heritabilities of RMSSD and HF reactivity to stress were 0.19 (0.05–0.32) and 0.21 (0.07–0.34), respectively. **Conclusions:** Independent of ethnicity and sex, substantial overlap exists between genes that influence HRV at rest and during stress. A small but significant genetic component is specific to the stress condition. These findings suggest that HRV regulation at rest and in response to stress is largely influenced by the same genes with a small contribution of stress-specific genetic effects.

P236

Functional SNPs Within the P2X7 Gene and Measures of Periodontitis in Patients with Stable Coronary Heart Disease and Healthy Controls: The Coronary Event and Periodontal Disease (CORODONT) Study

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Background: Genetic predispositions to an increased inflammatory response to infectious stimuli might play a pivotal role in the association between CHD and periodontal disease. The P2X7 receptor has been suggested as an important cell surface regulator of the key pro-inflammatory mediator IL-1β. We investigated the possible association between several functional SNPs within the P2X7 gene and a measure of periodontal disease in patients with stable CHD and healthy controls. Methods: Five P2X7SNPs (rs208294 (C489T); rs28360457 (G946A); rs1653624 (T1729A); rs3751143 (A1513C) and rs2230912 (A1405G)) were genotyped by pyrosequencing in 263 CHD patients and 526 population-based, age- and gender- matched controls without a history of CHD. Subgingival biofilm samples were analyzed for the main periodontal pathogens, such as A. actinomycetemcomitans, B. forsythus, P. gingivalis, P. intermedia and T. denticola, using DNA-DNA hybridization. The need for periodontal treatment in each subject was assessed by the community periodontal index of treatment needs (CPITN). Results: Neither clinical measures of periodontal disease nor various microbiological parameters differed significantly among several genotypes of the five P2X7 SNPs in patients with stable CHD and in healthy controls, despite the possible modulatory properties of these SNPs resulting in the amplification or down-regulation of an inflammatory response. In particular, with respect to the gain of function C489T SNP, mean CPITN after adjustment for age, gender and statin intake was found to be 2.80 vs 2.83 vs 2.85 in the CC-, CT-, and TT-bearing CHD patients (p ANOVA=0.94) and 2.69 vs. 2.69 vs. 2.62 in CC, CT and TT- controls, respectively (p ANOVA=0.77). Concerning oral microbiology, total periodontal pathogen burden was found to be 4.88, 4.73 ands 4.74 in CC, CT or TT genotype carriers in CHD patients (p ANOVA=0.70) and 4.61, 4.52 and 4.51 in CC, CT or TT genotype carriers, respectively, in controls (p ANOVA=0.59). Conclusions: We found no association between individual SNPs within the P2X7 gene and various clinical and microbiological measures of chronic periodontitis in patients with stable CHD and in healthy controls. The cooperative effect of individual SNPs awaits further testing.

P237

Monocyte Chemoattractant Protein-1 (MCP-1) Gene Polymorphisms and Incident Type 2 Diabetes Mellitus (T2DM) in Middle-Aged Men and Women from the MONICA/KORA Augsburg Case-Cohort Study, 1984–2002

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Background: It has been suggested that circulating levels of MCP-1 could be modulated by genetic variations within the gene coding for this protein, thereby accounting for the possible association between MCP-1 concentrations and risk of incident coronary heart disease (CHD) as well as incident T2DM. We have previously shown that various single nucleotide polymorphisms (SNPs) within the MCP-1 gene (CCL2) contributed to MCP-1 levels in the general population. However, no consistent association was found between these SNPs and incident CHD. Here we prospectively investigate whether various SNPs, covering the whole region of the CCL2 gene, might be associated with incident T2DM. Methods: A case-cohort study was conducted in initially healthy, middle-aged men and women based on data from the MONICA/KORA Augsburg studies collected between 1984 and 2002 (mean follow-up 10.1 yrs). Concentrations of MCP-1 were measured in 498 case subjects (307 men, 191 women) with incident T2DM and 1569 non-case subjects (835 men, 734 women). Taking into account possible gender differences, all analyses were carried out for men and women separately. Genotyping of 6 SNPs (rs1024610 (-2136A/T) and rs2857656 (-362C/G) in the promoter region; rs2857657 (+763C/G) in intron 1; rs4586 (+900C/T) in exon 2; rs13900 (+1542C/T) in exon 3, and one SNP in 3' flanking region (+3726T/C, rs2530797) was performed on the Sequenom MALDI-TOF MS system. Results: MCP-1 genotype distribution did not significantly differ among subjects with type 2 diabetes and non-case subjects (n = 2,067). We found no consistent association between these 6 SNPs within the CCL2 gene and incident T2DM in crude and in multivariable adjusted analyses, neither for men and women separately, nor in a model that included all study participants. Conclusions: Despite the fact that polymorphic alleles of rs1024610 and rs2857657 strongly contributed to increased MCP-1 concentrations in women in our previous study, no association was found between these 6 SNPs within the CCL2 gene and incident T2DM during mean 10-year follow-up.

P238

Functional SNPs in the P2X7 Ion Channel and Risk of Chronic Coronary Heart Disease: Results from the CORODONT Study

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Background: The purinergic receptor P2X7, functioning as an extracellular nucleotide-gated ion channel, may play an important role in local inflammatory cytokine release, a crucial step in early atherogenesis. Various single nucleotide polymorphisms (SNPs) which either activate or down-regulate the P2X7 gated calcium signalling, have been described. We sought to investigate whether the presence of individual SNPs within the P2X7 gene might be associated with genetic predisposition for an increased risk of CHD in a large case-control study. Methods: A total of 789 Caucasian subjects, 263 patients with angiographically confirmed, stable CHD and 526 population-based, age and gender matched controls without a history of CHD, were included in the study. Genotyping of the following P2X7 SNPs (C489T, rs208294; G946A, rs28360457; A1405G; rs2230912; A1513C; rs3751143 and T1729A; rs1653624) was performed by pyrosequencing and multivariable logistic regression analysis was applied to estimate the independent association of various P2X7 SNPs with the presence of stable CHD, while simultaneously controlling for confounding factors. Results: Among the 5 studied SNPs in the P2X7 gene, the frequency of the gain-of-function SNP C489T differed between subjects with stable CHD and controls (CC 27.7% CT 50.6 % TT 21.7% vs CC 34.8% CT 44.7 % TT 20.5%, respectively, $p < 0.0499$). However, neither the 5 P2X7 SNPs, nor the 5 more frequent haplotypes inferred from these SNPs were found to be associated with the presence of CHD in crude and in multivariable analyses. Specifically, the risk for presence of CHD in subjects homozygous for the mutant T allele of the gain of function SNP C489T (n=165) was not significantly increased (multivariable adjusted OR 1.06, 95% CI 0.53–2.14), and the same was true for subjects bearing the CT genotype (n=368) (OR 1.37, 95% CI 0.78–2.40) as compared to CC wild type carriers (n=256). Conclusions: Our preliminary findings suggest that functionally relevant SNPs in the P2X7 coding sequence do not play a major role in the susceptibility to CHD, despite the fact that individuals, carrying several of these polymorphic alleles might be exposed to moderately elevated concentrations of various proinflammatory mediators.

P239

Relationship Between Genetic Variants in Myocardial Sodium and Potassium Channel Genes and QT Duration in Diabetics: The Diabetes Heart Study

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Introduction: Several common genetic variants in myocardial sodium and potassium channel genes are associated with prolonged QT duration and increased risk of sudden cardiac death. However, it is unclear whether these genetic variants remain relevant in subjects who already have a predisposition to prolonged QT due to other underlying conditions such as diabetes. We tested single nucleotide polymorphisms (SNPs) in five candidate genes for association with QT interval duration in a family based cohort of subjects with type II DM (T2DM). **Methods**: The Diabetes Heart Study (DHS) is a cross-sectional study of sibling pairs concordant for T2DM. Thirty-six previously reported SNPs were genotyped in the KCNQ1, hERG, SCN5A, KCNE1, and KCNE2 genes in 901 individuals of European American ancestry (83% with T2DM) from 366 DHS families. The QT and QTc durations were determined using the Marquette 12SL program. Associations between the QT duration and the genotypes were evaluated using SOLAR, adjusted for heart rate, age, gender, T2DM status, and body mass index, while assuming a 2 degree of freedom model of inheritance. **Results**: Of the 36 SNPs evaluated, 6 were monomorphic in the DHS population, 3 failed to genotype using the Sequenom MassARRAY system, and 5 failed assay design. There was weak evidence for an association between increasing QT interval duration and the minor allele of rs1805124 in SCN5A (p=0.04); however, no association was observed with the QTc. The minor allele of rs1805123 in the hERG gene was associated with shorter QT duration (p=0.03) and QTc (p=0.08). Within the KCNQ1 gene, both the QT duration (p=0.03) and QTc (p=0.02) were significantly longer in those inheriting the minor allele of IVS12 + 14T>C. No other significant associations were observed between any of the other SNPs and either the QT or QTc. **Conclusions**: Selected genetic variants in previously identified candidate genes remain associated with QT duration in subjects with diabetes. More information is needed to determine the clinical implications of these associations in these subjects whose risk for sudden death is already significantly elevated.

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P240

DNA Repair Genes, Cigarette Smoking, and Intima-Medial Thickness: The Atherosclerosis Risk in Communities Study

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Although the association between cigarette smoking and atherosclerosis is well established and consistent across age, sex, racial, and geographic strata, the mechanisms by which smoking initiates vascular disease remain poorly understood. As differences in responses to mutagen exposure have been attributed in part to heritable variation in DNA repair capacity, we examined the degree to which variation in five DNA repair genes (hOgg1, APEX1, XRCC1, XPD and XRCC3) modified the association between ever-smoking and carotid artery mean intima-medial thickness (IMT) in the Atherosclerosis Risk in Communities (ARIC) cohort. A stratified random sample of 698 Caucasians and 367 African Americans was selected from eligible participants (n=14,255). Analyses were race-stratified and adjusted for age, sex, study center, alcohol intake and physical activity. Baseline mean IMT differences were estimated using hierarchical linear methods that incorporated prior probability distributions (priors) into models including all tagSNPs and models extended to examine gene-by-smoking interaction. Ever-smoking status was associated with a greater mean IMT when priors for genetic (within gene) and environmental effects were added to the first-stage model, with estimated mean differences ranging from 0.047 - 0.12. TagSNPs rs3136814 [APEX1, joint $\text{effect}_{X0/XX\ vs.\ 00}$ = 0.14 (0.03, 0.24)], rs3213282 [XRCC1, joint $\text{effect}_{X0\ vs.\ 00}$ = 0.09 (0.004, 0.17); joint $\text{effect}_{XX\ vs.\ 00}$ = 0.08 (-0.02, 0.19)], and rs3213245 [XRCC1, joint $\text{effect}_{X0\ vs.\ 00}$ = 0.09 (0.02, 0.17); joint $\text{effect}_{XX\ vs.\ 00}$ = 0.09 (-0.02, 0.20)] were associated with increases in the estimated effect of ever-smoking on mean IMT. Though imprecise, our results suggest that DNA repair pathway variants may modify the effect of cigarette smoking on subclinical atherosclerosis. Further work examining these pathways is warranted.

P241

The Association of Hypertension Treatment and Control with All-Cause and Cardiovascular Mortality Among US Adults with Hypertension

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Background. Mortality from the long-term sequelae of hypertension can be prevented through existing antihypertensive drug therapy and blood pressure control. This study examined all-cause and CVD mortality over a 10 year follow-up period for U.S. adults with hypertension by patterns of antihypertensive medication use and blood pressure control. Methods. Persons aged ≥ 18 years from the Third National Health and Nutrition Examination Survey 1988–1994 were identified as hypertensives based on either blood pressure ≥ 140/90 mmHg or currently taking antihypertensive agents for hypertension. Vital status in 2000 was ascertained by passive follow-up studies using the National Death Index. Cox proportional hazard regression analyses were performed to assess correlates of survival, controlling for multiple covariates. Results. At baseline, 52% of hypertensives reported taking prescription medication for controlling their blood pressure. Among treated hypertensives, 38% had their blood pressure controlled. Compared to untreated hypertensives, the adjusted relative risk of all-cause and CVD mortality for treated hypertensives were 0.97 (95% CI 0.83–1.14) and 1.02 (95% CI 0.80–1.28) respectively. Compared to treated controlled hypertensives, the adjusted relative risks of all-cause and CVD mortality for treated uncontrolled hypertensives were 1.42 (95% CI 1.10–1.82) and 1.80 (95% CI 1.30–2.49); for untreated uncontrolled hypertensives, 1.33 (95%CI 1.05–1.70) and 1.54 (95%CI 1.09–2.17) respectively. Hypertensives who received monotherapy with a calcium channel blocker or an angotensin-converting enzyme inhibitors had 61% (95% CI 1.12–2.32) and 56% (95%CI 1.07–2.27) greater risk of all-causes mortality versus those who received monotherapy with a diuretic. No significant associations were observed between drug classes and risk of CVD mortality. Conclusions. Both undiagnosed untreated hypertension and treated uncontrolled hypertension were associated with increased all-cause and CVD mortality compared to treated controlled hypertension. Controlling blood pressure is essential for reducing the excess mortality risk among the hypertensive population.

P242

Gap Analysis of American Heart Association Treatment of Hypertension Blood Pressure Goals

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Background: Based upon new clinical trial evidence and expert opinion, a recent scientific statement of the AHA regarding the treatment of hypertension set new treatment blood pressure goals of <140/90 for the low risk hypertensives, <130/80 for individuals at high risk for cardiovascular disease and <120/80 for individuals with left ventricular dysfunction. We were interested in ascertaining the population impact of these new BP goals in the United States. **Methods:** Using NHANES 1999–2004 data for adults age 18–84, we estimated the number and percentage (%) in the US population for each at risk category, % at target BP goals, % with hypertension and the degree of antihypertensive drug therapy for those with hypertension. The populations included: low risk hypertensives[Framingham risk score-(FRS)<10%], those with chronic kidney disease(CKD)[<60 ml/min estimated Creatinine Clearance], diabetes(DM), stroke (CVA), peripheral vascular disease(PVD), coronary heart disease(CHD),congestive heart failure(CHF), high coronary risk without vascular disease or diabetes (FRS≥10%). Hypertension (HTN) was defined as average BP>140/90 or antihypertensive medication therapy. SUDAAN 9.0 was used to account for complex sampling design of NHANES to estimate US population prevalence. **Results:** Hypertension was prevalent in over 55 million individuals (30.3%) in the US adult population. Of those with hypertension, only 31.8% were at the new BP goals. The percent of the population in various CHD risk categories, at target BP goal, the number with hypertension and the degree of drug therapy for those with hypertension is shown below. **Conclusion:** Over 47 million US adults are not at recommended BP targets. Most high risk cardiovascular risk individuals are not at recommended BP goals. The majority of hypertensives are on no or single drug therapy but for those with established vascular disease, the majority are on 2 or more drugs.

NHANES 1999–2004 ADULT POPULATION ESTIMATES

Population	N	%*	At BP Goal (N)	%	HTN (N)	No Drug Therapy (%)	1-Drug Therapy (%)	2-Drug Therapy (%)	3-Drug Therapy (%)	>3-Drug Therapy (%)
Low Risk	128,479,077	70.7	114,150,992	88.8	21,828,751	43.4	30.5	19.1	6.1	0.9
CHD	8,652,986	4.8	3,590,236	41.5	7,215,479	7.1	29.6	36.3	17.7	9.3
DM	13,342,316	7.4	5,611,900	42.1	8,886,024	12.5	34.6	28.3	16.1	8.5
CKD	17,285,173	9.5	5,605,156	32.4	13,206,962	23.1	27.5	26.6	15.5	7.2
PVD	4,601,823	2.7	1,630,844	35.4	3,511,867	19.8	28.1	27.8	15.5	8.8
CVA	4,102,158	2.3	1,416,369	34.5	3,097,158	9.3	28.7	34.3	18.7	9.0
High Risk	30,879,714	17.0	10,424,052	33.8	19,146,659	21.0	34.6	26.6	12.2	5.6
CHF	3,802,098	2.1	1,237,535	32.6	3,153,169	7.1	24.5	28.0	22.9	17.6
Total	181,617,539		134,544,709		55,101,100	30.6	31.7	23.7	10.3	3.7

*Total Percentage>100% because subjects can be in more than one category

P243

Elevated Blood Pressure Prevalence in Children Did Not Follow the Increase in Overweight: Results from a School-Based Study in a Rapidly Developing Country, 1998–2006

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Background: Blood pressure (BP) is strongly associated with body weight and there is concern that the pediatric overweight epidemic could lead to an increase in children's mean BP. **Objectives:** We analyzed BP trends from 1998 to 2006 among children of the Seychelles, a rapidly developing middle-income country in Africa. **Methods:** Serial school-based surveys of weight, height and BP were conducted yearly between 1998–2006 among all students of the country in four school grades (kindergarten, 4th, 7th and 10th years of compulsory school). We used the CDC criteria to define "overweight" (BMI ≥95th sex-, and age-specific percentile) and the NHBPEP criteria for "elevated BP" (BP ≥95th sex-, age-, and height specific percentile). Methods for height, weight, and BP measurements were identical over the study period. The trends in mean BMI and mean systolic/diastolic BP were assessed with linear regression. **Results:** 27,703 children aged 4–18 years (participation rate: 79%) contributed 43,927 observations on weight, height, and BP. The prevalence of overweight increased from 5.1% in 1998–2000 to 8.1% in 2004–2006 among boys, and from 6.1% to 9.1% among girls, respectively. The prevalence of elevated BP was 8.4% in 1998–2000 and 6.9% in 2004–2006 among boys; 9.8% and 7.8% among girls, respectively. Over the 9-years study period, age-adjusted body mass index (BMI) increased by 0.078 kg/m^2/year in boys and by 0.083 kg/m^2/year in girls (both sexes, P<0.001). Age- and height-adjusted systolic BP decreased by -0.37 mmHg/year in boys and by -0.34 mmHg/year in girls (both sexes, P<0.001). Diastolic BP did not change in boys (-0.02 mmHg/year, P: 0.40) and slightly increased in girls (0.07 mmHg/year, P: 0.003). These trend estimates were altered modestly upon further adjustment for BMI or if analyses were based on median rather than mean values. **Conclusion:** Although body weight increased markedly between 1998 and 2006 in this population, systolic BP decreased and diastolic BP changed only marginally. This suggests that population increases in body weight are not necessarily associated with corresponding rises in BP in children.

P244

Dietary and Supplemental Iron, Red Meat, and Blood Pressure: INTERMAP Study

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Background and objectives: Iron is a redox-active transition metal that may contribute to production of reactive oxygen species, oxidative stress and inflammation - all shown to influence blood pressure (BP) levels. We investigate comprehensively, for the first time, associations of dietary (total, heme and non-heme iron), supplemental iron, and - the major food source of heme iron - red meat, with individuals' BP in International Study of Macro- and

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Micro-nutrients and Blood Pressure (INTERMAP). Methods: Cross-sectional data including 4 standardized in-depth 24-hr dietary recalls, 2 timed 24-hr urine collections, and 8 BP readings were analysed for 4,680 men and women ages 40–59 years (17 population samples from Japan, China, UK and US). Results: In multiple linear regression analyses dietary total and non-heme iron were consistently inversely associated with BP. Adjusted for multiple confounders (including urinary sodium and potassium, alcohol intake, dietary cholesterol, saturated and polyunsaturated fats) systolic BP differences were -1.4 mm Hg ($p<0.001$) for dietary iron intake higher by 4.2 mg/1,000 cal (2 s.d.) and 2.14 mm Hg($p<0.001$) for dietary non-heme iron intake higher by 4.1 mg/1,000Kcal (2 s.d.). BP differences were smaller for diastolic BP. Heme iron intake from food was consistently positively associated with BP, though associations were weak and non-significant. Iron intake from diet and supplements combined was inversely associated with BP; however, associations were weaker than those of dietary iron alone. Red meat intake was directly associated with BP; 103 g/24-hours (2 s.d.) higher red meat intake was associated with 1.3 mm Hg higher SBP ($p<0.01$). Associations of red meat and BP persisted with adjustment for urinary sodium and potassium, alcohol intake, dietary cholesterol, saturated and polyunsaturated fats, heme iron, and animal protein intake. Conclusions: These findings, based on large sample size and robust methods, indicate a possible role for non-heme iron in lowering blood pressure. An unfavorable effect of red meat on BP was also observed. These findings must be confirmed in other populations, meanwhile current dietary guidelines for the prevention and control of high BP remain prudent.

P245

30-Year Survival for Black and White Individuals with Hypertension

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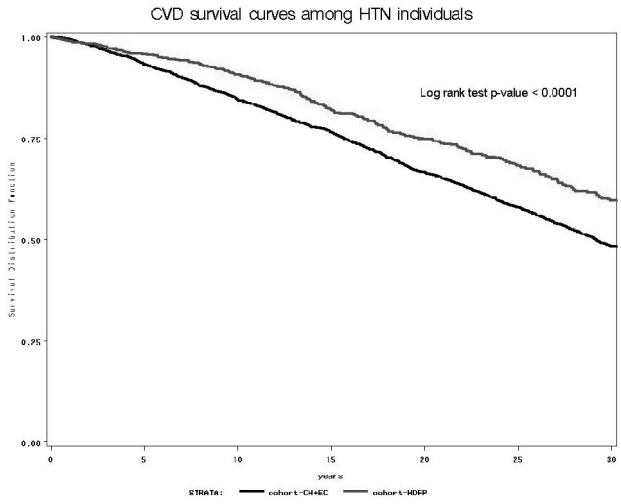
Introduction Treating hypertension has been long recognized as a major intervention for reduction of cardiovascular disease outcomes. The Hypertension Detection and Follow-up Program (HDFP) was one of the first major studies to demonstrate blood pressure reduction and the short-term benefits of stepped care (SC) compared with usual care (UC). Study objectives were to evaluate 30-year survival and cardiovascular outcomes of the Georgia cohort of HDFP (HDFP-GA) and to compare outcomes of these patients with 2993 hypertensive individuals from the Evans County Heart Study (ECHS) and Charleston Heart Study (CHS) cohorts. Methods HDFP-GA patients consisted of 688 individuals (black (n=267); white (n=421)) randomized to UC (n=341) and SC (n=347). The combined ECHS and CHS included 1369 black and 1624 white hypertensives. All-cause mortality and cardiovascular disease mortality were assessed as survival outcomes within the HDFP-GA population and compared to the ECHS and CHS combined cohorts. Results After 30-years, 66.9% of the HDFP-GA cohort died; with 32.8 % cohort mortality rate due to cardiovascular disease (CVD). Further, CVD rates for the SC (32.3%) and UC (33.4%) were similar as well as similar for the four race-sex subgroups. CVD survival rates for both SC and UC HDFP-GA arms were significantly better than population-based hypertensive individuals in the ECHS and CHS cohorts, with consistent benefits in all four race-sex groups. Conclusions These results identify systematic hypertension treatment and management as achieved by a disease management protocol to be beneficial for long-term cardiovascular disease outcomes compared with a general hypertensive population.



P246

What Factors Predict Hypertension Medication Nonadherence in Young Urban Black Males?

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Background: Young black males with high blood pressure (HBP) are under-studied and have lower rates of HTN treatment and control than whites. Medication non-adherence is a significant contributor to poor blood pressure control; however, few studies have prospectively assessed how the predictors of hypertension (HTN) medication adherence change over time. **Objective:** Identify longitudinal predictors of anti-hypertensive adherence using the Hill-Bone Compliance to HBP Scale, Medication-Taking subscale (HBS-MT) for 309 males enrolled in a randomized clinical trial evaluating the effectiveness of a HTN intervention. **Methods:** Black males with HTN aged 21 to 54 from inner-city Baltimore, MD participated in this trial. Controlling for age, marital status, employment, randomization group and baseline urine screen for illicit drugs, generalized estimating equations were used to identify predictors of medication adherence at 0, 24, 36, 48 and 60 months. Interactions with time were also evaluated. **Results:** Depression is positively associated (β=1.02, $p<0.001$) and satisfaction with medical care is negatively associated (β= -0.57, p= 0.003) with non-adherence. The association between medication class and non-adherence differs by time period (see table). Overall, Thiazide diuretic use (β= -1.65, p= 0.001) and B-blocker use (β= -1.91, p= <0.001) are negatively associated and Angiotensin Receptor Blocker (ARB) use (β= 1.81, p< 0.001) is positively associated with medication non-adherence. **Conclusions:** Depression and satisfaction with care are strongly related to medication non-adherence and medication class affects patterns of adherence.

TABLE: MEAN DIFFERENCES IN HBS-MT SCORES* BY MEDICATION CLASS OVER TIME

Medication class	Baseline	24 mo	36 mo	48 mo	60 mo
Thiazide diuretic use§	-1.7	-1.0	1.4	2.4	1.1
Beta-Blocker use§	-1.9	-0.6	-0.7	-1.3	-1.8
ARB use§	No data	-0.7	0.8	-1.0	-0.2

*HBS-MT scale is reverse-coded, such that lower scores indicate better medication adherence § Versus use of any other JNC-7 medication class (Thiazide diuretics, Beta-blockers, ACE-Inhibitors, Angiotensin Receptor Blockers, Dihydropyridine Calcium-channel blockers, Non-dihydropyridine Calcium-channel blockers, Combination medications)

P247

Relationships Between Cardiovascular Risk Factors and Biventricular Volume in the Diabetes Heart Study

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Introduction: Biventricular volume (BivV) is a newly described, easily acquired measure of cardiac size obtained from non-contrast, low dose (~1mSv), ECG gated CT scans. These measures may provide additional relevant information about cardiac risk at the time of screening coronary artery calcium-CT. To establish the validity of these measures as indicators of cardiac risk, we examined the association between traditional cardiovascular disease (CVD) risk factors and BivV in a cohort enriched with type 2 diabetes (T2DM). **Methods**: The Diabetes Heart Study (DHS) is a cross-sectional study of sibling pairs concordant for T2DM and other family members. In DHS, 1,241 participants (692 females and 549 males, 85% diabetic) had cardiac CT scans; BivV was measured from the cardiac CT scans, and associations with risk factors were assessed with t-tests, bivariate correlations, and multivariable regression analyses. **Results**: The average BivV in this sample was 379.4 ± 114.5 mL. In univariate models, the following variables were directly or inversely* associated with BivV at a significance level of $p<0.01$: age*, male gender, T2DM, hypertension, CVD, systolic blood pressure, HDL*, LDL*, height, weight, smoking pack years, and microalbumin. After adjustment for age, race, gender, height, and weight, the following variables were directly or inversely* associated with BivV at a significance level of $p<0.005$: hypertension, prevalent CVD, systolic BP, and urine microalbumin; or at the $p<0.05$ significance level: HDL-C*, estimated glomerular filtration rate*, years with diabetes (diabetic subjects only). The following variables were not significantly associated with BivV: Diastolic BP, LDL, use of lipid lowering drugs, current smoking, smoking pack-years, hemoglobin A1c. **Conclusions**: In this sample, most CVD risk factors were significantly associated with higher biventricular volumes in the expected direction. This supports the hypothesis that, similar to left ventricular hypertrophy, biventricular volume is related to CVD risk and may be useful in predicting CVD events.

P248

Influence of Environmental Mercury Exposure on Blood Pressure and Heart Rate Variability in an Aboriginal Population of the James Bay (North of Quebec, Canada)

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Background: Aboriginal populations inhabiting the North of Quebec are exposed to environmental mercury because their diet is still based on traditional food. Mercury, which is accumulated in fish as methyl mercury (MeHg), has been associated with increment in blood pressure (BP) and decreased heart rate variability (HRV) with inconsistent results. **Objective:** To assess the impact of mercury levels on BP and HRV among adult Cree of Mistissini taking into account potential confounding factors such as age, gender, cholesterol levels, insulin sensitivity, waist circumference, smoking habits, n-3 fatty acids and selenium. **Methodology:** During summer 2005, a Health Survey was conducted among Cree of Mistissini. Information was collected among 169 adults ≥ 18 years. BP was taken according to the WHO clinical guidelines for management of systemic hypertension while HRV was measured following a 2-hour Holter monitoring. Simple relation between MeHg and BP and HRV parameters was explored using Pearson correlations while multiple regressions were used to adjust for confounders. **Results:** Mercury was positively correlated with systolic blood pressure (SBP) (r= 0.48; $p<0.0001$) and pulse pressure (PP) (r= 0.46; $p<0.0001$) while the correlation with diastolic blood pressure (DBP) did not reach statistical significance. Following multiple regression analysis, the association between mercury and PP became non significant while the effect of mercury on SBP remained significant (β= 2.89; p= 0.02). In contrast, the association between mercury and DBP became significant once confounders were considered (β= 2.18; p= 0.047). Regarding HRV, mercury was negatively correlated with low frequency (LF) (r=

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-0.28; p= 0.0001), high frequency (HF) (r= -0.25; p= 0.0004), the squared root of the mean squared differences of successive RR intervals (rMSSD) (r= -0.17; p= 0.02) and the proportion of interval differences of successive RR intervals > 50 ms (pNN50) (r= -0.19; p= 0.02) but these associations became non significant after adjusting for confounders. **Conclusion:** A negative influence of mercury on BP was observed taking into account potential confounding factors while HRV parameters were not affected by mercury concentrations after adjusting for confounders.

P249

Tracking of Blood Pressure Variability: A 15-Year Longitudinal Study from Childhood to Early Adulthood

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Backgrounds: Although high blood pressure variability (BPV) has been increasingly used as a predictor of end-organ damage and cardiovascular events, little is known about its ability to track in childhood and early adulthood and its dependency on ethnicity and gender. **Methods:** The 24-hour ambulatory systolic (SBP) and diastolic blood pressure (DBP) were measured up to 12 times over a 15-year period in 295 European Americans (EAs) and 252 African Americans (AAs) with the average age of 14-year-old at initial visit. Pulse pressure (PP) was calculated as SBP-DBP. BPV was indexed by the standard deviation (SD) of the ambulatory BP recordings over the entire 24-hours and separately for the day-time and night-time sub-periods. To account for the influence of the nocturnal BP fall on the 24-hour BP SD, the weighted 24-hour BP SD, defined as the mean of the day-time and night-time SD weighted for their respective durations, was also used in this study. Generalized estimating equations were used to estimate the tracking coefficients of BPV. **Results:** All BPV measures showed significant but low stabilities over time (all tracking coefficients ≤0.35, with all p-values <0.001). The 24-hour SD had the highest tracking stability for SBP, DBP and PP, respectively (0.22, 0.30 and 0.35), followed by those of day-time (0.09, 0.20 and 0.31) and night-time (0.10, 0.11 and 0.16). The weighted 24-hour SD showed the tracking coefficients of 0.12, 0.22 and 0.33 which were lower than those of 24-hour while higher than those of day-time and night-time. In comparison of different BP components, PP showed the highest tracking coefficient, followed by DBP and SBP. No effect of ethnicity or gender was found for BPV tracking. **Conclusions:** The results showed that tracking coefficients of BPV were low over a period of 15 years from childhood to early adulthood. This indicates that BPV might not be a stable measure and may therefore have limited value in reliably predicting cardiovascular outcomes.

P250

Complementary Effects of Lifestyle Modification with Antihypertensive Therapy in the Management of Stage 1 Hypertension

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Hypertension is a significant risk factor for cardiovascular disease and stroke. Lifestyle behaviors including sodium restricted diets, exercise and weight loss have been demonstrated to help in the management of hypertension. The blood pressure lowering effect of lifestyle modification (LM) alone has not been extensively studied in comparison to combined therapy. Therefore, we measured the effects of LM alone and a combined treatment of lifestyle modification with antihypertensive medication valsartan-based regimen (LM-med) on blood pressure. Twenty- nine overweight and obese men and women age 41–71 with stage 1 hypertension (SBP 140–159 mm Hg, DBP 90 -99 mm Hg) were randomized into the LM or LM-med group. Participants in the LM group were instructed on lifestyle modification consistent with JNC VII treatment guidelines, which include reduction in sodium intake (less than 2400mg/day), moderate physical activity, smoking cessation, and limited alcohol consumption. Participants in the LM-med received similar instruction on lifestyle modification in addition to an appropriately prescribed regimen of antihypertensive medication. Participants also received instruction on weight loss and had bi-weekly follow-up visits with a dietitian and exercise physiologist. Although significant within group changes in weight after 12 weeks were observed, these changes were similar between the groups (LM: -4.11 ± 2.17 kg; LM-med: -2.36 ± 3.29 kg, p=0.140). After 12 weeks, SBP was significantly reduced within the groups (LM: -12.0 ± 11.26 mmHg; LM-med: -20.89 ± 13.52 mmHg, p<0.001) but not between the groups (p=0.087). DBP was significantly reduced within the groups after 12 weeks (LM: -7.7 ± 7.15 mmHg; LM-med: -14.31 ± 8.16 mmHg, p<0.001) and between the groups (p=.040). Sodium intake was significantly reduced in both groups after 12 weeks (LM: 3806.2 ± 1564.3 to 2460.4 ± 1510.3; LM-med: 3461.2 ± 1249.9 to 2765.1 ± 1526.7, p<0.001). These data suggests that the reductions in BP achieved with lifestyle modification are in addition to the reductions in BP achieved with drug therapy and that the simultaneous implementation of drug therapy with lifestyle modification is recommended for optimal management of patients with stage 1 hypertension.

P251

Racial and Regional Variations in the Incidence of Hypertension: 20-Year Follow-up in the CARDIA Study

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Objective: Cardiovascular disease (CVD) mortality, including stroke and coronary heart disease, varies by race, sex and region. To better understand these variations, we assessed 20-year incidence of hypertension, a CVD risk factor, by race-sex and region. **Methods:** Among 3,436 eligible black and white adults aged 18–30 years recruited in 1985–86 in the population-based Coronary Artery Risk Development in Young Adults (CARDIA) cohort, we examined cumulative hypertension (SBP ≥140 mmHg or DBP ≥90mmHg or anti-hypertensive medication at any examination) incidence from years 0 to 20 by race-sex and examination center, adjusting for baseline covariates with Cox regression models (Table 1). **Results:** 20-year hypertension incidence was highest among black men (34.5%; n=617; mean age 44.5 ± 3.7 years) and black women (37.6%; n=965; mean age 44.6 ± 3.9 years) compared to white men (21.4%; n=856; mean age 45.7 ± 3.4 years) and white women (12.3%; n=998; mean age 45.7 ± 3.4 years), (P<0.001). Birmingham participants had greater incident hypertension (33.6%) than those from Chicago, (23.4%), Minneapolis, (19%), and Oakland, (28.3%), (P<0.001). After adjustment, regional differences in hypertension incidence persisted within the overall cohort but some regional contrasts were no longer statistically significant within race-sex groups (Table 1). **Conclusion:** Hypertension incidence between age 24 and 45 years varies significantly by race-sex and region. Known risk factors for hypertension do not fully explain these differences.

TABLE 1: ADJUSTED HAZARD RATIOS AND 95% CONFIDENCE INTERVALS FOR CUMULATIVE 20-YEAR HYPERTENSION INCIDENCE, OVERALL, AND STRATIFIED BY RACE-SEX GROUP, AMONG ADULTS AGED 18–30 YEARS: THE CARDIA STUDY, 1985–2005

	Hazard ratio (95% CI) for Cumulative 20-Year Hypertension Incidence				
Baseline Variable	Overall Cohort (n=3286)	Black Men (n=599)	Black Women (n=901)	White Men (n=825)	White Women (n=961)
Age (per year)	**1.06 (1.04, 1.08)**	**1.04 (1.00, 1.09)**	**1.05 (1.02, 1.09)**	**1.09 (1.03, 1.14)**	**1.08 (1.02, 1.14)**
Black men	1.00	NA	NA	NA	NA
Black women	**0.82 (0.68, 0.99)**	NA	NA	NA	NA
White men	**0.58 (0.47, 0.72)**	NA	NA	NA	NA
White women	**0.33 (0.26, 0.43)**	NA	NA	NA	NA
Birmingham	1.00	1.00	1.00	1.00	1.00
Chicago	**0.66 (0.54, 0.81)**	**0.62 (0.41, 0.95)**	**0.69 (0.51, 0.93)**	**0.63 (0.41, 0.98)**	0.83 (0.47, 1.46)
Minneapolis	**0.58 (0.48, 0.71)**	0.67 (0.45, 1.01)	**0.62 (0.44, 0.87)**	**0.49 (0.33, 0.75)**	**0.54 (0.32, 0.91)**
Oakland	0.84 (0.70, 1.00)	0.96 (0.68, 1.36)	**0.71 (0.54, 0.94)**	1.01 (0.67, 1.53)	0.91 (0.55, 1.50)
Heart rate (per beat)	**1.01 (1.01, 1.02)**	**1.02 (1.01, 1.03)**	1.01 (1.00, 1.02)	**1.01 (1.00, 1.02)**	**1.01 (1.00, 1.03)**
BMI (kg/m^2)	**1.06 (1.05, 1.08)**	**1.06 (1.03, 1.09)**	**1.05 (1.03, 1.06)**	**1.13 (1.08, 1.17)**	**1.12 (1.08, 1.15)**
Current tobacco use	**1.26 (1.08, 1.47)**	**1.51 (1.10, 2.06)**	1.26 (0.98, 1.62)	0.87 (0.59, 1.27)	1.45 (0.95, 2.22)
Family history of hypertension	**1.54 (1.33, 1.77)**	**1.69 (1.27, 2.26)**	**1.36 (1.08, 1.72)**	1.31 (0.97, 1.78)	**2.06 (1.40, 3.03)**
Education ≥high school†	**0.65 (0.52, 0.82)**	0.84 (0.53, 1.31)	0.72 (0.51, 1.02)	**0.45 (0.24, 0.81)**	**0.36 (0.18, 0.73)**
Elevated uric acid§	**1.30 (1.08, 1.57)**	1.38 (0.99, 1.90)	1.33 (0.90, 1.96)	1.04 (0.73, 1.50)	1.13 (0.63, 2.03)
Heavy alcohol use‡	0.90 (0.72, 1.14)	1.15 (0.77, 1.74)	0.82 (0.51, 1.33)	0.84 (0.54, 1.31)	0.69 (0.38, 1.26)

*Bolded figures indicate 95% CI not containing one. †Education uses last available education. §Elevated uric acid: ≥7 mg/dL for men and ≥6 mg/dL for women. ‡Heavy alcohol: >14 drinks/wk (men) and >7 drinks/wk (women).

P252

Severity of Coronary Artery Disease Is Predicted by Exercise Pulse Pressure

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Introduction: Abnormal blood pressure (BP) response to exercise is associated with a compromised cardiovascular system and the presence of cardiovascular disease (CVD). Since pulse pressure (PP) is determined by the response of both systolic and diastolic BP, it may be a better indicator of cardiovascular function and CVD. Thus, an insufficient rise in PP during exercise may signify myocardial hypoxia and be a stronger and more clinically useful marker for coronary artery disease (CAD) severity. However, the association between PP and severity of CAD has not been well-defined. **Methods:** To determine the association between exercise PP and CAD severity, we assessed exercise parameters and angiographic findings in 282 patients (61 ± 11 years) undergoing cardiac angiography subsequent to a positive exercise tolerance test. Severe CAD was defined as a diameter stenosis of: 1) 50% or greater in left main coronary artery; 2) 70% or greater in three vessels; and 3) 70% or greater in two vessels with the proximal left anterior descending artery involved. Multivariate logistic regression models were applied. Data were adjusted for age, body mass index, cardiac medications, baseline measurements and the conventional cardiovascular risk factors. **Results:** Eighty-three (28.1%) of the patients had severe CAD and 212 (71.9%) had moderate or mild CAD. The strongest predictors of CAD severity were PP at the exercise workload of 5 METs (OR=0.982; CI: 0.97–0.99; p=0.001) and PP at peak exercise (OR=0.983; CI: 0.97–0.99; p=0.001). More specifically, the risk of severe CAD was reduced 18% for every 10 mm Hg increase in either PP. Cut-off analysis also revealed a PP threshold of 60 mm Hg at the exercise workload of 5 METs. The risk for severe CAD was 2.0 times higher for those with PP at the exercise workload of 5 METs or below this threshold (OR = 2.0; CI: 1.2–3.5; p <0.001). **Conclusions:** Failure of PP to rise above 60 mm Hg at the exercise workload of 5 METs constitutes a 2-fold increase in the likelihood of severe CAD. The risk of CAD severity is lowered by 18% for every 10 mm Hg increase in PP above this threshold.

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P253

Blood Pressure Control Among Patients After Coronary Artery Bypass Grafting Surgery in a Veterans Affairs Hospital

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Background: Controlling BP is very important in decreasing cardiovascular risk. Patients undergoing CABG are at high risk for recurrent cardiac events; blood pressure control is a cornerstone of secondary prevention in this high risk cohort. The current JNC-7 guideline advocates BP target of <140/90mmHg. Methods: We conducted a retrospective study of all 123 patients who underwent CABG between August 2004 and August 2006. We obtained blood pressure values and hypertensive medications prescribed prior to and six months post CABG. Target blood pressures were determined by the JNC-7 guidelines. Results: Six months after CABG, the SBP was lowered by 4mmHg (p=0.08) and DBP was lowered by 2mmHg (p=0.1). SBP was at goal for only 43% of patients prior to CABG and 44% of patients six months following CABG. DBP was at goal for 68% of patients prior to CABG and 73% of patients six months following CABG. No significant change occurred with use of beta-blockers (62% pre and 63% post, p=0.1), nitrates (22% pre and 11% post, p=0.1), or ACEI/ARBs (62% pre and 63% post, p=0.9). There was a significant reduction in the use of CCBs (27% pre and 17% post, p<0.0001). Patients were prescribed a similar number of anti-hypertensive medications both pre and post CABG (2.11 vs. 2.17 p=0.64). Conclusion: Surprisingly, we did not observe any change in blood pressure in this high risk cohort of patients who underwent CABG. With the exception of a decrease in CCB use, there were no differences in utilization of the other efficacious anti-hypertensive medications. Despite having less than half of the patients at goal BP, we did not observe any increase in the number of anti-hypertensive medications prescribed among our patient population. More aggressive management is clearly required in this high-risk population. Table

Variable	SBP	DBP
Baseline BP (n=122)	135	74
6 month BP (n=113)	131	72
ΔBP (mmHg)	4 p=0.0825	2 p=0.1134
% patients at target BP prior to CABG (n=122)	43%	68%
% patients at target BP post CABG (n=113)	44%	73%
Δ in rates of achieving target BP	p=0.5	p=0.5

P254

Differences in Blood Pressure Control in Urban and Rural Populations, Effects of Race, and Comorbidities: The Geisinger Clinic and University of Pennsylvania Populations

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While it is universally acknowledged that control of blood pressure in primary care is of major importance in reducing the burden of cardiovascular and related diseases, control is suboptimal in most populations. We evaluated BP control over a 3 year interval according to JNC-VII guidelines in primary care patients managed in two Pennsylvania health care systems, one urban (Penn = P, N=16,690) and one rural (Geisinger =G, N=79,934). Factors assessed included number of comorbidities (diagnoses occurring ≥2 times that could compete for clinician attention), number of primary care visits, age, sex, race, insurance and health system. The reduced JNC-VII threshold of 130/80 was applied for diabetes and chronic kidney disease. The G population was more Caucasian (C)(98 vs 49 percent), less African American (AA)(1 vs 46 %), marginally older (60.2 vs 59.2 years), and less female (56 vs 61 percent). Mean days of follow-up and number of BP readings were 1197 and 12.4 at G and 1010 and 9.9 at P. The mean number of comorbidites was 3.4 at G and 3.7 at P. and, by race, 3.45 for C, 3.90 for AA. Medicare coverage was slightly more common at P (32 vs 29 %) and commercial insurance slightly more common at G (63 vs 58 %). BP was controlled in a similar proportion of readings 66% and 65% (G and P). Binary logit models were constructed using percent of visits with BP controlled (%vBPc) as the dependent variable and including all the above factors. Overall, increasing comorbidity was associated with a slightly greater %vBPc (p<0.0001), with an effect size averaging 1–2% for each comorbidity. This did not vary by age, but was different by race. In AA, increasing comorbidity was associated with a decreased %vBPc. After accounting for race, there were no differences between the urban and rural health systems. In analyses restricted to C, increased comorbidity predicted higher %vBPc with all forms of insurance (including self-pay) in all age groups. In AA, a strong inverse effect of comorbidity on %vBPc was evident in patients over the aged ≥60 years with commercial insurance; this effect was weaker with Medicare. These findings suggest that racial mix may explain urban-rural contrasts in BP control, and management of comorbidities complicates control in AA, but not in C. More refractory BP in AA may be a factor.

P255

Metabolic Syndrome and Salt-Sensitivity of Blood Pressure Among Chinese Adults

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We studied the relationship between metabolic syndrome and blood pressure (BP) responses to dietary sodium intervention among 1,906 GenSalt study participants in rural China. The metabolic syndrome was defined as the presence of three or more of the following risk factors: elevated BP, low HDL-cholesterol, high triglyceride, elevated glucose, and abdominal obesity according to the criteria recommended in the National Cholesterol Education Program Adult Treatment Panel III guidelines. Dietary sodium intervention included a 7-day low sodium-feeding (51.3 mmol/day) and a 7-day high sodium-feeding (307.8 mmol/day). A total of nine BPs were measured during the 3-day baseline observation and the last 3 days of each intervention phase using a random-zero sphygmomanometer. Multivariate linear regression analyses were used to adjust for age, gender, education, cigarette smoking, alcohol consumption, physical activity, body mass index, and baseline 24-hour urinary excretion of sodium and potassium. Compared to participants with zero components of the metabolic syndrome, the mean systolic BP reduction (95% confidence intervals [CI]) during low-sodium intervention was -1.33 (-2.11, -0.55), -1.32 (-2.26, -0.39), -2.64 (-3.87, -1.41), and -5.10 (-6.84, -3.35) mm Hg for those with 1, 2, 3, and 4 to 5 components, respectively (p <0.0001 for linear trend). The corresponding mean systolic BP increase (95% CIs) during high-sodium intervention was 0.52 (-0.15, 1.19), 1.22 (0.41, 2.02), 2.13 (1.07, 3.18), and 4.33 (2.84, 5.83) mm Hg (p <0.0001 for linear trend). The multivariate-adjusted net change (95% CI) of systolic BP in participants with compared to their counterparts without the metabolic syndrome were -2.17 (-3.14, -1.20) mm Hg during low-sodium intervention and 1.97 (1.14, 2.40) mm Hg during high-sodium intervention, respectively (both p-values <0.0001). These results suggest that metabolic syndrome is significantly related to salt-sensitivity. Therefore, a low dietary sodium intake may be more effective in reducing BP among patients with metabolic syndrome.

P256

Prehypertension and Risk of Cardiovascular Disease in Chinese Adults

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Objectives: The excess risks associated with prehypertension and the cost-effectiveness of treatment have not been well examined. **Methods:** We conducted a prospective cohort study in a nationally representative sample of 169,871 Chinese men and women aged 40 years and older. Data on blood pressure and covariables were obtained at a baseline examination in 1991 using a standard protocol. Follow-up evaluation was conducted in 1999–2000, with a response rate of 93.4%. **Results:** Prehypertension was significantly associated with an increased relative risk (95% confidence interval) of cardiovascular disease incidence 1.34 (1.27, 1.42) and mortality 1.22 (1.15, 1.30), coronary disease incidence 1.32 (1.16, 1.50) and mortality 1.47 (1.23, 1.75), and stroke incidence 1.72 (1.59, 1.86) and mortality 1.67 (1.50, 1.86). The population attributable risk associated with prehypertension was 10.6% and 7.1% for cardiovascular disease incidence and mortality, 9.9% and 13.9% for coronary disease incidence and mortality, and 19.9% and 18.7% for stroke incidence and mortality. The five-year number-needed-to-treat to prevent a cardiovascular disease event or death was 53 and 185, 17 and 51, and 8 and 22 for prehypertension, stage-1 hypertension, and stage-2 hypertension, respectively. The number-needed-to-treat to prevent a cardiovascular disease event was significantly smaller in prehypertension patients with a history of clinical cardiovascular disease or diabetes (34 for incidence and 44 for mortality) compared to those without (115 for incidence and 352 for mortality). **Conclusions:** Prehypertension was related to an increased risk of cardiovascular disease. Treatment of prehypertension appeared cost-effective only among patients with a history of clinical cardiovascular disease or diabetes.

P257

Dietary Carbohydrate Intake of Individuals (Total, Starch, Total Sugar) and Their Blood Pressure: INTERMAP Study

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BACKGROUND: Clinical trial data suggest high-monounsaturated fatty acid (MUFA) or high-vegetable protein diets reduce blood pressure (BP) more than isoenergetic high-carbohydrate (CHO) diets. METHODS AND OBJECTIVES: Data collected in the cross-sectional INTERMAP Study include four 24-h dietary recalls; two 24-h urine collections; eight BP readings; and questionnaire data, for 4680 men and women ages 40–59 yr from 17 population samples in Japan, People's Republic of China, United Kingdom, and United States of America. These data were used to test the prior hypothesis that individuals' dietary starch intake is directly related to their BP, and to explore associations of total CHO and total sugar with BP. RESULTS: Starch intake (adjusted for sample, age, sex) was positively correlated with vegetable protein (r=0.58) and negatively correlated with saturated fatty acid (SFA; r=-0.41). Total CHO was negatively correlated with SFA, MUFA, polyunsaturated fatty acids (PFA), dietary cholesterol, alcohol and animal protein (r= -0.65 to -0.44). No high-order correlations were observed for total sugar. In multiple linear regression analyses – adjusted for urinary Na, urinary K, alcohol, cholesterol, PFA, et al. – starch intake higher by 14.1% kcal (2 s.d.) was associated with systolic/diastolic BP differences of -1.3/-1.2 mmHg (p<0.05/p<0.01). These were reduced to -0.7/-0.8 mmHg (p non-significant/p<0.05) with control for weight and height and reduced similarly by control for dietary fibre. Systolic/diastolic BP differences were eliminated by separate adjustment for vegetable protein. The magnitude and pattern of associations were similar for total CHO. Associations between total sugar intake and BP were mostly direct, weak, and non-significant. CONCLUSION: These findings reject the prior hypothesis and indicate weak inverse (not direct) relations of starch and total CHO to BP. Current dietary guidelines for hypertension prevention

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and control remain prudent. More research is needed on CHO and BP, including on individual sugars and glycaemic load.

P258

Hypertension Is Associated with Markers of Obesity, LDL Cholesterol, and Family History of Hypertension in Asian Indian Adolescents

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Introduction: Primary hypertension has become increasingly common in children. While there is an increase in prevalence of pediatric obesity in India, hypertension (HTN) remains understudied. This study explores the relationship of hypertension with the markers of obesity, LDL-cholesterol (LDL-C) and family history of HTN in Asian Indian adolescents. **Methods**: Cross sectional data of 1133 school and college going adolescents aged 14–20 yrs in New Delhi, India (collected using WHO multi-cluster sampling) were analyzed. Systolic hypertension (SHTN) and diastolic hypertension (DHTN) were defined using upper 90th percentile as >124 and > 82 mm Hg, respectively. Body fat% was calculated using bipedal bioelectric impedance. Sum of four skin fold thickness (biceps, triceps, sub-scapular and supra-iliac) was also used as a marker of obesity. Markers of obesity, fasting blood sugar (FBG), HbA1c and LDL-C were divided into quartiles and odds ratios (ORs) of HTN calculated for highest quartile with reference to the lowest. **Results**: The prevalence of SHTN and DHTN using above cutoffs were 9.8% and 9.2%, respectively. Overall, HTN was present in 14.3%. Boys (n=577) had significantly higher mean ± SD SBP (115.1 ± 9.9 versus 111 ± 9.3 mm Hg) and DBP (74.8 ± 7.3 versus 73± 6.5 mm Hg) than girls, p<0.001. All markers of obesity, but waist-hip ratio, were significantly associated with both systolic and diastolic hypertension after adjustment for age and gender [See Table]. While both SHTN and DHTN were associated with LDL-C; neither were associated with FBG or HbA1c. The odds of overall HTN associated with family history of HTN was 3.1 (2.2–6.4). **Conclusion:** Childhood hypertension is associated with markers of obesity, LDL-C and family history of hypertension in Asian Indian adolescents.

ODDS RATIOS, 95% CI""S, OF SYSTOLIC AND DIASTOLIC HYPERTENSION IN ASIAN INDIAN ADOLESCENTS; N=1133.

Outcome	Explanatory variables	Odds ratios	95%Confidence Intervals
Systolic Hypertension	BMI (kg/m^2)	2.0	1.1–3.3
	Waist Circumference (cm)	2.6	1.4–4.6
	Waist-Hip ratio	1.9	0.9–3.9
	4SF (mm)*	3.1	1.3–7.1
	Body fat mass (Kg)	2.0	1.1–3.4
	Fasting blood glucose (mg/dl)	0.7	0.4–1.3
	HBA1C (%)	0.6	0.3–1.1
	LDL-C (mg/dl)	1.9	1.1–3.3
Diastolic Hypertension	BMI (kg/m^2)	3.0	1.6–5.5
	Waist Circumference (cm)	6.7	3.0–14.8
	Waist-Hip ratio	2.6	1.2–5.5
	4SF (mm)	3.4	1.8–6.1
	Body fat mass (Kg)	3.5	1.5–8.2
	Fasting blood glucose (mg/dl)	0.9	0.5–1.5
	HBA1C (%)	0.6	0.3–1.0
	LDL-C (mg/dl)	2.1	1.2–3.8

4SF variable is defined as sum of biceps, tricpeps, sub-scapular and supra-iliac skinfold thickness in mm. Linear regression gave the following equations: SBP (mm Hg) = 105.1 + 0.1[Age-14yrs] + 4.4*(Boy) + 0.7*[BMI - 12]; (P<0.001) DBP (mm Hg) = 69.1 - 0.04*[Age-14yrs] + 1.9*(Boy) + 0.5*[BMI - 12]; (P<0.001)

P259

Does Elevated Cardiovascular Reactivity in Normotensives Predict Future Hypertension in a Lean Western African Population?

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Several studies have shown that exaggerated behavior responses to stress are related to elevated blood pressure. Our previous cross-sectional study of blood pressure reactivity to stress in a cohort of Nigerian civil servants showed greater task-induced blood pressure changes among men than women, among hypertensives than normotensives. To determine whether cardiovascular reactivity to mental stress could predict future elevated blood pressure, we followed 340 civil servants who were normotensive, aged 20 to 64 years (male: 40.4 ±7.1 (SD) years, female: 38.2±5.8 years) with relatively low BMI (male: 21.4 ±3.0, female: 24.3±4.5) at baseline. Cardiovascular reactivity was measured at baseline in subjects based on star tracing task and speech task induced blood pressure changes. Speech task induced systolic blood pressure (SBP) change greater than 30 mmHg was observed in 105 (34%) participants. After 7 years follow up, 51 participants (29 men, 22 women) in this cohort developed hypertension. In bivariate analyses, speech task induced SBP change was positively associated with hypertension development, as were baseline SBP, baseline DBP, waist circumference and age. In logistic regression analyses, participants whose reaction to the speech task was more than 30 mmHg increase in SBP, compared with those whose reaction was lower than 30 mmHg, were 2.0 times (95%CI: 1.0- 4.2) more likely to develop hypertension, adjusted for age, gender and baseline blood pressure (categorized as SBP 120–139 mmHg vs. SBP < 120 mmHg), despite the strong association of baseline SBP with future hypertension (OR: 16.4; 95%CI: 7.3–36.9). Other task induced blood pressure changes (speech task DBP change, star tracing BP change) were not predictors for future hypertensive status in our analysis. This study demonstrates that systolic blood pressure reactivity to a speech related task may predict hypertensive status after 7 years follow up, independent of baseline SBP. Therefore, cardiovascular reactivity may be useful for predicting future hypertension in African populations.

P260

Adherence to the US Joint National Committee (JNC7) Guidelines for Blood Pressure Control in a Veterans Health Institution 1 Year Post Percutaneous Coronary Intervention Among African Americans

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Background: Secondary prevention of hypertension in patients with known CAD reduces morbidity and mortality. The JNC7 guidelines target a goal BP of <140/<90 mmHg in non-diabetics and < 130/ < 80mmHg for diabetics. Previous studies have shown African Americans have difficult to control blood pressures that are typically worse than other patient populations. Beta-blockers (BB) and angiotensin antagonists (ACEi/ARB) have shown the most benefit in these individuals Methods: We conducted a retrospective, observational study of 379 unique patients who underwent PCI at an urban VA between 2004–2006. Blood pressure values and classes of anti-hypertensive medications were recorded at baseline, 6 and 12 months post-PCI. Findings: African Americans comprised 56.2% (213/379) of the patients. At baseline in the overall population, the percentage of patients at JNC7 goal SBP was 41.8% (89/213) in African-Americans, and 43.4% (72/166) in other patients. At one year follow up, the percentage of patients at JNC7 goal SBP was 54.8% (97/177) in African-Americans and 52.8% (75/142) among other patient populations. These were both non-significant differences. At 6 months there was a significant increase in all patients taking BB and ACEi/ARB; however, medication utilization decreased at 12 months to baseline levels. Conclusion: In patients undergoing PCI, there was not a significant difference in reaching JNC7 goals between African Americans and other patient populations. The overall use of blood pressure medications in these patients was high. As opposed to previous studies, there were no racial differences noted in regards to those reaching JNC7 blood pressure goals. The lack of disparity between races in blood pressure goals affirms the benefit for patient care in a system of equal access such as the VA.

P261

Risk Factors for Vascular Disease in an Indian Rural Population

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Little is known about the specific risk factors for vascular diseases in rural India. Aim. The aim of this study was to determine the prevalence of risk factors for vascular disease in a rural region of Andhra Pradesh. We also aimed to identify factors that were associated with hypertension. Methods. Trained health workers administered questionnaires to residents (at least 18 years of age) to obtain information about their lifestyle (smoking, alcohol consumption, physical activity). In addition, measurements of blood pressure, height, weight, waist-hip ratio, blood glucose, cholesterol, triglyceride and hemoglobin were performed. Multivariable backward stepwise logistic regression was used to assess the factors that were associated with hypertension (blood pressure >= 140/90 mmHg). Results. In total 1472 adults were included. The mean age was 39.8 years, and 46.3% were male. The prevalence of risk factors for vascular disease was different to that observed in developed countries. In total 52.0% were underweight (body mass index <19 kg/m^2), 19.3% had elevated blood cholesterol levels, 1.3% had elevated blood glucose levels and 41.2% of men were current smokers. Daily salt intake per person was approximately 5 times greater than the recommended daily salt intake for adults (<5g/day). The prevalence of hypertension was 10.0%. There were marked differences between men and women; 23.4% of women and 12.1% of men had low hemoglobin levels and 0.8% of women and 31.9% of men drank alcohol. Using multivariable logistic regression we found that age, ever drinking alcohol, body mass index and waist-hip ratio were positively associated with hypertension. Conclusion. There were a number of risk factors for vascular disease evident in this rural population. The prevalence of risk factors was greater among men and many of the risk factors were modifiable. Factors associated with hypertension were similar to those observed in developed countries. This information is being used to develop prevention strategies among this rural community.

P262

Association of Socioeconomic Status with Heart Rate Recovery Following Maximal Exercise in Children

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Attenuated 1-min heart rate (HR) recovery (defined as HR at peak exercise - HR at 1 min during recovery) on cessation of exercise is a recently described risk factor and is associated with all-cause mortality and sudden cardiac death in adults. Socio economic status (SES) affects health-related behavior and access to resources. Low SES is associated with attenuated HR recovery, higher incidence of cardiac disease and higher all-cause mortality in adults. The purpose of this study was to deteremine if SES is related to HR recovery in healthy children. **Methods:** HR recovery after cessation of a maximal treadmill exercise test (Bruce protocol) was assessed in 317 children (121 girls, 196 boys, median age 11.8 years, range 5–18 years) who underwent an exercise test during their clinical evaluation to exclude cardiac disease and were discharged as normal. The first-minute cool down period (1.5 mph, 0% inclination on treadmill) was standard for all subjects. American census 2000 database was used to extract 6 variables of wealth, income, education and occupation for the census tract of residence (average population 4000, relatively homogeneous with respect to population characteristics, economic

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status and living conditions) of each subject. A previously described and validated summary SES score (summed z value) was generated for each subject. Multivariable linear regression analyses were performed to determine predictors of 1- min HR recovery. **Results:** 1-min HR recovery declined with age, was higher in boys compared to girls and was lower in children with higher BMI. Children in the lowest SES quartile had lower exercise endurance (-1.9 minute, $P<0.01$) compared to those in the highest SES quartile controlling for age and gender. HR recovery was lower in children in the lowest SES quartile (-3.75 beats/min, $P=0.03$) compared to those in the highest quartile after controlling for age (-2.1 beats/min/year of age) and gender (+4.7 beats/min for boys) (adjusted R square=0.347, $P<0.001$). This association of SES with HR recovery remained significant after adding BMI to the model ($P=0.04$, adjusted R square for the model = 0.395). **Conclusion**: Children in the lowest quartile of SES have attenuated HR recovery after cessation of maximum exercise.

P263

Early Dynamic Cardiac Perturbations Are Encountered in Fetuses of Well-Controlled Mothers with Gestational Diabetes

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Background: Increasing evidences show that diabetes and its associated cardiovascular disturbances may well have a fetal origin. This intrauterine programming may be attributable to different maternal factors such as diet and metabolic control. **Aim:** To determine if fetal cardiocirculatory parameters are altered in pregnancies complicated by gestational diabetes characterized by a very good metabolic control. **Methods:** Echo-Doppler parameters of 34 fetuses of well-controlled mothers with gestational diabetes (GDM) were compared to a control group of 10 normal pregnancies. Cardiocirculatory variables, including the Tei index (reflecting the ventricular function), were measured between the 19th and 25th week of gestation, using an Acuson ultrasound system. Glycated hemoglobin level (HbA1c) was used as a marker of metabolic control. Statistical analyses were performed with the use of SPSS (version 11.5.) **Results:** The two groups were comparable based on age and comorbidities. The HbA1c for the GDM group was of 6.4%. Although results are comprised within normal values, significant differences ($p\leq0.05$) were found between GDM fetuses compared to normal pregnancies for interventricular septal thickness (2.12±0.03 and 1.94±0.05mm), left ventricular posterior wall thickness (2.11±0.04 and 1.89±0.05mm), cardiac circumferences (7.6±0.2 and 6.7±0.2mm), myocardial performance (Tei index) (0.230±0.002 and 0.219±0.006) and diastolic filling time (178±3 and 201±6ms), respectively. Babies born from GDM were also statistically smaller than those born from control mothers and were also characterized by smaller placentas. **Conclusion:** This is the first evidence, that very good maternal metabolic control does not prevent early alterations of cardiac morphology and diastolic function in fetuses of GDM. Other variables associated with the diabetic milieu should be considered. However, the significance of these early changes on the cardiovascular system later in life remains to be elucidated.

P264

Maternal Obesity, Offspring Birth Weight, and Offspring Blood Pressure at Age 17: The Jerusalem Perinatal Study

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BACKGROUND: Both maternal obesity and offspring birth weight (BW) have been shown to be associated with adult blood pressure. We sought to examine whether these associations appears earlier in life, during adolescence. **METHODS:** The Jerusalem Perinatal Study (JPS) collected extensive prenatal, perinatal and postnatal data on all 17,003 births during 1974–1976. Measurements of blood pressure and body mass index (BMI) at age 17 were obtained from military draft records for 11,729 individuals. BW was grouped into low (LBW: BW $\leq$ 2500 g), normal (NBW: 2500 g $<$ BW $\leq$ 4000 g) and high (HBW: BW $>$ 4000 g) categories. Logistic regression was used to examine the associations of maternal pre-pregnancy BMI (mBMI) and BW (LBW and HBW) with pre- and stage 1 high blood pressure (HBP - systolic blood pressure $\geq$ 130 mmHg or diastolic blood pressure $\geq$ 80 mmHg), after controlling for gender, gestational age, mother's smoking during pregnancy, and socioeconomic status. We also examined these characteristics in relation to subsets of offspring at age 17, HBP1 (HBP and BMI $\geq$ 25 kg/m^2) and HBP2 (HBP and BMI $<$ 25 kg/m^2). In the two latter models, the reference group included subjects with normal BP (SBP $<$130 and DBP $<$ 80 mm Hg) and BMI $<$ 25 kg/m^2. **RESULTS:** A positive association between mBMI and HBP was observed (odds ratio [OR] associated with 1 SD of mBMI - 1.107; $P<0.001$). No significant association was found between BW and HBP. For HBP1 a somewhat stronger association with mBMI was observed (OR, 1.666; $P<0.001$) and no association with BW was apparent. For HBP2 a significant association with LBW was revealed (OR, 1.247; $P=0.026$), independent of the positive association with mBMI (OR, 1.074; $P=0.002$). **CONCLUSIONS:** Maternal pre-pregnancy BMI is associated with their offspring's blood pressure levels at age 17. In non-overweight hypertensive adolescents (age 17), independent of mBMI, LBW is also significantly associated with an adverse BP phenotype. The biological pathways that underlie the associations of mBMI and BW with HBP in adolescents may differ for those with and without overweight/obesity. These findings warrant replication in other birth cohorts.

P265

Childhood Socioeconomic Circumstances Predict Inflammatory Markers in Framingham

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BACKGROUND: Childhood socioeconomic position (SEP) predicts cardiovascular disease (CVD) in most studies, however the physiological mechanisms are not well understood. **OBJECTIVES:** To evaluate the association between childhood SEP and circulating inflammatory markers including C-reactive protein (CRP), interleukin-6 (IL-6), intercellular adhesion molecule-1 (ICAM-1), P-selectin, tumor necrosis factor receptor II (TNFR2), lipoprotein-associated phospholipase A_2 (Lp-PLA_2) activity and monocyte chemoattractant protein-1 (MCP-1). **METHODS:** We examined 2386 participants of the Framingham Heart Study Offspring Cohort (mean age 62.1 y, 53.4% women) during 1998–2001. Childhood SEP was measured as mother's and father's educational attainment, obtained directly from parents. Multivariable regression analyses were performed, adjusting for age, sex, own educational attainment and clinical CVD risk factors (systolic blood pressure, antihypertensive and cholesterol-lowering medications, total:HDL cholesterol ratio, body mass index, smoking, fasting glucose and depression). **RESULTS:** In age- and sex-adjusted regression analyses, mother's education was significantly inversely associated with CRP, IL-6, ICAM-1, Lp-PLA_2 activity, and TNFR2 (Table 1). Father's education was significantly related to CRP, IL-6, ICAM-1 and TNFR2. Additional adjustment for own educational attainment and clinical risk factors substantially reduced effect sizes. **CONCLUSION:** Childhood SEP is related to several inflammatory markers, and the mechanisms responsible may be via individual's own educational attainment and clinical risk factors.

Table 1. Multivariate regression analyses for association of mother's education with inflammatory markers.

	Model Adjustment			
	Age, sex		Age, sex, offspring education, clinical risk factors	
	β*	95% CI‡	β	95% CI
CRP, ln mg/L	**0.269**	0.133 , 0.405	0.096	-0.033 , 0.224
IL-6, ln pg/mL	**0.126**	0.045 , 0.208	0.024	-0.058 , 0.106
sICAM-1, ln ng/mL	**0.040**	0.009 , 0.070	0.011	-0.019 , 0.041
TNFR2, ln pg/mL	**0.058**	0.021 , 0.095	0.023	-0.017 , 0.063
Lp-PLA_2, ln nmol/min/mL	**0.032**	0.001 , 0.062	0.016	-0.015 , 0.047
P-Selectin, ln ng/mL	0.023	-0.024 , 0.069	-0.011	-0.061 , 0.039
MCP-1, ln pg/mL	0.007	-0.035 , 0.049	-0.017	-0.064 , 0.029

*Regression coefficients (β) represent logarthmic change in biomarker units for <12 *vs.* >12 years mother's education. Analyses included category of 12 years mother's education (data not shown).

P266

Aromatase Inhibitors Anastrozole and Letrozole in Risk of Cardiovascular Disease: Meta-Analysis of Randomized Controlled Trials

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Context: Third-generation aromatase inhibitors (AIs) are increasingly utilized following or in place of tamoxifen for treatment of breast cancer. However, the cardiovascular disease (CVD) risks of AIs are not well understood. **Objective:** Evaluate the CVD risks of anastrozole and letrozole in postmenopausal women with breast cancer. **Data Sources:** Systematic search of EMBASE, MEDLINE (through March 2007), and Cochrane Central Register of Controlled Trials; references of retrieved articles, and contact with expert investigators. **Study Selection:** Randomized tamoxifen-controlled trials of anastrozole or letrozole among postmenopausal women with early or advanced breast cancer. Placebo-controlled AI trials and meta-analyses of CVD risks from placebo-controlled tamoxifen trials were selected for indirect comparative risk analyses of AIs. **Data Extraction:** Data on study design, participant characteristics, and incidence of hypercholesterolemia, ischemic heart disease, thromboembolic events, and cerebrovascular disease, were independently extracted by two investigators via standardized format. **Data Synthesis:** Results were pooled via random-effects models. Eight randomized controlled trials of anastrozole and letrozole enrolling 18,548 patients (range of mean age 58–68) were included; 432 thromboembolic events, 237 cerebrovascular events, 342 ischemic cardiac events, and 2249 incidents of hypercholesterolemia were reported. Compared to tamoxifen, anastrozole and letrozole decreased the risk of thromboembolic events (RR=0.54, 95%CI: 0.43–0.68; I2=10) and cerebrovascular events (RR=0.78, 0.61–1.00; I2=0); however, AIs were associated with increased the risk of hypercholesterolemia (RR=2.27, 1.87–2.76; I2=54) and ischemic heart disease (IHD) (RR=1.23, 1.00–1.52; I2=0). Estimating risks from placebo comparisons, AIs were not associated with risk of MI (RR=1.09, 95%CI: 0.57–2.09) or stroke (RR=1.31, 95%CI: 0.87–1.97) compared with placebo. **Conclusions:** Anastrozole and letrozole offer a mixed CVD risk profile compared to tamoxifen, decreasing thromboembolic and cerebrovascular events, but increasing hypercholesterolemia and IHD risk. Additional studies are warranted to investigate the safety of all AIs.

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P267

A National Study of Health Behaviors and Attitudes: What Is Preventing Prevention in the US?

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Information about motivators and barriers to better health could provide powerful insight to develop targeted strategies and interventions to help individuals make positive lifestyle changes to reduce the risk of chronic disease. The purpose of this study was to evaluate healthcare attitudes and practices in a diverse US population sample to determine if distinct population segments can be characterized. **Methods:** A stratified random sample weighted to the US census(N=6000, mean age 48 ± 15 years, 52% female, 71% non-Hispanic white) was drawn from an online national panel of 3.6 million persons who completed a standard survey. Based on responses to a series of self-descriptive statements, physical characteristics, behaviors, and locus of control, individuals were categorized into one of six groups 1) Leading the Way, 2) In it for Fun, 3) Value Independence, 4) I Need a Plan, 5) Not Right Now, or 6) Get Through Today. **Results:** Leading the Way and In it for Fun individuals reported significantly fewer barriers to managing weight than did all other groups ($p<0.05$) and to having a healthy diet vs. Value Independence, I Need a Plan, and Not Right Now groups ($p<0.05$). I Need a Plan individuals were more likely to report being too lazy or finding excuses to exercise vs all other segments ($p<0.05$). Those in the Get Through Today segment were significantly more likely to report having a medical condition that prohibits them from exercising vs other groups ($p<0.05$). Generally, Get Through Today individuals were the least likely to cite motivators to healthy behavior. Those in the Value Independence and I Need a Plan segments were more likely to report taste as the biggest driver of food purchases vs. other segments ($p<0.05$). Leading the Way and In it for Fun segments cited health benefits as the most important driver of food purchases vs. other segments ($p<0.05$). Leading the Way and I Need a Plan individuals were more likely to report using a healthcare professional as a resource for health information vs other segments ($p<0.05$). **Conclusion:** Distinct population segments can be identified that have unique motivators and barriers to engaging in healthy lifestyles. These data suggest that key health messages and interventions may be most effective if targeted to specific population segments.

P268

Glomerular Filtration Rate and Risk of Coronary Heart Disease in the VA Normative Aging Study

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Background: While end-stage renal disease is a well-recognized risk factor for cardiovascular disease (CVD), the relationship between glomerular filtration rate (GFR) and long-term risk of CVD in apparently healthy individuals remains unclear. **Methods:** We prospectively examined the relationship between baseline GFR and risk of coronary heart disease (CHD) in the Veterans Administration Normative Aging Study, a longitudinal cohort of healthy adult men. Beginning in 1979, serum creatinine was measured in 1,574 participants who were followed for incident CHD events. We calculated baseline GFR using the Modification of Diet in Renal Disease (MDRD) study equation (GFR = 186.3 x $(S_{cr})^{-1.154}$ x $(Age)^{-0.203}$). We used Cox proportional hazards models to calculate relative risks (RRs) and 95% confidence intervals (CIs) for the association between baseline GFR and risk of non-fatal myocardial infarction (MI) and CHD death. The multivariable model adjusted for age, smoking history, alcohol use, and family history of heart disease. In additional analyses, we included the following potential mediators: body mass index, systolic blood pressure, total cholesterol, and diagnosis of diabetes. **Results:** The mean age was 57.0 ± 8.0 years, and the mean baseline GFR was 67.5 ± 13.5 mL/min/1.73 m^2. During a maximum follow-up of 22.1 years, there were 239 incident CHD events (144 non-fatal MIs and 95 CHD deaths). Age-adjusted RRs (95% CI) for CHD for decreasing quintiles of GFR were 1.00 (ref), 1.12 (0.73–1.70), 1.16 (0.76–1.77), 0.94 (0.61–1.49), and 1.47 (0.98–2.21). Multivariable-adjusted RRs (95% CI) were 1.00 (ref), 1.12 (0.73–1.70), 1.19 (0.78–1.83), 0.94 (0.60–1.47), and 1.45 (0.97–2.19). Further adjustment for potential mediators attenuated the RRs only slightly. For the lowest decile of GFR values, there was a greater than 2-fold increased risk (RR 2.05; 95% CI, 1.29–3.25), compared with the highest quintile of GFR. **Conclusions:** In this prospective cohort of initially healthy men without pre-existing CVD, a non-linear, increased risk of CHD was observed only in the lowest decile of GFR (<52 mL/min/1.73 m^2). This contrasts with previous studies, and the level of GFR at which cardiovascular outcomes become apparent in the general population warrants further study.

P269

Risk Factors for Left Ventricular Dilation in Young Adults: The Bogalusa Heart Study

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Background: Cardiac enlargement is an important predictor of adverse cardiovascular (CV) events. Left ventricular (LV) dilation is a precursor both of LV dysfunction and clinical heart failure. LV dilation has not been well studied among younger adults. Methods: Risk factors for LV end-diastolic dilation were examined in 841 young adult subjects (341 male, 490 female) who participated in the Bogalusa Heart Study. Ventricular dimensions were determined by M-mode echocardiography following and indexed to height using a standard method. Logistic regression models were used, stratified by race and sex, to assess the relationship CV risk factors with quantile of LV end-diastolic dimension. Results: In sex-specific models adjusted for age, race, blood pressure, and measure of insulin resistance, body mass index in the obese range was a significant predictor of LV dilation in the highest quintile among both men and women (Odds Ratio [OR], 3.06; 95% Confidence Interval [CI], 1.67 to 5.61 in men; OR, 2.38; 95% CI, 1.45 to 3.91 in women). Among men, race was a marginally associated (OR, 1.76; 95% CI, 0.92 to 3.38) with higher blood pressure levels in blacks, while among women, no difference was observed. Triglycerides>155 mg/dL was marginally significantly associated with LV dilation in men, while LDL cholesterol>160 mg/dL was marginally significantly associated with LV dilation among women. Conclusion: In this study, LV diameter varied with concentrations of triglycerides and LDL-cholesterol among men and women, respectively. However, the strongest and most consistent relationship was with BMI. Obesity was the most consistent predictor of LV dilation in a generally healthy, asymptomatic, young adult population.

P270

Increased Risk of ACS in Cocaine Users: A Case-Control Study to Assess the Extent and Composition of Coronary Atherosclerosis by Contrast-Enhanced MDCT

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Background: Increased risk of acute coronary syndromes (ACS) in cocaine users may be mediated through advanced coronary atherosclerosis. **Methods**: In this case-control study, we compared the extent and composition of coronary atherosclerotic plaque (AP) as detected by 64-slice cardiac multidetector computed tomography (MDCT) in cocaine users and controls selected from a large cohort of consecutive patients who presented with acute chest pain but non-diagnostic ECG and negative initial troponin to the emergency department (ED). Two blinded readers determined the presence of non-calcified AP, calcified AP, and mixed AP, and significant stenosis (>50%) per coronary segment. An expert panel determined the presence of ACS and identified cocaine users based on documented present or past use. Cocaine users were matched to controls 1:3 with respect to age and gender. All analysis was adjusted for smoking, hypertension, diabetes mellitus, hyperlipidemia, and history of CAD. **Results**: Overall 44/412 (9%) reported use of cocaine. The analytic cohort consisted of 176 subjects (mean age: 46±6 years, 86% male). In multivariate adjusted regression analysis cocaine use was associated with an almost 10 fold increased risk for ACS. In contrast, there was no association between cocaine use and extent of plaque or stenosis (table). **Conclusion**: Our data suggest that among patients presenting with acute chest pain to the ED cocaine users have a 10 fold increase in risk for ACS as compared to matched controls, independent of the extent and composition of coronary plaque as detected by cardiac MDCT. Thus, increased risk of ACS in cocaine users may not be mediated through advanced coronary atherosclerosis.

TABLE: ASSOCIATION BETWEEN COCAINE USE AND PLAQUE, STENOSIS AND ACS

	Multivariate Regression adjusted for risk factors		Multivariate Regression adjusted for risk factors + plaque and stenosis	
	OR for cocaine use	95%-CI	**OR for cocaine use**	**95%-CI**
Non-calcified Plaque	0.83	0.65–1.07	0.67	0.39–1.16
Mixed Plaque	0.83	0.60–1.15	1.03	0.44–2.40
Calcified Plaque	0.97	0.85–1.11	0.99	0.81–1.22
Stenosis [number]	1.42	0.85–2.39	1.54	0.57–4.14
ACS	5.67*	1.21–26.60	9.78*	1.29–74.03

Odds ratio (OR) per coronary segment containing plaque (non-calcified, mixed, or calcified); CI: confidence interval; * $p<0.05$

P271

Lifestyle Intervention and 18-Month Change in Aortic Pulse Wave Velocity in Postmenopausal Women: The Women on the Move Through Activity and Nutrition (WOMAN) Clinical Trial

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Objective**:** To evaluate the lifestyle intervention effects on 18 month (18m) change in aortic pulse wave velocity (aPWV) in the Women On the Move through Activity And Nutrition (WOMAN) randomized trial. Methods: Eligibility criteria included: postmenopausal, non-diabetic, current or recent hormone therapy (HT) user, age 52–62, BMI: 25–40 kg/m^2, waist circumference (WC) ≥80 cm, BP controlled to ≤ 140/90 mmHg throughout the trial, LDL-C:100–160 mg/dl, and not on lipid-lowering medications. Eligible women (n=508, mean age=57) were randomized to the Lifestyle Change (LC) (diet and physical activity) or Health Education (HE) control group. APWV was assessed from carotid- to-femoral waveforms at baseline (BL) and 18m. Change analyses used linear models adjusted for baseline levels of the change variable(s), age, and use of HT or antihypertensive medications at BL and 18M. Results: Valid aPWV measures were available at BL (mean=881 cm/s) and 18m for 369 women. Use of HT and anti-hypertensive medications at BL and 18m were 62% and 30%, and 23% and 26%, respectively. At 18m, the intervention (LC) had a non-significantly greater reduction in aPWV than HE (-9.7±12.7 vs. -4.6±13.8 cm/s), despite a previously reported significant reduction in weight and WC (but not SBP). At 18m, aPWV change demonstrated a threshold effect at the highest quartile of reduction

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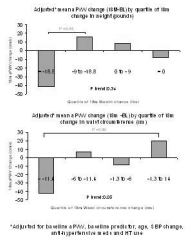
in weight or WC (Figure.) Conclusions: Among postmenopausal women with well-controlled blood pressure, change in aPWV was not significantly different between the intervention and control group at 18 months. Reduction in aPWV was most apparent among those with the largest reductions in 18m weight or waist circumference.



P272

Cost-Effectiveness of Screening BNP Levels in Patients at Risk of Asymptomatic Left Ventricular Dysfunction

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Purpose: We sought to evaluate the cost-effectiveness of screening 'high-risk' patients for (asymptomatic) left ventricular dysfunction (LVD) with brain natriuretic peptide (BNP), and subsequent treatment of those identified with LVD with enalapril. Methods: A Markov-based decision analytic model was constructed with three health states in each arm: 'Alive with asymptomatic LVD', 'Alive with (clinically manifest) heart failure' and 'Dead'. The annual risks of developing heart failure and death among people with asymptomatic LVD, and the annual risks of hospitalization and death among people with heart failure, were calculated from the Studies of Left Ventricular Dysfunction (SOLVD). Costs to the health sector comprised those associated with screening, drug treatment and hospitalization for heart failure, and were sourced from a prospective, longitudinal study conducted by Liao and collegues (2006) that compared long term costs and resource use of patients with heart failure. Results: At a five-year time horizon, the incremental cost-effectiveness ratios (ICERs) of a BNP-based screening strategy in terms of dollars per life year gained were $40,306, $28,767 and $25,414 for populations with 10%, 20% and 30% underlying prevalences of asymptomatic LVD, respectively. ICERs decreased with increasing time horizons and an increasing underlying risk of LVD among the target population. Conclusions: Screening for asymptomatic LVD and subsequent treatment with enalapril represents a cost-effective means of reducing heart failure-associated morbidity and mortality.

	Underlying prevalence of asymptomatic LVD		
Years to model	0.1	0.2	0.3
5	$40,306 ($16,126 - $212,825)	$28,767 ($12,289 - $165,579)	$25,414 ($8,257 - $180,132)
6	$28,484 ($13,761 - $134,460)	$21,345 ($9,346 - $128,511)	$19,577 ($8,221 - $82,671)
7	$21,671 ($11,080 - $102,735)	$16,754 ($7,829 - $68,922)	$14,979 ($6,735 - $74,126)
8	$17,424 ($9,341 - $77,245)	$13,591 ($6,730 - $54,686)	$12,217 ($5,783 - $45,303)
9	$14,836 ($7,523 - $46,963)	$11,395 ($5,767 - $45,272)	$10,274 ($4,980 - $31,030)
10	$12,380 ($6,920 - $43,856)	$9,844 ($5,031 - $31,115)	$8,850 ($4,485 - $31,776)

P273

Performance in Risk Prediction for Cardiovascular Events Using Adaptive Tree-Based Method

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Background Risk prediction is important in disease prevention. Risk stratification has been made by the risk score such as Framingham method developed on the basis of regression models. Although this approach is not based on clinically oriented thinking, a tree based method is simple and similar to clinical inquiry process. Therefore, we examined the accuracy and interpretability of the tree based method for the REACH Japanese data and compared with the result of regression approach. Methods We used a CART method that is a binary tree method to predict an event. Entropy criterion was used for splitting. As compared to this, we performed logistic regression analysis. We used the REACH Japanese data (N=5015). The REACH registered patients with or at risk of atherothrombotic disease. We defined the event to be a composite of cardiac death or nonfatal stroke/MI within a year. Risk prediction was made by stratification of gender. Variables to consider were age, number of risk factors, smoking, waist circumference, ischemic stroke, ischemic heart diseases, peripheral artery diseases, hypertension, diabetes, use of statin, atrial fibrillation, and heart failure. The predictive event was confirmed if the predicted event rate was greater than the average in each model. Results Out of 5015 patients, 149 (3.0%) occurred the event. The rate was higher in men (3.4%) than women (2.1%) even if mean age was 3 years higher in women. The CART model selected only 6 variables for men and 5 variables for women. Agreement was 56% for men, 63% for women. The logistic model used all the 12 variables, and the agreement was 60% for men, 69% for women. Sensitivity (probability of predicting the event by the model among actual event cases) was 0.74 for men, 0.78 for women in the CART model; 0.53 for men, 0.47 for women in the logistic model. Specificity (probability of predicting no event by the model among actual no-event cases) was 0.56 for men, 0.63 for women in the CART model; 0.61 for men, 0.70 for women in the logistic model. Conclusions The CART model showed a good performance in accuracy of prediction as logistic models despite the CART model used less variables than logistic models for prediction. It would also enable us to stratify the risk population according to the event rate at each final node.

P274

Withdrawn

P275

High-Dose Aspirin Therapy Does Not Erase Sex Differences Seen in Platelet Aggregation with Low-Dose Aspirin Therapy

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Background: Low-dose aspirin (ASA) therapy for primary prevention of cardiovascular diseases is not as effective in women. As a possible reason, women have greater platelet activation prior to and following low-dose ASA therapy. To examine whether therapy with a higher ASA dose reduces the greater residual platelet aggregation observed in women, we compared the effect of ASA 81 mg/day with ASA 325 mg/day in both sexes. **Methods**: Healthy family members (N=106) of patients with premature coronary heart disease participated in a trial of 14 days of ASA 81 mg/ day followed by 14 days of 325 mg/day. Platelet function was measured at baseline and following both doses. Ex vivo testing included platelet aggregation in whole blood (WB) to arachidonic acid (AA), adenosine diphosphate (ADP), and collagen and in vivo testing was measured using urinary 11-dehydro thromboxane B2 (TxM) **Results**: At baseline, women had greater platelet activation in all measures, significant only in response to ADP and collagen (Table 1). After therapy with both doses, both sexes had marked suppression of platelet aggregation to AA in WB and TxM, representing the direct cyclooxygenase-1 (COX-1) pathway. For indirect COX-1 pathways, women had significantly more residual platelet activation to collagen and ADP after both ASA doses. When women's platelet function after ASA 325 mg/day was compared with men after ASA 81 mg/day, women continued to have greater residual platelet aggregation in response to collagen ($p=0.01$) and ADP ($P<0.001$). **Conclusion**: Therapy with low dose ASA results in marked inhibition of platelet activation directly related to COX-1 pathway. Sex differences in the indirect COX-1 pathways remained at both doses of ASA. Overall, women had greater residual platelet activation after the higher dose of ASA even when compared to men treated with a lower dose of ASA. Although these results suggest that women would not benefit from a higher dose of ASA, the clinical effect was not examined.

PLATELET FUNCTION AT BASELINE AND AFTER ASPIRIN 81 MG/DAY AND 325 MG/DAY IN MEN AND WOMEN

	Aggregation to 0.5 mM Arachidonic acid (ohms)		Aggregation to Collagen 5μg/ml (ohms)		Aggregation to ADP 10μM (ohms)		Urinary TxM (ng/mmol creatinine)	
Sex (ASA Dose/day)	Mean (SD)	Sex Difference p-value	Mean (SD)	Sex Difference p-value	Mean(SD)	Sex Difference p-value	Mean (SD)	Sex Difference p-value*
Women (Baseline)	13.5 (4.1)	0.12	22.3 (6.2)	0.05	13.0 (3.8)	<0.001	305 (533)	0.69
Men (Baseline)	12.2 (3.9)	19.9 (5.9)	9.7 (4.2)	236 (203)				
Women (81 mg)	1.28 (3.6)	0.33	19.2 (6.4)	0.017	12.6 (4.4)	<0.001	65.3 (69)	0.15
Men (81 mg)	0.71 (2.4)	16.2 (5.8)	9.3 (4.6)	50.4 (39)				
Women (325 mg)	1.10 (4.3)	0.99	19.2 (6.1)	0.02	13.1 (4.2)	<0.001	58.5 (81)	0.24
Men (325 mg)	1.11 (3.6)	16.3 (5.6)	9.3 (3.8)	43.3 (46)				

* p-values for TxM are on log-transformed data

P276

Effects of Statins on Aggression Differ by Gender: Results of a Double-Blind Placebo Controlled Trial

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Background: Case reports have suggested that some persons may express increased aggression with statin use. However it is unknown whether statins increase or reduce aggression on average. **Subjects**: 1016 adult men and women without diabetes or heart disease, with LDL-cholesterol 115–190mg/dL. **Design**: Randomized double-blind placebo-controlled trial of simvastatin 20mg, pravastatin 40mg or placebo for six months. Aggression was assessed using the Overt Aggression Scale-Modified aggression subscale (OASMa). **Analysis**: Scores were comparable across groups at baseline. Sex-stratified t-tests of differences in means of on-treatment aggression scores between statins and placebo were examined with and without exclusion of outliers. Regression assessed significance of a "sex-by-statin" interaction term. **Results**: Results (excluding outliers) showed strong trends in opposite directions for men (reduced aggression) and women (increased aggression). Inclusion of outliers weakened findings for men. Regression analysis affirmed a significant interaction of statins and gender on aggression ($p = 0.019$ for interaction term). Men on statins (but not placebo) who sought early conclusion of participation showed increased aggression on

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treatment (difference p = 0.008). **Conclusion:** Effects of statins on aggression differed significantly for men vs women. Borderline significant trends toward benefit (men) and harm (women) merit replication with larger samples.

TABLE 1. T-TEST RESULTS: EXCLUDING OUTLIERS

	N	Mean Final OASMa Score (SD)	Score Difference From Placebo (SE)	2-sided P vs Placebo	*2-sided P for Women Substituting Male Sample Sizes**
MEN (negative difference values represent trends to reduced aggression)					
Placebo	220	2.50 (4.87)	—	—	—
All-statin	441	1.82 (4.12)	-0.686 (0.357)	0.055†	—
Simvastatin	221	1.67 (4.03)	-0.830 (0.426)	0.052†	—
Pravastatin	220	1.96 (4.01)	-0.541 (0.425)	0.204	—
WOMEN (positive difference values represent trends to increased aggression)					
Placebo	103	1.26 (2.62)	—	—	—
All-statin	206	1.97 (3.40)	0.704 (0.382)	0.0663†	*0.0072†*
Simvastatin	102	2.11 (3.69)	0.846 (0.447)	0.0599†	*0.0058†*
Pravastatin	104	1.83 (3.10)	0.565 (0.399)	0.1589	*0.0398†*

SD = standard deviation; SE = standard error * For this analysis female means and SDs were employed, substituting male sample sizes, to better permit comparison of effects in men vs women. † Statistically significant

P277

Protective Effect of Donepezil on Cardiovascular Mortality

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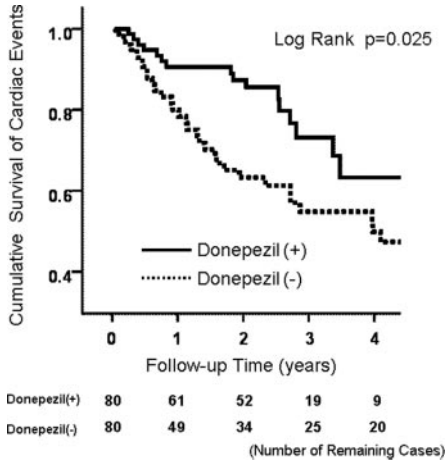
Introduction: Diminished cardiac vagal activity and increased heart rate predict a high mortality rate for chronic heart failure (CHF). Chronic electrical stimulation of the vagus nerve improves long-term survival in rats with CHF after large myocardial infarction. Donepezil hydrochloride (donepezil), a reversible acetylcholinesterase inhibitor which increases vagal effects is widely used to treat Alzheimer's disease. There are no data yet on potential cardiovascular (CV) benefit of donepezil. **Hypothesis:** We tested the hypothesis that donepezil might have a favorable effect on CV mortality. **Methods:** We conducted a retrospective cohort study from the data of 1008 patients with Alzheimer's disease or vascular dementia admitted to Vanderbilt University Hospital between 1994 and 2003. Eighty patients were Tennessee residents and were prescribed donepezil at discharge (DPZ(+)). We randomly chose 80 patients who were not prescribed donepezil at discharge (DPZ(-)) as comparable control subjects. Kaplan-Meier survival curves and Cox proportional-hazards models were used to evaluate the risk of all mortality and fatal CV events. **Results:** In the DPZ(-) group, 36 patients (45 %) had fatal CV versus 18 patients (23 %) in the DPZ(+) group for the same follow-up period. The DPZ(-) group had a significantly higher risk of death as well as fatal CV events (RR, 1.48; 95% CI, 1.00 - 2.19; RR, 1.85; 95% CI, 1.03- 3.34, respectively) after adjustment for age, sex, race, past medical history of coronary artery disease and diagnosis of Alzheimer's disease or vascular dementia. **Conclusions:** Patients with Alzheimer's disease or vascular dementia who were given donepezil had reduced CV mortality.



P278

Life-Years Gained from Modern Cardiological Treatments and Population Risk Factor Changes in the US, 1980–2000

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Objective. We estimated life-years gained from cardiological treatments and cardiovascular risk factor changes in the US between 1980 and 2000. Methods. We used the previously validated IMPACT model to integrate data on the number of coronary heart disease patients, treatment uptake, treatment effectiveness, risk factor trends and effectiveness, and median survival among US adults between 1980 and 2000. The treatment interventions included acute myocardial infarction, unstable and stable angina, heart failure, hypertension and elevated cholesterol. The population level risk factors included changes in smoking prevalence, systolic blood pressure, cholesterol (attributed mainly to diet), physical inactivity, obesity, and diabetes. We estimated the life-expectancy gains for each intervention by using the IMPACT model estimates of deaths prevented or postponed by 2000, multiplied by the gender and age-specific median survival for each group. Minimum and maximum estimates of life-years gained were then calculated using the analysis of extremes method. Results. Compared with 1980, there were 341,745 fewer coronary deaths in 2000 with the IMPACT model explaining 308,965 (90%). This represented approximately 3,147,855 life-years gained among people aged 25–84 years (range: 2,448,890 - 3,744,955). ;2,143,720 were in men (68%). Cardiological treatments for patients accounted for approximately 1,092,260 life-years gained (range: 751,740 - 1,398,630) whereas population risk factor changes accounted overall for approximately twice that, with 2,055,600 life-years gained overall (range: 1,697,150 - 2,346,325). Large gains from improvements in population smoking, cholesterol, physical inactivity and blood pressure in men (approximately 2,770,590 life-years gained) were substantially offset by additional deaths attributable to adverse population trends in obesity and diabetes (approximately -714,990 life-years lost). Conclusions. Compared with cardiological treatments, modest reductions in major risk factors gained over twice as many life-years. Unfortunately, these gains were diminished by increases in the prevalence of obesity and diabetes. More effective public health policies are now required.

P279

Prevalence of Heart Failure in REGARDS: A Unique Opportunity to Study Racial and Geographical Variations in Heart Failure Epidemiology

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Background: The natural history of heart failure (HF) may vary by race and region. However, relevant data, derived primarily from the Framingham Heart Study, Cardiovascular Health Study, Minnesota Heart Study and Rochester Epidemiology Project, are limited by predominantly white populations from restricted geographical areas. **Methods:** Between January 2003 and August 2007, REGARDS (REasons for Geographic And Racial Differences in Stroke) has recruited 28467 community dwelling participants, age ≥45 (mean, 65) years, 55% women, 43% African Americans from 48 contiguous states (56% from 8 Southern states). HF was defined as self-reported symptoms of orthopnea and paroxysmal nocturnal dyspnea (n=1436), two of the major Framingham criteria, and the use of HF medications (diuretics and either of digoxin, an ACE inhibitor, an ARB, or a beta-blocker approved for HF), a modified Cardiovascular Health Study criterion (n=4030). **Results:** Of the 357 (1.3%) participants with HF, 59% were African Americans, 65% were women, 54% were from Southern states, 90% had hypertension, 51% had coronary artery disease, 53% had diabetes and 55% had chronic kidney disease (eGFR<60 ml/min/1.73m^2). Compared to 0.9% white participants, 1.7% African Americans had HF (OR, 1.93; 95% CI, 1.56–2.38; p<0.0001). Compared to whites, more African Americans with HF had hypertension (93% v 86%; p=0.030) and diabetes (60% v 42%; p=0.007). Among those with HF, the prevalence of hypertension and diabetes from Southern and non-Southern states were 91% v 88% (p=0.365) and 51% v 54% (p=0.503), respectively. There were no racial or geographical differences in the prevalence of coronary artery disease or chronic kidney disease among HF patients. **Conclusion:** Among REGARDS participants HF was more common among African Americans (v whites), who also had higher prevalence of hypertension and diabetes. REGARDS provides a unique opportunity to study racial and geographical variations in the natural history of HF.

TABLE 1. REGARDS PARTICIPANTS WITH AND WITHOUT HEART FAILURE

N (%), mean (±SD)	Heart failure (n=357)	No heart failure (n=28110)	P-value
Age	64.5 (±8.3)	65.5 (±9.4)	0.0237
African American	209 (59%)	11877 (42%)	<0.0001
Women	232 (65%)	15466 (55%)	0.0002
Hypertension	321 (90%)	16298 (58%)	<0.0001
Coronary artery disease	176 (51%)	6262 (23%)	<0.0001
Diabetes mellitus	180 (53%)	5898 (22%)	<0.0001
Chronic kidney disease	185 (55%)	11468 (43%)	<0.0001

P280

Ethnic and Gender Differences in Heart Rate Variability at Rest and in Response to Stress: A Longitudinal Study in Youth and Young Adults

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Backgrounds: Evidence on ethnic and gender differences in heart rate variability at rest and in responses to stress, especially from longitudinal studies, is scarce and warranted. **Methods:** Two evaluations were performed approximately 1.5 years apart on 399 youth and young adults (189 European Americans [EAs] and 210 African Americans [AAs]; 190 males and 209 females; mean age: 23.1± 2.8 at initial test). Root mean square of successive differences (RMSSD) of normal R-R intervals and high-frequency power (HF), which specifically reflect vagal control of cardiac regulation, were calculated from 3 segments of 30-second continuous RR intervals at rest and 5 segments of 30-second RR intervals during a video game challenge. The responses of RMSSD and HF to stress were indexed by the (stress-rest)/rest ratio. Repeated measures ANOVA were used to compare RMSSD and HF across visits. **Results:** Compared with EAs, AAs showed significantly higher levels of RMSSD and HF at rest across the two visits. The age and gender adjusted means (standard error, SE) for AAs and EAs were 73.8 (2.3) and 67.9 (2.3) ms

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(p=0.009) for RMSSD and 1926.4 (106.9) and 1692.3 (108.3) ms^2 (p=0.005) for HF, respectively. When comparing the RMSSD and HF responses to stress across the two visits, we found that females displayed a larger decrease during stress than males. The age and ethnicity adjusted means (SE) of the responses for males and females were -0.13 (0.02) and -0.18 (0.01) (p=0.018) for RMSSD and -0.15 (0.04) and -0.27 (0.04) (p=0.020) for HF, respectively. No significant gender difference on RMSSD and HF at rest or significant ethnic difference on the response to stress was observed. Furthermore, no significant ethnicity by visit interaction on RMSSD and HF levels at rest or significant gender by visit interaction on their responses to stress was observed. **Conclusions:** AAs show higher vagal control of cardiac function at rest than EAs and females show greater vagal response to stress than males. These ethnic or gender differences are consistent across 1.5 years.

P281

Differential Associations of Individual Risk Factors with Lifetime Risks for Cardiovascular Disease in Blacks and Whites

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BACKGROUND: Although associations of individual risk factor (RF) levels with lifetime risk for cardiovascular disease (CVD) have been reported in whites, data are sparse for non-whites. Therefore, we sought to compare black/white differences in remaining lifetime risks for CVD events by individual risk factor level. METHODS: Using data from the National Heart Lung and Blood Institute, we pooled participants from the Atherosclerosis Risk in Communities, Cardiovascular Health, Chicago Heart Association, EPESE, Framingham Heart, Framingham Offspring, Hispanic EPESE, Honolulu Heart, Kaiser Old, NHANES I, NHANES II Mortality, People's Gas, Puerto Rico Heart Health, Tecumseh, and Western Electric Studies. We incorporated RFs measured at or near ages 45, 55, 65, and 75 years for non-whites and whites separately in sex-stratified analyses. Using a modified lifetable analysis, we estimated remaining lifetime risks for CVD events (fatal CVD, fatal/non-fatal MI, and fatal/non-fatal stroke) to 85 years and 95 years of age with death free of CVD as a competing event. Analyses were performed with stratification on levels of individual RFs [blood pressure, total cholesterol, smoking, body mass index (BMI), and others] at the selected ages. RESULTS: We included 59,107 participants (48.8% women; 9.6% black) followed for 871,635 person-years. Representative data comparing remaining LR for CVD death by extremes of risk factor levels in blacks and whites separately at age 55 are shown in the table. Although the confidence intervals are wide for blacks, there appeared to be differences between blacks and whites with regard to the associations of hypercholesterolemia and BMI (in women). However, there were no differences associated with stage II hypertension or smoking. CONCLUSIONS: In this first report of LR for CVD by individual RFs in non-whites, the observed differences could reflect black/white differences in competing risks for non-CVD death or other factors.

TABLE: REMAINING LIFETIME RISKS* FOR CARDIOVASCULAR DISEASE DEATH AT AGE 55 YEARS BY ELEVATED RISK FACTOR LEVELS IN BLACKS AND WHITES

	Black	White
	Men	
Total Cholesterol > 240 mg/dL	22.9 (8.4–37.5)	42.5 (40.0–45.0)
Stage II Hypertension or Treated	36.5 (21.1–52.0)	42.9 (39.9–45.9)
BMI > 30	47.6 (26.1–69.1)	42.8 (38.9–46.8)
Current Smoking	36.2 (20.6–51.8)	38.2 (36.2–40.3)
	Women	
Total Cholesterol > 240 mg/dL	36.9 (19.1–54.8)	19.0 (17.2–20.8)
Stage II Hypertension or Treated	31.6 (14.8–48.3)	35.1 (31.7–38.5)
BMI > 30	49.8 (25.9–73.7)	31.0 (27.1–35.0)
Current Smoking	35.2 (19.5–50.8)	26.4 (24.0–28.8)

Stage II Hypertension defined as systolic blood pressure ≥ 160, diastolic blood pressure ≥ 100; BMI: body mass index * to age 90 for all risk factors except total cholesterol in women (age 85 years)

P282

Segment-Specific Association of Race and Cardiovascular Risk Factors with Aortic Diameter in the Study of Women's Health Across the Nation (SWAN) Heart Study

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Background: Arterial pathogenesis is influenced by vascular geometry and in women, atherosclerosis of the aorta predates coronary disease. Little, however, is known about the impact of cardiovascular risk factors on aortic morphology. We hypothesized that atherosclerotic risk factors, including race, will exhibit segment-specific association with aortic diameter in 544 Caucasian and African-American women (mean age: 50 years, mean BMI: 29 kg/sq.m), enrolled in the Pittsburgh and Chicago sites of SWAN, an ongoing, multi-site longitudinal study of the menopausal transition. Methods: Aortic diameter, in millimeters, was recorded at five segments - aortic root (AR), ascending (AA), descending (DA), thoracic (TA) and abdominal aorta (AbA) - using a novel, reliable electron beam tomography protocol. Mixed linear models, that accounted for within-person correlation, were used to obtain parameter estimates and test interaction of risk factors with aortic segment. Results: African-Americans (n=199, 37%), compared to Caucasians, had larger diameters in every segment (p <0.05 for all but aortic root and abdominal aorta), that persisted after adjustment for age, weight, site and degree of education (Table). The relationship between aortic diameter and other risk factors also varied by segment (Table), e.g., a 10-mmHg increase in DBP was associated with a 0.68 mm increase in the ascending aorta but only 0.38 mm increase in the aortic root. Conclusion: These data demonstrate novel segment-specific impact of race and other risk factors on aortic morphology in women. Segment-specific variation in aortic diameter, as a marker of vascular adaptation, deserves further exploration.

Table: Segment-Specific Parameter Estimates For Associations Of Race And Cardiovascular Risk Factors With Aortic Diameter (Millimeters)

	Aortic root (N=316)	Ascending Aorta (N=443)	Descending Aorta (N=534)	Thoracic Aorta (N=478)	Abdominal Aorta (N=310)	P value Interaction of Risk factor with Aortic segment
			Univariate models			
Age (per 1 year)	0.10	0.18 ‡	0.28 ‡	0.21 ‡	0.10 *	0.001
Weight (per 10 kg)	0.05‡	0.08‡	0.05‡	0.04‡	0.04‡	0.04
			Age and Weight-adjusted models			
Blood pressure (per 10 mmHg)						
Systolic	0.10	0.31 ‡	0.34 ‡	0.21 ‡	0.01	<0.001
Diastolic	0.38 *	0.68 ‡	0.60 ‡	0.34 ‡	0.15	<0.001
Pulse pressure	-0.14	0.15	0.28 ‡	0.20 †	-0.01	<0.001
Blood Glucose (per 10 mg/dl)	0.14	0.08	0.10 *	0.02	-0.04	0.04
Insulin (per 1 microIU/ml)	0.08	0.19	0.15	-0.05	-0.26*	0.02
Visceral adipose tissue (per 10 sq.	-0.03	-0.01	0.01	-0.02	-0.05†	0.003
Lipoprotein A1 (per 10 mg/dl)	0.00	0.19	-0.14	-0.05	-0.04	0.02
Factor VII (per 10%)	0.03	0.09	0.04	-0.15	-0.08 *	0.04
			Model adjusted for age, weight, site and degree of education			
African-Americans (vs Caucasians)	0.18	0.46	0.81 ‡	0.54 †	0.01	0.004

*P <0.05, † P <0.01, ‡ P<0.001

P283

Place of Birth, Cardiovascular Risk Factor Profile, and Cardiovascular and Total Mortality in an Insured Hispanic Cohort

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Foreign-born Hispanics are seemingly healthier and experience lower cardiovascular disease (CVD) and all-cause mortality risks than US-born Hispanics or non-Hispanic whites. The extent to which this epidemiological paradox is explained by early-life experiences, socioeconomic status, health behaviors and/or access to medical care remains unsettled. Our cohort comprised 5,237 members of the Northern California Kaiser Permanente Medical Care Program (NC-KPMCP) who attended multiphasic health checkups between 1965 and 1973 and self-reported Hispanic ethnicity. The distribution of place of birth, a proxy measure of early-life experiences, was as follows: 36% (1,883 of 5,237) in the US, 34% (1,804 of 5,237) in Central/South America, 21% (1,106 of 5,237) in Mexico and 9% (444 of 5,237) in the Caribbean Islands. Mortality follow-up was available through 2004, with total accrual of 170,268 person-years. As shown in the Table, those born in Central/South America and in the Caribbean Islands had higher and those born in Mexico lower education level; all three groups born outside the US had lower prevalences of current smoking and obesity. Hypertension was highest among those born in Mexico. Prevalence of self-reported diabetes and hypercholesterolemia (total cholesterol > 240 mg/dl) did not differ by place of birth. Compared to those born in the US, CVD mortality rates tended to be lower in all three Hispanic groups born outside the US. However, after multivariate adjustment, there were no significant differences in CVD mortality risk. All-cause mortality rates were lower among those born in Central/South America and the Caribbean Islands but higher among those born in Mexico. After controlling for risk factors, those born in Mexico remained at 1.2-fold increased risk of all-cause mortality. This study reinforces the notion that Hispanics subgroups in the US, even in a setting that controls for access to care, differ in terms of risk factor profile and mortality. risk.

ASSOCIATION OF PLACE OF BIRTH WITH RISK FACTORS AND MORTALITY AMONG HISPANICS IN THE NC-KPMCP

Risk Factors and Outcomes	United States	Central/South America	Mexico	Caribbean Islands	p-value
N	1,883	1,804	1,106	444	
Male, %	47	40	49	46	< .001
Some college or higher, %	29	38	18	37	< .001
Current smoking, %	41	36	34	35	< .001
Obesity, %	15	6	11	9	< .001
Diabetes, %	2	2	3	2	.63
Hypertension, %	34	32	39	36	.005
Hypercholesterolemia, %	27	27	30	28	.24
Age-adjusted CVD mortality rate*	13.7	11.2	13.2	10.5	
Adjusted relative risk (95% CI)**	1.00	0.95 (0.74–1.23)	1.12 (0.86–1.44)	0.88 (0.60–1.29)	
Age-adjusted all-cause mortality rate*	46.7	41.0	49.3	42.7	
Adjusted relative risk (95% CI)**	1.00	1.03 (0.89–1.20)	1.20 (1.03–1.40)	1.01 (0.81–1.26)	

* Rates are per 10,000 person years. ** Age, gender, education level + the 5 CVD risk factors

P284

Cumulative Socioeconomic Position from Early Childhood to Mid Adulthood and Incident Hospitalized Heart Failure in Blacks and Whites: The ARIC Study

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An association between socioeconomic position (SEP) in adulthood and incident heart failure (HF) has been reported; however the role of SEP over the life-course on incident HF remains unknown. We examined cumulative SEP measures from early childhood (at age 10 years), young-adulthood (at age 30 years) into mid-adulthood (45–64 years) and incident hospitalized HF over 18-years of follow-up (1987–2004) among 11,671 Atherosclerosis Risk in Commu-

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nities Study participants. Proxies for SEP during the life epochs included: measures of household income, education, manual occupation, managerial role, and home ownership. A composite cumulative SEP score was generated and categorized into race-specific quintiles. Hospitalized HF was ascertained via annual contacts, review of medical records, and death certificates. Participants with prevalent HF at baseline were identified via the Gothenburg criteria, and were excluded. Initial hospitalized HF was defined as the first occurrence of either ICD-9 428 or an underlying cause of death of 428 or ICD-10 150 for hospitalization without a previous record of 428. The age-adjusted incidence rate was higher for Black men (19.3/10^5py) and women (18.1/10^5py) than White men (3.7/10^5py) and women (2.5/10^5py). More Whites (43.1%) than Blacks (37.3%) had a SEP score in the upper two quintiles. Cox Proportional Hazards regression was used to estimate hazard ratios (HR) and 95% confidence intervals (CI) by ethnicity adjusted for age, gender, and center. A graded inverse association between cumulative SEP and incident HF was evident for both Blacks and Whites, indicating that socioeconomic circumstances across the life-course influence HF risk.

Age, gender, and center adjusted HR (95% CI) for the association between cumulative SEP and incident HF.

Blacks (n=2684)

Ranks	SEP score	N	Events	HR	CI
0 (lowest)	0-1	408	63	2.83	1.74, 4.59
1	2-3	715	76	1.99	1.24, 3.19
2	4-5	560	58	2.00	1.23, 3.25
3	6-8	525	30	1.09	0.63, 1.88
4 (highest)	9-15	476	23	ref	---

Whites (n=8987)

0 (lowest)	0-4	1357	175	2.63	2.00, 3.47
1	5-6	1734	125	1.53	1.15, 2.03
2	7-8	2025	121	1.35	1.02, 1.79
3	9-10	1887	88	1.08	0.80, 1.45
4 (highest)	11-15	1984	85	Ref	---

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P285

Racial Differences in Diurnal Blood Pressure and Heart Rate Patterns: Results from the Dietary Approaches to Stop Hypertension Feeding Study

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Background: Several studies have suggested that blacks, on average, have a blunted decline in nocturnal blood pressure (BP) as compared to non-blacks. It is unknown whether differences in traditional determinants of BP, specifically diet and obesity, account for observed differences in diurnal patterns. Methods: We conducted an analysis of The Dietary Approaches to Stop Hypertension (DASH) feeding study that enrolled adults with prehypertension or stage 1 hypertension. ABPM data were obtained at the end of a 3 week run-in period on 333 participants, all of whom ate the same diet. Mean ambulatory daytime (6AM-11PM) and nighttime (11PM-6AM) systolic BP, diastolic BP, and heart rate (HR). Dipping was defined as a nighttime drop of <10% from mean daytime values. Results: Office BP was similar in blacks and non-blacks, as were 24-hr and daytime BP and HR. However, blacks exhibited a statistically significant, blunted nocturnal decline in BP and HR. Blacks were significantly more likely than non-blacks to have systolic non-dipping (44.9% (84 of 187) vs. 26.7% (39 of 146), P=0.001) diastolic non-dipping (20.9% (39 of 187) vs. 11.6% (17 of 146), P= 0.03) and HR non-dipping (40.9 % (76 of 187) vs. 19.9% (29 of 146), P<0.0001). These differences persisted after adjusting for site, sex, age, body mass index, alcohol, activity, office BP (or HR), education and income. Conclusions: Blacks with similar office BP, and who consumed the same diet as non-blacks, had a blunted nocturnal decline in SBP, DBP and HR, even after controlling for factors that influence BP.

P286

Risk Factors for Subclinical Cardiovascular Disease in Different Hispanic Ethnic Groups

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Background:The aim of this study was to determine if there are differential associations between CVD risk factors and measures of subclinical CVD across different Hispanic groups. Methods: Subjects were a subset of participants from the Multi-Ethnic Study of Atherosclerosis (MESA). In MESA, there were 1,493 Hispanic subjects, of whom 54% were Mexican American (MA), 13% were Puerto Rican American (PR), 12% were Dominican American (DA) and 17% were classified as 'Other' Hispanic Americans (OH). Standardized protocols were used to quantify coronary artery calcium (CAC) and other measures of subclinical CVD. Results: The mean age of the sub-sample was 61.3 years and 52% were women. The Table provides the associations between CVD risk factors and CAC by Hispanic group. The magnitude of the associations between CAC and age, sex and body mass index were similar across all Hispanic groups. However, there were differences in the magnitude and significance of the associations between CAC and hypertension, hypercholesterolemia and cigarette smoking. Specifically, the odds associated with hypertension were 2-fold higher in PR and MA; 5-fold higher for hypercholesterolemia in DA and PR; and 2.5 - 3-fold higher for smoking in DA and PR. The differential associations of CVD risk factors by Hispanic ethnic group were also present for aortic valve calcium (AVC), thoracic aortic calcium (TAC), left ventricular mass (LVM), carotid intimal medial thickness (CIMT) and the ankle-brachial index (ABI). Conclusions: These results suggest a potential difference in the relevance of a given risk factor for subclinical CVD that may be dependent on the ethnicity of the Hispanic subgroup.

TABLE - HISPANIC GROUP SPECIFIC ODDS OF CAC > 0 FOR THE CVD RISK FACTORS

	DA (38%)‡		*MA (49%)‡*		*OH (40%)‡*		*PR (41%)‡*	
Variable*	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age (1 year)	1.08	1.03–1.13	1.10	1.08–1.13	1.10	1.06–1.14	1.13	1.08–1.18
Sex (male vs. female)	3.49	1.46–8.34	2.81	1.95–4.03	4.92	2.58–9.37	2.75	1.29–5.84
Body Mass Index (1 unit)	1.06	0.97–1.15	1.05	1.01–1.08	1.00	0.93–1.07	0.98	0.91–1.06
Hypertension (yes vs. no)	0.86	0.37–1.99	1.95	1.37–2.78	1.29	0.68–2.47	2.27	1.04–4.97
Hypercholesterolemia (yes vs. no)†	5.10	2.0–13.03	1.62	1.15–2.26	0.97	0.52–1.81	4.94	2.30–10.64
Diabetes Mellitus (yes vs. no)	0.66	0.23–1.89	1.45	0.97–2.17	1.26	0.55–2.92	0.36	0.13–0.97
Smoker (yes vs. no)	3.27	1.43–7.47	1.46	1.04–2.06	1.76	0.94–3.30	2.58	1.18–5.61

*All variables in the same multivariable logistic model †Total Cholesterol to HDL Cholesterol ratio > 5.0 or Taking a Cholesterol Medication ‡Hispanic Group (Prevalence of CAC)

P287

Hyperuricemia and Cardiovascular Disease in African Americans in the Jackson Heart Study

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Background Hyperuricemia has been associated with an increased risk of hypertension (HTN) and cardiovascular disease (CVD). In a large clinical trial, diuretics were shown to lose their cardio-protection in patients whose uric acid levels increased. In several studies of the general population, including NHANES I, hyperuricemia was found to be independently associated with cardiovascular events. As most studies were performed in European Americans, the relationship between uric acid and cardiovascular disease in African Americans is unknown. To explore this relationship, data from the baseline visit of the JHS, an epidemiological cohort study in African Americans, were examined. **Methods** For these analyses, hyperuricemia was defined as serum uric acid concentrations >6.5 mg/dl in males and >6.0 mg/dl in females or treatment with allopurinol. Hypertension was defined as blood pressure > 140/90 mmHg or antihypertensive treatment while presence of CVD was determined based on 12-lead ECG and self-reported history of MI or stroke. **Results** Of 5058 participants with sufficient data (excluding heavy drinkers), the overall prevalence of hyperuricemia was 29%, was higher in males (39%) then females (24%), and increased with age from 22% in those 21–54 years old to 36% in those 55 and older. HTN and CVD prevalence was significantly higher (81% and 15%, respectively) among hyperuricemics than in the rest of the cohort (56% and 9%, respectively). In multivariable logistic regression analyses adjusting for sex, age, and established risk factors such as type 2 diabetes, high cholesterol, low GFR, and obesity, hyperuricemia was independently associated with HTN in the overall cohort ($p < 0.0001$, adjusted odds ratio OR 2.8, 95% CI: 2.31 to 3.29) as well as after excluding those on diuretics (OR 1.6, 95% CI: 1.28 to 1.94). Similar analyses showed an independent association of hyperuricemia with CVD only in individuals not taking diuretics ($p= 0.0165$, OR 1.5, 95% CI: 1.07 to 2.03). **Conclusions** These results indicate a strong relationship (in addition to traditional risk factors) between hyperuricemia and CVD (including hypertension) in African-Americans and underscore the need for further investigation of uric acid as a cardiovascular risk factor in this population.

P288

Subclinical Cardiovascular Disease in Different Hispanic Ethnic Groups

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Background: The aim of this study was to determine if the distributions of several subclinical measures of cardiovascular disease (CVD) differ significantly among 4 different Hispanic ethnic groups. Methods: Subjects were a subset of participants from the Multi-Ethnic Study of Atherosclerosis (MESA). In MESA, there were 1,493 Hispanic subjects, of whom 54% were Mexican American (MA), 13% were Puerto Rican American (PR), 12% were Dominican American (DA)and 17% were classified as 'Other' Hispanic Americans (OH). Standardized protocols were used to quantify coronary artery calcium (CAC), aortic valve calcium (AVC), thoracic aortic calcium (TAC), left ventricular mass (LVM), carotid intimal medial thickness (CIMT) and the ankle-brachial index (ABI). Results: The mean (SD) age of the sub-sample was 61.3 (10.3) years and 52% were women. The overall prevalence of CAC > 0, AVC > 0, TAC > 0 and an ABI < 1.0 was 45%, 21.4%, 25% and 9.9%, respectively, while the mean LVM and internal CIMT was 146.5 (38.1) grams and 1.04 (0.6) mm, respectively. The Table shows the prevalences and mean values of these measures adjusted for age, sex, body mass index, hypertension, high cholesterol, diabetes and cigarette smoking by Hispanic group. Mexican Americans had the highest values for CAC, TAC, common and internal CIMT while Puerto Rican Americans had the highest values for AVC, an ABI < 1.0 and LVM. Conversely, no Hispanic group was consistently lowest for the subclinical measures of CVD. The excess subclinical CVD found in MA and PR was the same before adjustment for body mass index, hypertension, high cholesterol, diabetes and cigarette smoking. Conclusions: The prevalences and mean levels of subclinical CVD vary among different Hispanic ethnic groups but Mexican Americans and Puerto

Rican Americans have higher levels of most of these measures. The excess subclinical CVD in these two Hispanic groups does not appear to be due to levels of CVD risk factors.

Subclinical Measure	DA (N = 179)	MA (N = 806)	OH (N = 194)	PR (N = 254)
Coronary Artery Calcium (%)	47.9	51.2	44.8	48.0
Thoracic Aortic Calcium (%)	23.4	30.2	25.3	27.3
Aortic Valve Calcium (%)	13.8	16.3	15.4	20.2
Mitral Valve Calcium (%)	9.1	12.6	11.5	8.4
ABI < 1.0 (%)	11.6	14.4	9.5	16.4
Common Carotid IMT (mm)	0.85	0.88	0.86	0.85
Internal Carotid IMT (mm)	1.03	1.13	1.12	1.11
Left Ventricular Mass (grams)	149.4	149.3	147.3	151.4

P289

Self-Monitoring of Blood Glucose by Race/Ethnicity and Income in US Adults with Insulin-treated Diabetes

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Objective: Self-monitoring of blood glucose (SMBG) by persons with diabetes may vary by race/ethnicity and income. We assessed the association of race/ethnicity and SMBG by income in a national sample of US adults with insulin-treated diabetes. **Research Design and Methods:** Among 16,630 adults aged ≥19 years with insulin-treated diabetes responding to the 2000–2004 Behavioral Risk Factor Surveillance Survey (BRFSS), we examined SMBG (≥daily) by race/ethnicity and income. We adjusted associations between SMBG and race/ethnicity and income for age, sex, education, insurance, health status, diabetes-related visits, diabetes duration, diabetic retinopathy, diabetes education, oral diabetes medication, and year. Results are weighted to reflect national population estimates. **Results:** For all racial/ethnic groups, adults with diabetes reporting income <$20,000 were more likely to be age ≥65 years, female, less educated, or uninsured than those reporting higher income. At incomes ≥$20,000, Hispanics and blacks similarly reported less SMBG compared with whites (78%, 77%, 85%; P<0.001). However, among those with income <$20,000, Hispanics performed SMBG less than blacks and whites (65%, 79%, 85%; P<0.001). Receipt of diabetes education varied significantly by race/ethnicity in the income <$20,000 group only (Hispanics 49%, blacks 64%, whites 62%; P<0.001). After adjustment, the racial/ethnic differences in SMBG persisted (Table 1). **Conclusions:** Among adults with insulin-treated diabetes, Hispanics and blacks performed SMBG less than whites. This disparity worsened for Hispanics with income <$20,000. Strategies to improve SMBG education and resources for low-income Hispanics with diabetes likely will reduce this ethnic disparity.

TABLE 1: ADJUSTED ODDS RATIOS (95% CONFIDENCE INTERVALS) FOR DAILY SELF-MONITORING OF BLOOD GLUCOSE AMONG ADULTS WITH INSULIN-TREATED DIABETES: THE BEHAVIORAL RISK FACTOR SURVEILLANCE SYSTEM FROM YEARS 2000 TO 2004*†

	OR (95% CI) for Daily Self-Monitoring of Blood Glucose	
	Income <$20,000	Income ≥$20,000
Variable	Model A **n=6,175**	**Model B n=9,081**
Race/ethnicity Hispanic vs. White Black vs. White	**0.33 (0.24, 0.47) 0.61 (0.46, 0.82)**	**0.62 (0.43, 0.92) 0.55 (0.42, 0.72)**
Age >30 years vs. 19–30 years	**0.76 (0.64, 0.91)**	0.90 (0.80, 1.02)
Female vs. male sex	1.14 (0.87, 1.51)	**1.33 (1.09, 1.63)**
Education <high school	0.79 (0.61, 1.03)	**0.71 (0.53, 0.97)**
No health insurance	**0.58 (0.41, 0.84)**	0.84 (0.58, 1.23)
Low heath status§	**0.71 (0.53, 0.96)**	1.10 (0.89, 1.35)
Any diabetes-related provider visit within past 12 months vs. no visits	**1.21 (1.04, 1.40)**	**1.55 (1.37, 1.75)**
Duration of diabetes <10 years vs. ≥10 years	0.90 (0.68, 1.19)	0.84 (0.68, 1.04)
Diabetic retinopathy	**1.42 (1.10, 1.82)**	1.10 (0.89, 1.37)
Receipt of diabetes education	**1.62 (1.24, 2.12)**	**1.32 (1.06, 1.64)**
Use of oral diabetes medication	0.90 (0.70, 1.16)	**0.64 (0.52, 0.78)**
Survey period (2001–2004 vs. 2000)	**1.18 (1.08, 1.29)**	**1.19 (1.11, 1.28)**

†Model A, Income <$20,000: F(degrees of freedom (df) 13)=8.27; P<0.0001. Model B, Income ≥$20,000: F(df 13)=10.81; P<0.0001. §Low self-reported health status defined as poor or fair on a 4-point Likert scale. *Each column represents one model. Models adjusted for race/ethnicity, age, sex, education, health insurance, self-reported health status, number of diabetes-related provider visits, duration of diabetes, diabetic retinopathy, receipt of diabetes education

P290

Different Effect of Gender on Heart Rate Variability Accounts for Decreased Heart Rate Variability Among Elderly Blacks: The Cardiovascular Health Study

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Background- Heart rate variability (HRV) reflects cardiac autonomic function, with higher HRV associated with better survival. We observed that heart rates (HRs) were significantly increased and time domain HRV decreased in elderly blacks compared to whites, and that there was a relationship of HRV to gender among white but not black participants. We therefore tested whether adjustment for clinical and demographic factors could account for these effects. Method: Time domain HRV from the initial 24-hr Holter recording from participants in the Cardiovascular Health Study, a population-based study of adults >65 years old was compared between white male (M), white female (F), black M and black F participants. N=379 blacks, [144 M (74±5yrs), 235 F (74±6 yrs)] and N=1,111 whites [545 M (74±6 yrs), 666 F (71±5 yrs)] had recordings adequate for time domain HRV measures. Covariates included: age, smoking, diabetes, heart disease, hypertension, medications, body weight, fitness, and cognitive function. UNIANOVA adjusted for factors which were significantly different by race and gender for each HRV measure. Results: Even after adjustment for covariates, white M continued to have the lowest HRs (71±0.5 bpm) and highest HRV (e.g., SDNN=126±2 ms). HRs remained significantly higher and HRV significantly lower than among white F (heart rate=74±0.5 bpm, SDNN=115±2 ms, p<0.001 compared to white males). Among blacks, despite adjustment for covariates, there continued to be little effect of gender on HR (73±0.5 bpm for black M vs. 75±0.6 bpm for black F, p=0.070 as compared to p<0.001 for white M vs. white F). Time domain HRV was also not different by gender among blacks (e.g., SDNN=112±3 ms for both). HRs and time domain HRV were similar among white F and both M and F blacks. Thus, while white M had significantly decreased HRs and increased HRV compared to F, black M had values similar to those of black and white F, resulting in increased HRs and decreased HRV among blacks compared to whites in the CHS. Conclusions- The lack of a gender effect on HR and HRV among blacks helps explain the disparity in HR and HRV between elderly black and white participants in the CHS. Elderly black males have increased HRs and decreased time domain HRV that remain unexplained by underlying factors.

P291

Heterogeneity in Cardiovascular Risk Factors Among Asian-American Subgroups

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Background: Despite the increasing ethnic diversity of the U.S. population, limited information is available about cardiovascular risk among Asians, one of the nation's fastest growing minority groups. Asian Americans are often aggregated for data collection convenience, and important differences in risk factor profiles may be overlooked. **Methods:** Persons of Asian Indian, Chinese, Filipino, Japanese, Korean, and Vietnamese descent were identified using validated given and surname lists in a clinic database. For each ethnic group, proportions with the following were determined using values in the past two years: diabetes (ICD-9 250.X or fasting glucose >= 126 mg/dL x 2), hypertension (ICD-9 401.0, 401.1, 401.9, 796.2 or systolic blood pressure (BP) > 140 mmHg or diastolic BP >90 mmHg), low HDL-C (<40 mg/dL in men, <50 mg/dL in women), high triglycerides (triglycerides >150 mg/dL), metabolic syndrome (according to standard ATPIII criteria), and Body Mass Index in kg/m^2 (BMI) >= 23, BMI>=25, BMI>=30. Chi-square tests of independence were used to compare risk factors among the ethnic groups, stratified by gender. **Results:** We identified 19,967 persons (11,103 women, 8,837 men) over the age of 35 of Asian descent. Characteristics in each subgroup are listed below. Filipino men and women in our population had a greater proportion of CVD risk factors (diabetes, hypertension, metabolic syndrome, overweight and obesity) when compared to other Asian ethnic groups. Low HDL-C was most prevalent in Asian Indians. **Conclusion:** Our results reveal significant heterogeneity among Asian ethnic subgroups with regard to cardiovascular risk factors. Future studies should strive to disaggregate these ethnic groups to better understand and define risk. Table: Demographics of Asian Women and Men in Clinic Population

WOMEN	**Overall**	**Asian Indian**	**Chinese**	**Filipino**	**Japanese**	**Korean**	**Vietnamese**	***p****
N	11130	2036	5986	560	1386	458	704	
Age (years), mean (sd)	48.6 (12.8)	46 (11)	49 (13)	50 (12)	53 (15)	49 (13)	47 (12)	<.0001
Diabetes, % (count)	5 (478)	7 (125)	4 (196)	13 (62)	5 (54)	4 (13)	5 (28)	<.0001
Hypertension, % (count)	24 (2573)	25 (499)	21 (1193)	45 (240)	32 (422)	20 (84)	20 (135)	<.0001
Low HDL-C, % (count)	23 (1126)	37 (374)	20 (503)	26 (75)	17 (87)	17 (23)	20 (64)	<.0001
High Triglycerides, % (count)	19 (1049)	25 (257)	16 (473)	28 (88)	20 (132)	19 (31)	18 (68)	<.0001
Metabolic Syndrome, % (count)	5 (495)	7 (128)	4 (210)	10 (56)	5 (64)	2 (10)	4 (27)	<.0001
BMI (kg/m^2)>=23, % (count)	47 (3395)	70 (884)	39 (1539)	76 (276)	49 (425)	36 (90)	38 (181)	<.0001
BMI >=25, % (count)	28 (2007)	49 (620)	20 (792)	54 (197)	31 (270)	18 (46)	17 (82)	<.0001
BMI >=30, % (count)	7 (474)	14 (175)	4 (140)	18 (66)	8 (72)	2 (5)	3 (16)	<.0001
MEN	**Overall**	**Asian Indian**	**Chinese**	**Filipino**	**Japanese**	**Korean**	**Vietnamese**	***p****
N	8837	2582	4250	396	772	348	489	
Age (years), mean (sd)	48.3 (12.2)	45 (10)	50 (13)	50 (11)	53 (14)	47 (13)	48 (11)	<.0001
Diabetes, % (count)	9 (648)	12 (249)	6 (223)	18 (61)	9 (58)	8 (22)	9 (35)	<.0001
Hypertension, % (count)	33 (2783)	30 (740)	32 (1299)	53 (200)	46 (322)	31 (98)	27 (124)	<.0001
Low HDL-C, % (count)	21 (1100)	31 (497)	17 (420)	20 (53)	13 (57)	14 (25)	15 (48)	<.0001
High Triglycerides, % (count)	37 (1988)	40 (651)	33 (864)	43 (116)	35 (160)	43 (79)	37 (118)	<.0001
Metabolic Syndrome % (count)	7 (632)	9 (228)	6 (234)	15 (58)	8 (61)	7 (23)	6 (28)	<.0001
BMI (kg/m^2)>=23, % (count)	78 (3797)	81 (1137)	74 (1797)	91 (201)	86 (314)	80 (129)	73 (219)	<.0001
BMI >=25, % (count)	51 (2471)	55 (770)	46 (1104)	73 (162)	61 (225)	50 (81)	42 (129)	<.0001
BMI >=30, % (count)	9 (449)	12 (165)	6 (150)	23 (51)	17 (61)	9 (14)	3 (8)	<.0001

*p values are displayed for $\chi 2$ tests of independence or ANOVA which tests for simultaneous difference in means across ethnicities.

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P292

Understanding Age and Black-White Disparities in Cardiovascular Disease

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Introduction: Black-white disparities in cardiovascular disease (CVD) morbidity and mortality have been described; however, the effect of age on differential CVD prevalence and mortality has not been well studied. **Methods:** Cross-sectional analyses of self or administratively identified blacks and whites age 35 years or older from the National Health and Nutrition Examination Survey (1999–2002) and the Centers for Disease Control and Prevention Compressed Mortality File (1999–2003). We defined CVD as a composite measure of self-reported heart failure, stroke, or myocardial infarction. We determined rates of prevalent CVD among blacks and whites, age-adjusted prevalence rate ratios (black vs. white), as well as rate ratios within defined age categories. We tested for age-race interactions and linear trends. We determined mortality rates due to CVD and calculated the percentage of all CVD deaths within each age strata for blacks and whites. **Results:** Blacks in younger age groups have significantly higher rates of CVD compared with whites, whereas prevalence rates are similar between the two groups among those over age 65 (Table 1). Nearly a third (28%, 69008 of 245149) of all CVD deaths among blacks occur in those less than 65 years, compared with only 12% (249513 of 1968976) among whites. Among those 35–44 years of age, the increased prevalence in blacks was partially attenuated after adjustment for CVD risk factors (RR 2.22, 95% CI 0.99–4.81) plus socioeconomic factors and measures of healthcare access (RR 1.91, 95% CI 0.87–4.06). **Conclusions:** Overall age-adjusted CVD rate comparisons in blacks and whites mask higher disease rates observed in blacks at younger ages that dissipate with older age. Understanding when CVD develops in blacks is important for public health and policy interventions aimed at reducing racial disparities in health.

TABLE 1. CVD PREVALENCE AND RATE RATIOS AMONG BLACK AND WHITE ADULTS, NHANES, 1999–2002

	Prevalence Rates per 100, 000 population		Rate Ratio (95% CI)	*P* Value
Overall			Black vs. White	
Unadjusted	9149	10399	1.13(0.89, 1.45)	
Age-adjusted			1.46(1.08, 1.96)	
By age categories				P for interaction .17 P for linear trend .03
35–44 yrs	1933	4754	2.46 (1.08, 5.44)	
45–54 yrs	4207	7209	1.71 (0.81, 3.49)	
55–64 yrs	10188	15750	1.55 (1.00, 2.30)	
65–74 yrs	16252	19444	1.19 (0.79, 1.74)	
75+ yrs	27622	26064	0.94 (0.70, 1.24)	

P293

Prevalence, Comorbidity, and Outcomes in Hospitalized Patients with Heart Failure for Whites and African Americans: Implications and Benchmarks

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Objective: To test the hypothesis that African American (AA) population has higher prevalence of hospitalization rate from heart failure (HF) and they have different comorbidities and outcomes as compared to whites. **Methods:** Data from the 2004 National Hospital Discharge Survey were analyzed to test the study hypothesis in those aged ≥35 years and with 1st-listed diagnosis HF (ICD9–428). Census estimated population data were used to calculate age and gender-specific hospitalization rates. Poisson regression analysis was used in statistical tests. **Results:** In 2004, age-adjusted HF hospital discharge rates per 1000 were 11.5 and 5.6 in whites and AA males (race diff. $p<0.001$). The corresponding rates in females were 8.8 in AA and 4.4 in whites ($p<0.001$). AA males with HF had significantly higher comorbidity from hypertension [odds ratio (95%CI): 2.67 (2.61–2.70)], and lower comorbidities from coronary heart disease (CHD) [0.63 (0.62–0.65)], diabetes [0.78 (0.77–0.80)], renal failure [0.61 (0.59–0.63)] and pulmonary heart disease (PHD) [0.62 (0.78–0.86)] than white males. Similar to males, AA females with HF had significantly higher comorbidity from hypertension [OR (95%CI): 2.32 (2.28–2.38)] and lower from CHD [0.73 (0.72–0.74)] than white. But, AA females with HF had significantly higher comorbidities from diabetes [OR (95%CI): 1.46 (1.43–1.48)], renal failure [1.14 (1.11–1.17)], and PHD [1.38 (1.34–1.45)] than white females. Average days in-hospital care were 5.4 (95%CI: 5.1–5.6) and 5.3 (4.9–5.) in white and AA males; and 5.6 (5.4–5.8) and 5.6(5.3–5.9) in white and AA females. Age-adjusted in-hospital mortality rates (per 1000) were 2.8 (95%CI: 2.6–2.9) and 2.5 (2.4–2.7) in white and AA males; and 1.8 (1.6–1.9) and 1.9 (1.8–2.0) in white and AA females. Among AA, 76% of HF patients were discharged to home and 11% to long-term health facility, but these corresponding rates were 62% and 16% for whites. **Conclusion:** AA had significantly higher HF hospitalization rates than whites, and males had higher rates than females. Significantly differences in comorbidity from five major HF-related diseases were observed between whites and AA. These results highlight the potential and the different strategies of prevention and management of HF in whites and AA.

P294

Cardiovascular Risk Factor Variation Within a Hispanic Cohort: SWAN, the Study of Women's Health Across the Nation

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Objective: Data regarding ethnic variability in risk factors are limited for groups other than Caucasians and African Americans. Although Hispanics have less favorable cardiovascular risk profiles relative to other ethnic groups, little is known regarding variability among ethnic sub-groups of Hispanics. We examined the relationship between cardiovascular risk factors and country of origin and acculturation measures in a cross sectional sample of 277 women aged 42–52 at baseline from SWAN, the Study of Women's Health Across the Nation. Methods: Women recruited to the New Jersey site of the SWAN baseline sample were separated into 4 groups based upon self reported country of origin: Central or South American (C/S American; n=135), Puerto Rican (PR, n=56), Dominican (D, n=42) and Cuban (Cu, n=44). BMI, smoking status, blood pressure (BP), lipid profiles, and presence of hypertension (HBP), hyperlipidemia, diabetes and metabolic syndrome were compared across the 4 sub-ethnicities using univariate and multivariable analytic models. Acculturation was measured based upon response to questions about familiarity with English. Results: PR women had lower mean LDL (109±27 mg/dl) than D (127±28 mg/dl; $p<0.05$), Cu (127 ± 27 mg/dl; $p < 0.05$) or C/S (121±28 mg/dl; NS). HDL was lowest in PR and Cu women (47.5±10 mg/dl and 47±10 mg/dl respectively) and highest in C/S (50±13 mg/dl) and D (53±12) (Overall p=0.05, pairwise comparisons NS). Prevalent metabolic syndrome was greatest in PR women (44.4% versus 31.2%, 11.1% and 26.8% in C/S American, D and Cu, respectively, p=0.009). PR women were more likely to smoke (26.8% versus 11.3, 12.8 and 25% in C/S American, D and Cu women, p=0.02). Neither BP, diabetes nor prevalence of HBP differed significantly across groups. Group differences in lipids were not explained by acculturation, financial strain, education, physical activity, smoking or dietary fat intake. Conclusions: There is significant heterogeneity in cardiovascular risk status among middle-aged PR, Cu, D and C/S women, not explained by acculturation or socioeconomic indicators. Differences in cardiovascular risk among Hispanics may be important for screening and targeting of preventive interventions.

P295

Acculturation, Health Beliefs, and Barriers to Cardiovascular Disease Prevention Among Racial and Ethnic Minorities

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Background: Acculturation has been correlated with elevated cardiovascular disease (CVD) risk factors. The purpose of this study was to examine the association between acculturation and health beliefs, perceptions, and barriers to CVD prevention which has not been previously defined. **Methods:** Racial/ethnic minority participants (n=169, 36% minority) in the NHLBI **F**amily **I**ntervention **T**rial for **Heart** Health **(FIT Heart)** (N=472) were included in the primary analysis (mean age 42 ± 13 years, 69% female). Acculturation was assessed using a validated survey (score <3 is less acculturated and ≥3 is more acculturated). Health beliefs, perceptions, and barriers to CVD prevention were assessed using standardized questions based on Likert scales. Multivariable regression models included the potential confounders: age, sex, education and insurance. **Results:** Acculturation was significantly lower among racial/ethnic minorities vs. whites even after adjustment for confounders ($p<0.01$). Less acculturated racial/ethnic minorities had greater agreement compared with more acculturated minorities with the following: 1) My chances of getting CVD in the next few years are great (62% vs. 32%, $p<0.01$), 2) I am afraid to have screening tests out of fear that something is wrong (35% vs. 18%, p=0.03), and 3) when you try to prevent illness, it can be more trouble than it is worth (41% vs. 22%, p=0.03). Less vs. more acculturated minorities were also more likely to agree that to avoid heart disease it is the doctor (79% vs. 42%, $p<0.01$) or God/ a higher power (59% vs. 33%, p=0.01) who can help the most, and were less likely to agree that they themselves were the greatest factor influencing their health vs. more acculturated minorities (64% vs. 79%, p=0.04). Adjusted results were not materially different. **Conclusions:** Acculturation is associated with altered health beliefs and perceptions that may impact adoption of CVD prevention strategies. Less acculturated minorities were more likely to have an external locus of control compared to more acculturated minorities. Racial/ethnic minorities also had a greater perceived susceptibility to CVD if they were less acculturated which may represent a unique opportunity for education and early intervention.

P296

Trans Fatty Acids and Serum Lipids in the Inuit of Nunavik: A Baseline Survey

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The main effects of trans fatty acids (TFA) on serum lipid levels have been evaluated in controlled dietary trials and in Caucasian populations. Our study looked at these effects in a cross-sectional, observational setting in Northern Québec (Nunavik). A total of 908 Inuit participants aged 18 years-old and more were enrolled in the baseline survey of the Inuit Health in Transition Cohort Study. We performed multiple regression analysis using serum lipid levels as dependant variables and the percentage of TFA in red blood cell (RBC) membrane phospholipids as the main predictor. The following factors were considered as potential confounders: age, sex, smoking, alcohol, omega-3/omega-6, saturated fatty acids, waist girth, HOMA and physical activity. The final model was selected according to best-fit criteria. A bootstrap approach was then applied to account for the complex sampling design and non-response rate of the survey sample. The mean level of TFA reached 1.22±0.03% of phospholipids in RBC membranes, ranging from 0.76±0.06% in the oldest to 1.42±0.09% in the youngest age group ($p<0.0001$). We found a positive association between TFA and LDL-cholesterol (p=0.04) and a negative association with HDL-cholesterol (p=0.0001). Consistently, there was a positive association between TFA and the ratio of total- to HDL-cholesterol (p=0.003) and a negative one with apolipoprotein AI (p=0.01). The association with total cholesterol did not reach statistical significance, nor did triglycerides, LDL size, and apolipoprotein B. In every model tested, TFA explained only a very small proportion of the variance of the outcome of interest. The tendencies observed in the general Inuit population of Nunavik are partly in accordance with what has been previously described.

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Together with lack of power and residual confounding, the high intakes of omega-3 fatty acids, inverse association of TFA intakes on age, and metabolic patterns observed in this group could obscure or counteract some known effects of TFA. As the percent of energy derived from imported, potentially TFA-rich foods grows while the regional and Canadian governments restrict the use of industrially produced TFA, the later may or may not become a significant cardiovascular risk factor in this population.

P297

Duration of Residence and Coronary Artery Disease in Fijian-South Asians: How Does Risk Change with Time?

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Background: South Asians (SA) have a higher prevalence of coronary artery disease (CAD) compared with residents of many other countries. The migration of SA from developing to industrialized nations may further increase the prevalence of CAD. However, there is no data on how the prevalence of CAD risk factors changes in migrants over time. We assessed the prevalence of CAD risk factors in Fijian-SA as a function of duration of residence in North America after migrating from Fiji. **Methods:** We assessed local Fijian-SA migrants for presence or absence of CAD. Presence of CAD risk factors, lifestyles, and migration pattern were also assessed. Subjects were classified as late migrants (LM) if they arrived in North America $\leq$ 20 years prior to study enrollment, or early migrants (EM) if they arrived $>$ 20 years prior to enrollment. Regression analyses were done to calculate odds ratios (OR) for CAD and associated risk factors for LM vs. EM, adjusting for age and sex differences between the two groups. **Results:** The cohort (n=442) consisted of 28% LM (n=125) and 72% EM (n=317). Both groups were well matched for age (55.6 $\pm$ 11.5 vs. 55.8 $\pm$ 11.3 years [P=0.88]) and sex (71% vs. 63% male [p=0.10]), for LM and EM respectively. After adjustment for age and sex, the prevalence of CAD was significantly higher in LM vs. EM (OR=1.87 [95% CI, 1.19–2.93]). The prevalence of diabetes mellitus (OR=1.82 [95% CI, 1.18–2.81]) and dyslipidemia (OR=1.93 [95% CI, 1.23–3.01]) were significantly higher in LM when compared to EM. There was no significant difference in the prevalence of hypertension, smoking, amount of exercise, waist:hip ratio, and recommended daily fruit and vegetable intake for either group. **Conclusions:** Amongst Fijian-SA migrating to North America, LM had a higher prevalence of CAD. When risk factors were examined, LM had a higher prevalence of diabetes and dyslipidemia compared to EM. These differences may reflect positive lifestyle adaptations made by migrants on arrival or improved health care access. Further investigations into the effect of migration on cardiovascular risk amongst ethnic populations are warranted.

P298

Cardiovascular Risk in a Previously Undescribed Hispanic Population

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BACKGROUND Even though Hispanics form the largest ethnic minority in the US, Mexican-Americans are the only segment of the Hispanic population whose cardiovascular (CV) risk has been well studied. In Miami-Dade, FL, where 69.5% of the population is Hispanic but only 3.8% are Mexican, The Florida Heart Research Institute screened 2,804 Hispanics, (1,799 women, 1,005 men) from this largely non-Mexican population for CV risk factors, and compared them to a control group of 1,498 non-Hispanic whites (NHW), (860 women, 638 men). **METHODS** Data from people participating in voluntary, free cardiovascular screenings, between 1997 and 2006, included measurements of blood pressure (BP), height, weight, fasting blood glucose, and lipid profile, and calculation of. Body Mass Index (BMI) and Framingham Risk Scores. Data were stratified by age ($\leq$45 and $>$45 for men, $\leq$55 and $>$55 for women), gender and ethnicity. χ-square tests and t-tests were used to determine significant differences between groups, with a significance level (α) set at 0.05. **RESULTS** Among men $>$45, Hispanics are more likely to be overweight or obese (p $<$.001), exhibit Stage 2 hypertension (p = .021), and lower HDL (p$<$ .019). Similarly, among women $>$55, Hispanics are more likely to be overweight (p$<$.001) or obese (p = .002), exhibit Stage 2 hypertension (p = .001) and lower HDL (p$<$.001). Hispanic women $<$55 were also more likely than NHW women to be overweight (p$<$.001) or obese (.001). Use of BP medication and smoking was similar between groups. When Framingham risk scores were compared, Hispanics did not display significantly higher scores than NHWs solely due to the older age (p$<$0.001) of the NHW subjects in this cohort. **CONCLUSIONS** Despite comparable Framingham scores, the Hispanics in this study demonstrate a risk pattern distinct from that previously described for the Mexican American population. They are at elevated CV risk, specifically as regards obesity, hypertension and HDL, which define targets in this population for focused intervention.

P299

Increased Cardiovascular Mortality in Minority Ethnic Groups: A Result of Increased Incidence or Case Fatality? Four New Studies and a Meta-Analysis in South Asians

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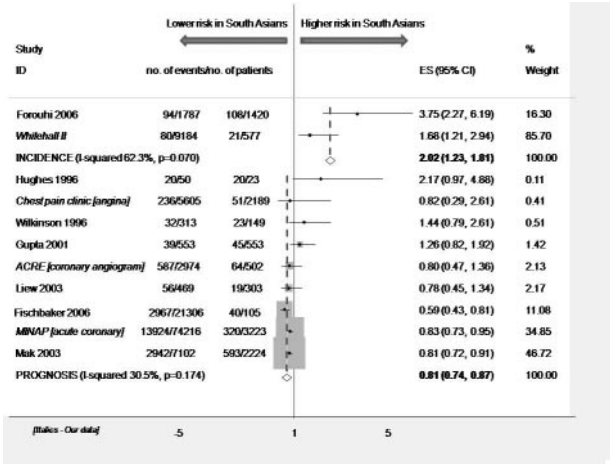
Background The relative contribution of incidence and case fatality to the high CV mortality rates observed in South Asians in high income countries throughout the world is not known. **Objective** We sought to report four new studies and systematically evaluate the published evidence on both incidence of coronary disease and case fatality in South Asians compared to majority populations **Methods** We contribute three new prognostic studies with 14244 events in acute coronary syndrome patients, 651 events in an angiographic cohort of stable coronary disease and 287 events in an incident angina cohort, and one new aetiological study contributing 101 events. A systematic literature review was carried out using MEDLINE 1966–2007 and citations from references. We calculated pooled odds ratios, and 95% confidence intervals using a random effects model. **Results** In addition to our own Whitehall II study, we found only one other study on incidence**.** South Asians had higher rates of incident coronary events (pooled OR 2.02, 95% CI 1.23–1.81). For prognosis, we identified six additional studies; survival after presentation with coronary disease was better in South Asians (pooled OR 0.81 95% CI 0.74–0.87). **Conclusion** We found higher incidence of disease in South Asians than in their white counterparts, but that once they presented with disease, their prognosis was better. The dissociation between the aetiological and prognostic findings has implications for the understanding of disease progression, and suggests that public health efforts to reduce disparities in mortality should focus on primary prevention rather than provision of healthcare to those with disease.



P300

4 of 5 First Fatal CHD Events Now Occur Out of Hospital: Trends Using Data from the Swedish Hospital Discharge and Death Registries, 1987 to 2003

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We investigated trends 1987 to 2003 in the proportion who died out of hospital in a first CHD event (AMI or CHD death) in the Swedish record linked database, which registers all hospitalizations and deaths in Sweden by use of personal identification numbers. Altogether, 376,666 men and women aged 35 to 84 years had a first fatal or non-fatal CHD event, 32% of whom died before reaching hospital (18% in persons $<$ 55 years, increasing to 42% in those aged 75 to 84 years). An additional 11% died in hospital or in the first 28 days following admission. Among 248,169 persons hospitalised with a first AMI, 28-day mortality decreased from 21% in 1987–89 to 10% in 2002–3 (age-adjusted odds ratio (OR) 0.39 (0.38 to 0.41)), ranging from a decrease from 7% to 3% among patients $<$ 55 years, to a decrease from 31% to 17% in those aged 75 to 84. Among all 376,666 first fatal or non-fatal events, out of hospital-deaths decreased from 38% to 28% (OR 0.62 (0.61–0.64)). Expressed as a proportion of all first CHD events fatal within 28 days (n=168,481) only 24% occurred after hospitalization, decreasing from 26% to 21% from 1987–89 to 2002–3. For person aged $<$ 55 years, only 17% occurred after hospitalization, decreasing from 22% to 14%, whereas among those aged 75 to 84 years the change was minimal, or from 26% to 24%. For those dying within 28 days, the odds of dying out-of-hospital, compared to baseline in 1987–89, was 1.73 (1.34–2.22) among persons aged $<$ 55, and 1.10 (1.04–1.17) among those aged 75 to 84 years. Conclusion: the great majority of all fatal first events in CHD occur outside hospital, and this proportion is increasing, particularly in younger CHD victims. In order to achieve further reduction in case fatality, primary prevention is becoming increasingly more important.

P301

Effects of Geographical Area of Residence and Deprivation on Access to Coronary Angiography and on Mortality After Acute Myocardial Infarction in Quebec, Canada

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Background Universal health care systems seek to improve the health status of all citizens by ensuring access to care on basis of need rather than socioeconomic status (SES). The performance of the Quebec universal health care system was examined with respect to the effects of the SES on access to coronary angiography and on mortality 1-year after the first acute myocardial infarction (MI). **Methods** Patients hospitalized for their first acute MI in the Quebec hospital discharge database between January 1997 and December 2001 were linked to the Quebec mortality database. The SES was determined with the provincial deprivation index which has 2 dimensions: material and social deprivation. Six months access to coronary angiography and 1-year mortality were considered in the proportional-hazards survival regression analysis which measured the impact of deprivation and the geographical area of

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residence of the patient. These models also take account of several other variables including age, sex, severity of the disease, speciality of attending physician, hospital volume, presence of on-site facilities and distance to nearest tertiary facility. **Results** The study cohort consisted of 50 242 patients. A strong relation is observed between the material deprivation form ($p<0.0001$) as well as the social one ($p=0.0008$) and the 1-year mortality. The most materially and socially deprived have 17% (95% confidence interval, 1.09–1.26) and 13% (1.05–1.22) more risk of death within 1-year respectively compared with the most advantaged. However, for access to coronary angiography, geographical area of residence is determining whereas deprivation does not have any influence. Living in the great area of a big city (Montréal), being treated by a cardiologist, in a teaching hospital, offering coronary angiography services are factors associated with an increased access to this diagnostic technique, 6 months following a first acute MI. **Conclusions** In the province of Quebec, despite universal health care system, SES had pronounced effects on mortality 1-year after acute MI. As opposed to 1-year mortality, access to coronary angiography is not associated to SES but rather to geographical proximity of a large city offering several specialized care in cardiology.

P302

Trend of Acute Myocardial Infarction Hospitalization in the United States, 1979–2000

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Background. Age-adjusted mortality rates from acute myocardial infarction (AMI) in the US have declined during the past half century. Our earlier report of hospitalization rates for AMI revealed no decline of hospitalization from 1988–1997. We now extend these observations to document trends in hospitalization rates and in-hospital mortality from AMI for 27 years from 1979 to 2005. **Methods.** Hospitalization rates for AMI were determined by age and sex using data from the National Hospital Discharge Survey and US civilian population from 1979 to 2005, aggregated by every three years, standardized with 2000 US population. Co-morbid conditions, use of cardiac procedures, and in-hospital mortality were estimated. **Results.** The rate of AMI hospitalization was 215 per 100,000 in 1979–1981, and increased to 342 in 1985–1987. Thereafter, the rate stabilized for the next decade before declining slowly after 1996 to reach 242 in 2003–2005. The trends were similar for men and women, although rates for men were almost twice that of women. Hospitalization rates increased substantially with age and were highest among those aged 85 years and above. From 1979 to 2005, while median hospital stay for AMI decreased from 12 to 4 days, intensity of hospital care increased, including use of coronary angioplasty from 2.9% in 1985–1987 (when it was first started) to 29.9% in 2003–2005; coronary bypass from 0.5% in 1979–1981 to 10.7% in 1994–1996 and 8.3% in 2003–2005; use of thrombolytics increased from 2.1% in 1997–1999 (when it was started) to 8.3% in 2003–2005. From 1979–81 to 2003–05, reported co-morbidity from diabetes (14.7% to 23.2%) and hypertension (14% to 46.7%) increased. Importantly, AMI complicated by heart failure nearly tripled from (13.1% to 33.3%). Nevertheless, in-hospital mortality declined from 17.8% in 1979–1981 to 8.0% in 2003–2005. **Conclusion.** Over the past quarter century, hospitalization for AMI declined slightly in the US, but complications from heart failure increased. Since their initiation, the use of cardiac procedure has increased. In hospital mortality decreased more than 50%, which could be contributed by both intensity of hospital care and shortening hospital stay.

P303

Trends in Coronary Heart Disease Incidence and Mortality Rates in US Women

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Background: Gender and racial disparities in CHD death rates in the United States show improvement, but whether women and minorities are still lagging behind white males in recent years is unclear. **Methods:** Using data from the National Center for Health Statistics, we examined trends in CHD death rates (ICD-10 I20-I25 and I00-I99) between 1997 and 2004 among whites and blacks in the United States. Log link and Poisson regression was used to derive race-and gender specific data after adjusting for age in 10-yr increments. **Results:** In the study period, there was a significant decrease in CHD death rates for both whites and blacks and for both women and men (all $P<.001$). The decrease in CHD deaths, however, was larger for whites (-21.8%) than blacks (-15.9%), and larger for women (-22.3%) than men (-20.7%). The largest improvement was seen in white women (-22.7%) and the lowest improvement in black men (-16.6%). Between 1997 and 2004, the standardized ratio of male-to female CHD mortality increased from 1.12 to 1.15 in whites, and from 1.15 to 1.17 in blacks. Between 2003 and 2004 only, there was a drop of almost 17,000 female deaths. **Conclusion:** CHD death rates have declined considerably in American whites and blacks and in both sexes during 1997–2004. Greater improvements were observed for whites and women; the greatest reductions overall were observed in white women.

	CHD Death Rate (per 100000)				CHD Deaths (percent of total)			
Year	Black Women	Black Men	White Women	White Men	Black Women	Black Men	White Women	White Men
1997	237.8	273.5	302.1	338.4	20.5	18.6	23.5	25.4
1998	233.3	266.8	296.1	329.5	20.1	18.6	22.9	24.8
1999	239.8	269.4	295.8	325.2	20.3	18.8	22.3	24.4
2000	234.8	260.6	284.7	314.5	19.9	18.5	21.5	23.7
2001	227.7	255.1	274.1	302.0	19.5	18.3	20.8	22.9
2002	219.9	248.3	263.7	296.3	18.9	18.0	20.0	22.5
2003	209.9	244.1	253.3	285.3	18.3	17.8	19.3	21.9
2004	195.5	227.9	233.4	267.5	17.5	17.1	18.5	21.1

P304

Disparities in Emergency Care for Chest Pain Visits with Acute Ischemic Heart Disease in the United States: National Hospital Ambulatory Medical Care Survey, 2003–2005

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Background: Chest pain (CP) is one of the most frequently reported chief complaint (CC) for visits to the emergency department (ED) in the US, and is the most important symptom for ischemic heart disease (IHD). Immediate medical care to identify those with IHD is critical. We examined disparities of medical care among those with CP during ED visits. **Methods:** The National Hospital Ambulatory Medical Care Survey is a national survey of visits to emergency and outpatient departments of non-Federal, short-stay, and general hospitals in the US. ED visits among adults aged $>=25$ years, reporting "chest pain" as "reason for visit" were included. We examined whether receipt of ED care services varied by race (whites vs non-whites), age (25–64 years vs $\geq$65 years) and sex (men vs women). **Results:** Among 19,327,000 ED CP visits (9.1% (95% Confidence Interval (CI) 8.7%–9.4%) of all ED visits), 15%, 13% and 72% of the visits had a primary diagnosis of acute ischemic heart disease (IHD), other cardiovascular disease (CVD) and non-CVD, respectively. Proportion of acute IHD was higher among those aged $\geq$65 years (21.9% vs 12.5%, $p<0.001$), whites (16.8% vs 12.3%, $p<0.001$) and men (17.2% vs 12.9%, $p<0.001$) than those of younger than 65 years, nonwhites and women. Logistic regression analysis, adjusting for demographic characteristics, insurance status and clinical characteristics, revealed that among ED CP visits with acute IHD, whites were 1.6 times more likely to be seen by an ED staff within 10 minutes of arriving (95%CI=1.1–2.6); 1.8 times more likely to be provided with EKG test (95%CI=1.1–3.7) and 1.5 times more likely to be prescribed with antianginal drugs (95%CI=1.1–2.4) than nonwhites. Comparing with women, men were 1.5 times more likely to be seen by an ED staff within 10 minutes of arriving (95%CI=1.03–2.31), 1.5 times more likely to be provided with EKG test (95%CI=1.05–2.66) and 1.7 times more likely to be prescribed with β-blockers (95%CI=1.1–1.5) than non-whites. No difference of emergency care service provided was noted between visits of older than 65 years and those of younger. **Conclusions:** This report suggests that disparities in the provision of emergent care for CP patients with acute IHD. Non-white, women were less likely to receive the cares than white and men patients.

P305

A Prospective Study of Change in Sleep Duration and Associations with Mortality in the Whitehall II Cohort

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Study Objectives: Although sleep curtailment has become widespread in industrialised societies, little work has examined the effects on mortality of change in sleep duration. We investigated associations of sleep duration and change in sleep duration with all-cause, cardiovascular and non-cardiovascular mortality. **Design:** Prospective cohort study. Data are from baseline (Phase 1, 1985–88) and Phase 3 (1991–93), with mortality follow-up of 17 and 12 years respectively. **Setting:** The Whitehall II study of 10,308 white-collar British civil servants aged 35–55 at baseline. **Participants:** 9,781 participants with complete data were included in the analyses at Phase 1, and 7,729 of the same participants were included in the analyses at Phase 3 and the analyses of change in sleep duration. **Interventions:** None. **Measurements and Results** U-shaped associations were observed between sleep ($\leq$5, 6, 7, 8, $\geq$9 hours) at Phase 1 and Phase 3 and subsequent all-cause, cardiovascular and non-cardiovascular mortality. A decrease in sleep duration among participants sleeping 6, 7 or 8 hours at baseline was associated with cardiovascular mortality, hazard ratio 2.4 (95% confidence intervals 1.4–4.1). However, an increase in sleep duration among those sleeping 7 or 8 hours at baseline was associated with non-cardiovascular mortality, hazard ratio 2.1 (1.4–3.1). Adjustment for the socio-demographic factors, existing morbidity and health-related behaviours measured left these associations largely unchanged. **Conclusions** This is the first study to show that both a decrease in sleep duration and an increase in sleep duration are associated with an increase in mortality via effects on cardiovascular death and non-cardiovascular death respectively.

P306

How Likely Are Warfarin Drug Interactions? Results from a Prospective Cohort Study

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Purpose There is a long list of medications that may interact with warfarin, but many are based only on case reports and controversy exists about their true effect. This study used a prospect cohort to evaluate 3 groups of drugs: drugs with (1) known interactions (positive controls), (2) debated interactions and (3) theorized interactions. **Patients and Methods**: The IN-RANGE study was a prospective cohort study of 390 patients with data collected on medications and other factors that can alter warfarin response. The primary outcome was mean change in INR after starting one potentially interacting medication compared to INRs following periods with no change in medications. Multivariable analyses adjusted for changes in warfarin dose, diet, and alcohol intake. Sensitivity analysis limited consecutive study visits to within 30 days of each other and no changes in warfarin dose. **Results** Both positive controls, acetaminophen and amiodarone, had warfarin dose-adjusted increases in INR: 0.15 ($P = 0.007$, [95% CI, 0.04 to 0.27]) and 0.19 ($P = 0.06$, [-0.01 to 0.38]), respectively. In the second and third group of

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debated or theorized interactions, only azithromycin increased INR (+0.43, P =0.002, [0.16 to 0.70]). There were no significant increases for fluorquinolones (-0.02, P = 0.87, [-0.28 to 0.24]), omeprazole (+0.25, P = 0.19, [-0.12 to 0.62]), SSRIs (+0.26 P =0.49, [-0.48 to 0.99]), simvastatin (+0.22 P = 0.53, [-0.47 to 0.91]), or all statins (+0.05 P = 0.75, [-0.25 to 0.34]). Sensitivity analysis, however, revealed potentially underestimated interactions for statins (INR +0.43 P = 0.003, [0.14 to 0.73]). Adjusting for alcohol and diet did not change the results. **Conclusion** This study supports a number of known and important warfarin drug interactions such as acetaminophen, but the evidence also suggests that many of the drug interactions identified by theoretical mechanisms or case reports may not interact to raise INR.

P307

Predictors and Barriers to Timely Medical Follow-up After Cardiovascular Disease Risk Factor Screening According to Race/Ethnicity

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Few data have evaluated if racial/ethnic differences exist to follow up after CVD risk factor screening. The purpose of this study was to assess follow up practices among individuals found to have elevated risk factors in a screening and educational outreach for family members of patients hospitalized with CVD. **Methods:** Participants in the NHLBI **F**amily **I**ntervention **T**rial for **Heart** Health (**FIT Heart**) who were randomized to a special intervention group, underwent standardized risk factor screening, and were found to have hypertension, pre-hypertension, suboptimal lipids, and/or abnormal blood glucose were included in this study (N=214, mean age 49 ± 13, 64% female, 33% non-white). Participants were contacted at 2 weeks, 6 weeks, and 3 months post screening to determine if medical follow up was initiated. Barriers to non-adherence to recommendations were assessed using standardized interviewer assisted questions. Descriptive statistics were stratified by race/ethnicity and logistic models were conducted to determine independent predictors of follow up. **Results:** At two weeks post screening, significantly more whites had medical follow up compared to non-whites (34% vs. 20%, p=.04). Racial/ethnic minorities were more likely to report that not having a doctor was a barrier (30% vs. 11%, p=.02). There were no significant racial/ethnic differences in follow up at 6 weeks or 3 months, however, non-whites were more likely to return to the study staff for follow up rather than seek care from a personal health care provider (32% vs. 15%, p=.001). In logistic regression models, independent predictors of non-follow up at two weeks were younger age (p=<.006), unemployment (p=.02), and not speaking English (p=.04). After three months, significant racial/ethnic differences in reported barriers to follow up included; not having a doctor (36% of non-whites vs. 7% of whites, p=0.001) and having limited time (47% of whites vs. 25% of non-whites, p=.05). **Conclusion:** Racial/ethnic minorities with abnormal CVD risk factors after screening may have delayed medical follow up compared to whites, and this may be attributable to lack of access to a doctor. These data suggest that improving access to care may reduce racial/ethnic disparities in risk factor management and CVD outcomes.

P308

A Sustainable Community Action for Cardiovascular Prevention: The CUORE Project Experience

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Background: Assessment of global absolute cardiovascular risk (GACR) using the Italian risk score of the CUORE Project was recently introduced in Italy and a plan for primary prevention of cardiovascular disease was implemented involving general practitioners (GPs). GACR function is based on gender, age, diabetes, smoking habit, systolic blood pressure, total and HDL-cholesterol and anti-hypertensive medication. The preventive plan aims to reduce/ maintain the Italian population at favourable risk profile. **Methods**: The implementation of the preventive plan includes: 1. web-site from which GPs may download the 'cuore.exe' software to assess 10-year GACR in men and women ages 35–69 years free of cardiovascular diseases; 2. national training course on the assessment of GACR, risk communication, healthy lifestyle counselling, medication treatment; 3. self-training module to collect data using the 'cuore.exe' software; 4. accessible web-site tool – the Observatory of GACR – to pool data collected by GPs, support GPs with quality control, disseminate results in order to monitor GACR by genders, age and geographical area and evaluate its efficacy in primary care. **Results**: Presently, 2,858 health professionals have downloaded the 'cuore.exe' software, 3,300 GPs attended the training course (1,600 residential; 1,700 e-learning) and used the self-training module. Data were collected and sent to the Observatory of GACR by 213 GPs. GACR was calculated for 11,382 persons: 604 men and 28 women were found at high risk (≥ 20%); 3,439 men and 2,295 women at adverse risk to be kept under control by lifestyle; 1,698 men and 3,318 women at low risk (<3%). **Conclusions**: The preventive plan launched within the CUORE Project is expected to be feasible thanks to the support by the Ministry of Health, National Institute of Health and Italian Drug Agency and the involvement of GPs, cardiologists and other health professionals. The Observatory of the GACR is expected to become an important tool for encouraging GPs to shift interest from care to prevention, improving the quality of data collected in clinical practice, monitoring cardiovascular risk and risk factor, planning further preventive actions, and supporting policy makers at national and regional level.

P309

Validation of the 8-Item Morisky Medication Adherence Scale with Pharmacy Fill Data in Patients with Hypertension

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Background The availability of validated self-report tools to assess medication adherence could enhance the patient-provider encounter. We evaluated the validity of the 8 item self-report Morisky Medication Adherence Scale (MMAS) with pharmacy fill data in a sample of community dwelling patients with hypertension. **Methods** Eighty-nine treated hypertensive patients, identified in the administrative databases of a managed care organization, completed a structured questionnaire that included the 8-item MMAS. Patient-level pharmacy fill data were obtained from the administrative databases and used to calculate four adherence measures: continuous single-interval medication availability (CSA), continuous single-interval medication gaps (CSG), medication possession ratio (MPR), and continuous multiple-interval medication gaps (CMG). MMAS was categorized as high, medium, and low (MMAS score =8, 6 to <8, and <6, respectively) and pharmacy fill non-persistency was defined as <0.8 for CSA and MPR and >0.2 for CSG and CMG. **Results** On the basis of MMAS, 57%, 34%, and 9% had high, medium, and low medication adherence. Also, 25% of patients had non-persistent CSA, CSG, and MPR and 37% had non-persistent CMG. After adjustment for age, race, and sex, patients with medium and low adherence were 3.20 (95% CI: 1.37 - 7.47) and 7.58 (2.78 - 20.7) times, respectively, more likely to have non-persistent pharmacy refill adherence by CSA and CSG, than patients with high adherence (p-trend<0.001). Also, patients with medium and low adherence were 2.92 (1.17 - 7.27) and 5.62 (1.96 - 16.1) times, respectively, more likely to have non-persistent pharmacy refill adherence by MPR than patients with high adherence (p-trend<0.001). **Conclusions** The MMAS is significantly associated with anti-hypertensive pharmacy refill adherence and may be useful in clinical practice.

P310

Abnormal Heart Rate Turbulence Predicts High Risk of Cardiovascular Mortality Among Elderly Persons with Elevated CRP: Results from the Cardiovascular Health Study

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Background: Heart rate turbulence (HRT) quantifies the autonomic response to ventricular premature beats. Abnormal HRT predicts cardiovascular (CV) mortality among elderly participants in the Cardiovascular Health Study (CHS). Increased C-reactive protein (CRP) also predicts CV outcomes. This study examines whether the relationship of CRP to CV mortality is mediated in part by HRT. Methods: 24-hour Holter recordings and CRP were obtained at baseline in 1249 CHS participants. Prevalent CV disease (CVD) was identified in 368 participants. Median follow up was12.3 years (245 CV deaths). HRT was calculated from Holter recordings. A stratified analysis of tertiles of CRP with CV mortality, further categorized by abnormal HRT [abnormal turbulence slope (TS<3 ms/beat), abnormal turbulence onset (TO>0), or both abnormal] was performed using Cox regression analysis. Analyses were adjusted for the Framingham risk score (FRS). Because the FRS was designed for individuals without CVD, analyses were stratified on prevalent CVD. Results: Neither increasing FRS nor abnormal HRT predicted CV mortality in the lowest tertile of CRP. Both increasing FRS and abnormal HRT predicted CV mortality in mid and high CRP. These two CRP categories were combined to form a single "elevated CRP" category. FRS predicted CV mortality in participants with elevated CRP [RR=1.02 (95% CI=1.01–1.09, p=0.008) with CVD and RR=1.05 (95% CI=1.03–1.07, p<0.001) without CVD]. Abnormal TS, adjusted for FRS, predicted increased risk of CV death [RR=2.1 (95% CI=1.3–3.4, p=0.004 with CVD and RR=2.3 (95%CI= 1.3–4.0, p<0.001) without CVD]. Combined abnormal TS and TO, adjusted for FRS, predicted greater risk of CV death [RR=8.0 (95% CI=4.6–14.0, p<0.001) without prevalent CVD and RR=2.63 (95% CI=1.4–4.9, p=0.002) among participants with CVD]. Conclusions: The relationship of elevated CRP levels with CV mortality in the elderly is mediated in part by abnormal HRT. Measurement of HRT may provide improved risk stratification in people with increased CRP independent of prevalent CVD, and may identify an especially high risk group among those without CVD.

P311

Does Leukocytosis Predict Recurrent Ischemic Events After Coronary Artery Bypass Graft Surgery?

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Objectives: High white blood cell (WBC) count, before coronary artery bypass grafting surgery (CABG), can be associated with an increased risk of recurrent ischemic events after surgery. **Background**: Studies have shown that inflammatory agents play a role in pathogenesis of coronary artery disease. However, data regarding the role of high WBC count and post CABG ischemic events are limited. The present study was designed to evaluate the role of high WBC count before CABG in predicting the risk of ischemic events after CABG. **Methods**: This prospective study was carried out on 380 patients who underwent CABG surgery. Patients with a recent history of myocardial infection, trauma or surgery, and gastrointestinal bleeding were excluded. Patients were followed for one-year after surgery. Recurrence of ischemic events

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was defined as a new onset myocardial infarction after surgery, unstable angina leading to hospitalization, stable angina, or revascularization. **Results:** During the follow up period, 119 patients (31.3%) developed recurrent ischemic event. Mean WBC count before CABG surgery in patients with recurrent ischemic event was 7264 mic/lit, which was significantly higher than the others, with a mean WBC count of 6721 mic/lit (p=0.011). Patients with a WBC count more than 8000 mic/lit were at the highest risk for recurrent ischemic event (OR=2.14, 95%CI=1.18–3.94). After adjustment for age, sex, diabetes, family history, smoking, hyperlipidemia, waist circumference, creatinine level and body mass index, the relationship between high WBC count and recurrent ischemic event remained significant (OR=2.21, 95%CI=1.18 to 4.13, p=0.013). **Conclusions:** High WBC count before CABG surgery is an independent risk factor for ischemic events after the surgery.

P312

Nonfatal Cardiac Events After Myocardial Infarction Increase the Risk of Sudden Death: A Community Study

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Background: Predicting the risk of sudden death after myocardial infarction (MI) is challenging. While baseline characteristics may be insufficient for this purpose, little is known about the relationship between post-MI non-fatal events, such as recurrent ischemic events (RIE) or heart failure (HF), and the risk of sudden death. **Objectives:** to evaluate the relationship between RIE and HF and sudden death after MI in the community. **Methods:** Olmsted County residents with validated incident MI were identified. Sudden death was defined as out-of-hospital death with the underlying cause of death coded as ICD9 410–414 on the death certificate. RIE was defined as recurrent MI or unstable angina and HF was validated using the Framingham criteria. **Results:** From 1979 to 2002, 2,732 incident MIs (mean age 68±14 years; 57% men) occurred. During a follow-up of 5.7 ± 4.7 years, 1,583 (58%) patients experienced RIE, 1,224 (45%) HF and 705 (26%) died suddenly. Age, female sex, hypertension, diabetes mellitus, anterior MI and comorbidity were all associated with an increased risk of sudden death (all $p < 0.001$). After adjustment for age and sex, interim RIE and HF were associated with a substantial increase in the risk of sudden death: hazard ratio [HR] 2.5, 95% confidence interval [CI] 2.1 to 3.0; $p<0.0001$ and HR 4.6, 95% CI 3.9 to 5.5; $p < 0.0001$, for RIE and HF respectively. **Conclusion:** In a large, population-based MI incidence cohort, the occurrence of non-fatal cardiac events, RIE or HF, was associated with a large increase in the risk of sudden death, suggesting that interim cardiac events should be taken into account in sudden death risk stratification.

P313

Modeling the Decline in Coronary Heart Disease Deaths in Italy, 1980–2000: Assessing Contributions from Risk Factors and Treatments

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Introduction Coronary heart disease (CHD) mortality rates in Italy are lower than in Northern Europe. Furthermore, Italian CHD mortality rates have been falling since 1975. **Hypothesis** To examine how much of the fall in CHD mortality between 1980 and 2000 could be attributed to trends in risk factors, and medical and surgical treatments. **Methods** A previously validated model was used to combine and analyse data on uptake and effectiveness of specific cardiological treatments and risk factor trends in the Italian population of 57 million, stratified by age and sex. Published trials, meta-analyses, official statistics, longitudinal studies, and surveys were the main data sources. **Results** Between 1980 and 2000, CHD mortality rates in Italy fell by 41% in men and 43% in women aged 25–84; with 42,930 fewer deaths in 2000 (24,950 in men, 17,970 in women) than expected. About 40% the mortality fall was attributed to treatments: substantial contributions came from specific treatments for heart failure, angina, and secondary prevention; CABG surgery and angioplasty were estimated to explain approximately 2% of the total mortality fall. About 55% the mortality fall was due to population changes in major risk factors. In men, greater improvements in cholesterol (33%) and blood pressure (25%) rather than smoking (7%) and physical activity (7%); adverse trends were seen in BMI (-1%) and diabetes (-4%); in Women more than 50% of the mortality fall was attributable to improvements in blood pressure (29%) and cholesterol (26%); lower contributions came from physical activity (3%), BMI (1%), and diabetes (0.2%); worrying adverse trend was seen in smoking (-1%). Conclusions Approximately more than half the CHD mortality fall in Italy between 1980 and 2000 was attributable to reductions in major risk factors, mainly systolic blood pressure and cholesterol in men and women and smoking in men, and approximately less than half to evidence-based medical therapies. The rise in smoking rates in women generated additional deaths. Our findings emphasise the importance of a comprehensive strategy which actively promotes primary prevention, particularly a healthy diet, physical activity, and tobacco control, and which maximises population coverage of effective treatments.

P314

Two-Decade Long (1986–2005) Trends in Receipt of Coronary Reperfusion and Coronary Revascularization Approaches in Patients Hospitalized with Acute Myocardial Infarction: A Community-Wide Perspective

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Background: Limited data are available describing contemporary trends in the utilization of coronary reperfusion approaches and revascularization procedures in patients hospitalized with acute myocardial infarction (AMI). The objectives of our population-based investigation were to examine long-term trends (1986–2005) in the utilization of various thrombolytic agents, percutaneous coronary interventions (PCI), and coronary artery bypass graft surgery (CABG) in a community sample of patients hospitalized with AMI. We examined the demographic and clinical characteristics of patients receiving these procedures and also determined whether the profile of patients receiving these different treatment approaches has changed over time. Methods: The study sample consisted of 9,422 greater Worcester (MA) residents hospitalized with confirmed AMI at all metropolitan Worcester medical centers in 11 annual periods between 1986 and 2005. Information on patient demographics, clinical course, and treatment practices was obtained through the review of hospital medical records. Results: Increases were observed in the utilization of PCI (2.0% to 50.7%) between 1986 and 2005; however, CABG utilization increased moderately in the 1990s (1.5%–6.1%), remaining stable thereafter, and subsequently declining to utilization rates of 3.8% in 2005. Use of thrombolytics increased from 1986 to 1995 (9.3% to 25.2%) and decreased markedly between 1997 (20.8%) and 2005 (0.8%). Several demographic and clinical characteristics were associated with the receipt of these treatment approaches and interventional procedures including advanced age, obesity, and Q wave MI. In addition, the profile of patients receiving these different treatment approaches changed over time. Conclusions: The results of this study of patients hospitalized with AMI in a large New England community suggest evolving trends in the treatment of patients with AMI with the increased utilization of mechanical interventions to restore coronary reperfusion. Our findings also suggest that there remains room for improvement in the therapeutic management of patients hospitalized with AMI, including several high-risk groups.

P315

How Reliable Are Cardiovascular Mortality Statistics in the Elderly?

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Death certificates are the main data source for many mortality studies, yet previous studies suggest that death certificates compared with other data sources may misclassify the underlying cause of death. We compared nosologist coding of death certificate's underlying cause of death with validated cause of death for 3194 deaths 1989–2004 in the Cardiovascular Health Study (CHS), an observational study of coronary heart disease (CHD) and stroke in older adults. Deaths were investigated using medical records, death certificates, proxy interviews and autopsies, and underwent central adjudication for underlying cause of death. Independently, death certificates were coded for underlying cause of death by a trained nosologist without any other supporting information about the death or the CHS classification. Comparison of CHS vs. nosologist underlying cause of death resulted in kappas as follows: atherosclerotic CHD=0.6127 (95%CI: 0.5815–0.6438), cerebrovascular disease=0.5930 (95% CI: 0.5451–0.6409), other atherosclerotic disease=0.4339 (95%CI: 0.3339–0.5340) and other cardiac disease=0.3286 (95% CI: 0.2484–0.4088). Although CHS and the nosologist classified a similar number of cases as CHD deaths (832/26.1% CHS vs. 877/27.4% nosologist), only 612 cases were considered CHD by both methods. CHD remained the leading cause of death in all age/sex/race categories by both methods. Almost 20% of the deaths CHS classified as definite fatal MI were not classified as CHD deaths by the nosologist. Agreement between the nosologist and CHS classified CHD did not vary by whether the deaths were witnessed (69.5%) vs. unwitnessed (67.3%). CHS classified 41.7% of deaths as out-of-hospital, 34.5% in-hospital, and 17.5% in a nursing home. Agreement between CHS and the nosologist's classification did not vary by location of death or by time between onset of symptoms and death. Agreement between CHS and the nosologist also did not vary by whether the death was classified by CHS as primary arrhythmic, secondary arrhythmic or pump failure/CHF. Based on these data, cardiovascular studies that use only death certificates to determine cause of death may result in substantial misclassification and potential bias.

P316

Neighborhood Income and Individual Education: Impact on Survival After Myocardial Infarction in the Community

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Background: Although socioeconomic status (SES) is a multidimensional construct, previous studies examining its impact after myocardial infarction (MI) have focused on single indicators measured at a single level. Further, data derived from community cohorts are lacking. We evaluated the association of neighborhood-level income and individual-level education with post-MI mortality in community patients. **Methods and Results:** Residents of Olmsted County, MN, who experienced an MI meeting standardized criteria between 2002 and 2006 (n = 705; mean age 69 [SD 15] years; 44% women) were prospectively enrolled and followed. The neighborhood's median household income was estimated by census tract data, while education was self-reported. Demographic and clinical variables were obtained from the medical records. Low SES, as defined by either area of living or education, was associated with older age, female sex, and more comorbidities. During follow-up (median 13 months), 155 patients died. Both neighborhood income ($34,205, $50,091, and $60,652 in the lowest through highest tertiles) and education were associated with mortality (Figure). Adjustment for demographics and various prognostic indicators attenuated these estimates, yet excess risk persisted for low neighborhood income (HR = 1.54; 95% CI: 1.02–2.32, for lowest vs. highest tertile). **Conclusions:** In this geographically defined cohort of MI, low individual education and neighborhood income were associated with a worse clinical presentation. Moreover, both measures showed a dose-response relationship with mortality. These findings emphasize the importance of addressing health disparities after MI.

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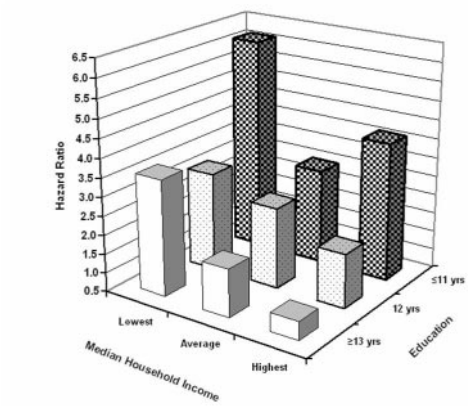

P317

Recent Trends in Hospitalized Myocardial Infarction

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Background: The monitoring of trends in cardiovascular disease events can provide important insights into the effectiveness of primary and secondary prevention efforts. We examined recent trends in hospitalized myocardial infarction (MI) between 1998 and 2006 by sex and race-ethnicity in a large and diverse integrated health care delivery system with over 3.2 million members. **Methods:** MI was identified by an ICD-9 dismissal diagnosis code of 410 among adults aged 35 years and older. Age-adjusted attack rates of hospitalized MI were calculated using Poisson regression. **Results:** Between 1998 and 2006, there were 55,109 hospitalizations for MI, of which 66% occurred in men and 30% in persons aged 75 years or older. Overall age-adjusted attack rates of hospitalization for MI declined steadily over the 9 year period. In 1998, the attack rate was 37 per 10,000 persons (95% CI, 33 to 42 per 10,000 persons) and in 2006 the rate was 29 per 10,000 persons (95% CI, 26 to 32 per 10,000 persons). Annual age-adjusted rates of hospitalizations for MI were consistently higher among men than women. The age-adjusted attack rate of hospitalization for MI decreased an average of 4.2% per year (95% CI, -5.0 to -3.3%) in men and 3.9% per year (95% CI, -5.2 to -2.7%) in women. Significant declines in average annual percent change in MI were also observed among all race-ethnicity groups. The average annual percent change (95% CI) in MI was -3.7% (-5.0 to -2.4%) in Whites, -3.6% (-4.4 to -2.7%) in Blacks, -3.1% (-4.0 to -2.1%) in Hispanics, and -2.8% (-4.1 to -1.5%) in Asians. **Conclusion:** While ecologic in nature, these secular declines suggest that improvements in treatment of risk factors and secondary prevention may have had a demonstrable impact on the occurrence of MI in this population. Future analyses will explore the contribution of individual level factors on these trends and their role in CHD mortality.

P318

Neighborhood Socioeconomic Status and Treatment of Myocardial Infarction: Atherosclerosis Risk in Communities Study

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Pharmacologic treatments are efficacious in reducing post-myocardial infarction (MI) morbidity and mortality. While disparities in the receipt of evidence-based treatments have been documented by age, race and gender, in the U.S. the influence of socioeconomic factors has not been systematically examined. We evaluated the association of neighborhood census tract median household income (nINC) with pharmacologic treatments received during hospitalization or at discharge among validated, definite or probable incident MI (n=9,200) in the Atherosclerosis Risk in Communities (ARIC) Community Surveillance Study (1993–2002). We grouped nINC into tertiles (low, medium and high) and examined treatments with known efficacy in this context (aspirin, β-blockers, angiotensin converting enzyme [ACE] inhibitors, and antihyperlipidemics, for which data became available in 1998). Overall, receipt rates were: 90% for aspirin, 83% for β-blockers, 48% for ACE inhibitors and 54% for antihyperlipidemics. Twenty-four percent of patients were treated optimally, defined as receiving agents in three or more of the medication classes. We used weighted poisson regression implemented using generalized estimation equations to estimate prevalence ratios and 95% confidence intervals (PR, 95% CI) adjusted for clustering of cases within census tracts. In gender-stratified models ($p<0.01$ for interaction) including age, race, and study community, those from low nINC areas were less likely to receive optimal treatment than those from high nINC areas among males (0.66, 0.52–0.83) but not among females (1.01, 0.77–1.33). There were no differences by gender between the medium and high nINC groups. In medication-specific analyses among patients without contraindications, low nINC was associated with a lower likelihood of treatment with aspirin among blacks only and antihyperlipidemics among males only. Medium nINC was associated with a lower likelihood of treatment with ACE inhibitors among blacks only. While receipt of individual treatments during the peri-infarction period was high, fewer than 25% of MI patients received optimal treatment, as defined here. nINC may be one of several contextual factors influencing the complexities of medical care practice patterns.

P319

Long-Term Prediction of Heart Failure Hospitalization: The Atherosclerosis Risk in Communities Study

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Most epidemiologic studies of heart failure (HF) are limited to hospitalized HF or death. Simple criteria of known validity to assess HF in outpatient or population settings are few. The Gothenburg criteria include self-reported cardiac and pulmonary conditions, atrial fibrillation on an ECG, the use of diuretics or digitalis, and selected items from a basic physical examination. We studied whether hospitalization for HF over an average 15.9 years of follow-up is predicted by items of the Gothenburg criteria recorded at the baseline examination (1987–1989) of the 15792 participants in the Atherosclerosis Risk in Communities (ARIC) study. Discharge codes for all hospitalizations reported by the cohort members were abstracted; the first hospitalization with an ICD9 428 code was used to define hospitalized HF. After exclusion of individuals who at baseline reported being treated for heart failure, the age-adjusted incidence of hospitalized HF per 1000 person-years ranged from 4.28 (95% CI, 3.92 - 4.63) for the lowest of the Gothenburg scores, indicating no HF, to 19.20 (95% CI, 16.28 - 22.11) for the highest of the possible scores (Table). A monotonic, positive association was found between Gothenburg scores and the long term risk of hospitalized HF in this population-based cohort of middle-aged African American and white men and women. Assessment of the predictive value of individual score items can be informative in estimating the community burden of HF.

AGE-ADJUSTED INCIDENCE OF HEART FAILURE BY GOTHENBURG SCORE AND HAZARD RATE RATIOS BY RACE AND GENDER

		Hazard Rate Ratios (95% CI)			
Gothenburg Score at Baseline	Incidence Rate (per 1,000 person-years)	White Men	White Women	African American Men	African American Women
0	4.28 (3.92, 4.63)				
1	5.71 (4.96, 6.46)	2.24 (1.78, 2.81)	0.88 (0.63, 1.23)	1.87 (1.19, 2.93)	1.05 (0.75, 1.48)
2	8.90 (7.94, 9.85)	3.06 (2.49,3.77)	2.34 (1.83, 3.00)	3.11 (2.18, 4.41)	1.62 (1.22, 2.15)
3	19.20 (16.28, 22.11)	6.43 (4.70, 8.79)	5.71 (4.20, 7.75)	4.64 (2.68, 8.04)	2.77 (1.95, 3.94)

P320

Left Ventricular Function and Heart Failure After Myocardial Infarction: Impact of the New Definition in the Community

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Background: The 2000 ACC/ESC myocardial infarction (MI) diagnostic criteria increased the number of MIs by identifying cases meeting only troponin-based criteria due to the greater sensitivity of this biomarker. It is important to characterize these cases newly identified as MI. Yet, data on ventricular function and on the incidence of heart failure (HF) among MIs meeting only troponin criteria compared to cases meeting CK-MB based criteria are scarce overall and absent in a community population. **Objectives:** To evaluate systolic and diastolic function by echocardiography and the occurrence of HF among persons with MI diagnosed by troponin-based criteria only compared to those cases meeting CK-MB criteria in the community. **Methods:** Between 11–2002 and 05–2006, we prospectively identified all MIs in the community. Cases were validated using standardized criteria that rely on cardiac pain, Minnesota coding of the ECG, and biomarkers. Both biomarkers, troponin and CK-MB, were prospectively measured in all cases. **Results:** 482 cases (age 68 $\pm$ 15; 45% women) with validated MI underwent echocardiograms at a median (Q1-Q3) of 1 (1–2) days post-MI. Among those, 363 cases met CK-MB-based criteria and 119 met only troponin criteria. Systolic dysfunction (EF$<$ 50%) was present in 160 (33%). Moderate/severe diastolic dysfunction was present in 255 (53%). Cases meeting only troponin criteria had slightly higher EF (55$\pm$ 13 vs 52$\pm$13 for CK-MB, $p<0.01$) and lower wall motion score index (1.3 $\pm$ 0.4 vs 1.5 $\pm$ 0.5 for CK-MB; $p<0.01$). Moderate/severe diastolic dysfunction was similar in both groups (52 vs 53 for CK-MB; $p=0.72$). After a mean follow-up of 1.1 $\pm$ 0.7 years, 142 episodes of HF were noted. The timing of the occurrence of HF was similar according to the biomarker ($p=0.15$). After adjusting for age, sex, comorbidities, the risk of HF was markedly lower among cases meeting only troponin-based criteria (RR 0.56; 95% CI 0.37, 0.85; $p=0.01$). **Conclusions:** Among community-based contemporary MI cases, the ACC/ESC criteria identify cases with more preserved systolic function but equal prevalence of diastolic dysfunction. Cases meeting only troponin-based criteria experience less HF than cases meeting CK-MB criteria.

P321

Coronary Heart Disease Mortality in Sweden Is Decreasing: Mortality Rates Halved Between 1986 and 2002

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Objectives Coronary heart disease mortality rates have been decreasing in Sweden since the 1980s. We used the validated IMPACT model to examine how much of the decrease in

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Sweden between 1986 and 2002 that could be attributed to medical and surgical treatments and how much to changes in cardiovascular risk factors. **Methods** The IMPACT mortality model was used to combine and analyse data on uptake and effectiveness of cardiological treatments and risk factor trends in Sweden. The main data sources were official statistics, national quality registers, published trials and meta-analyses, clinical audits and national population surveys. **Results** Between 1986 and 2002, coronary heart disease mortality rates in Sweden decreased by 51.7% in men and 51.5% women 25 to 84 years old. This resulted in 12 345 fewer deaths in 2002. Some 39.9% of this decrease was attributed to treatments in individuals (including 11.9% to secondary prevention, 6.7% to heart failure treatments, 5.9% to initial treatments of acute myocardial infarction, and 6.7% to hypertension treatments) and 53.7% to population risk factor reductions (principally cholesterol, 38.5%; smoking, 10.4%; blood pressure, 4.5% and physical activity, 5.5%). Adverse trends were seen for diabetes, overweight and obesity. **Conclusions** More than half of the coronary heart disease mortality decrease in Sweden between 1986 and 2002 was attributable to reductions in major risk factors, principally a decrease in total serum cholesterol levels in population along with reduction in smoking. These findings emphasize the value of a comprehensive strategy that promotes primary prevention such as tobacco and diet but also physical activity. It also emphasizes the importance of effective; evidence based medical treatment and intervention, especially secondary prevention.

P322

Cardiovascular Risk Factor Trends in the US Population and Options for Reducing Future Coronary Heart Disease Mortality

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Objective: The US Government Healthy People 2010 objectives include a 20% reduction in age-adjusted coronary heart disease (CHD) mortality rates from 1998 levels. This paper examines the potential for cardiovascular risk factor changes to achieve that target. **Study Design:** Analysis of risk factor trend data using a previously validated CHD mortality model. This comprehensive model integrates information on trends in all the major cardiovascular risk factors, stratified by age and sex. Addressing the US projected population aged 25 to 84 years in 2010 (198 million), the potential reductions in CHD mortality from the base year 2000 were calculated for three contrasting scenarios. **Results:** If age-adjusted CHD mortality rates observed in 2000 remained unchanged, some 388,470 CHD deaths (aged 25–84) would occur in 2010. **a) Recent risk factor trends simply continuing to 2010** should result in approximately 19,000 fewer coronary deaths (minimum estimate 10,000, maximum estimate 25,000). This represents approximately 51,000 fewer deaths attributable to improvements in cholesterol, blood pressure, smoking, and physical activity, negated by approximately 32,000 additional deaths attributable to adverse trends in obesity and diabetes. **b) Successfully reaching all the Healthy People 2010 risk factor targets** (total cholesterol 199 mg/dl, systolic blood pressure 120 mmHg, 12% smoking, 6% diabetes, 80% physically active, and body mass index 25 kg/m^2 in men and 26 kg/m^2 in women); would result in approximately 182,000 fewer deaths (minimum 125,000, maximum 244,000). **c) Everyone reaching the levels already seen in the "low-risk strata" of US surveys (total cholesterol 178 mg/dl, systolic blood pressure 115 mm Hg, zero smoking, zero diabetes, all physically active, and body mass index 24.5 kg/m^2)** could potentially achieve approximately 372,000 fewer deaths (minimum 281,000 maximum 507,000). These estimates remained stable after sensitivity analysis. **Conclusion:** Successfully achieving the Healthy People 2010 targets could approximately halve predicted CHD deaths. Policies to achieve modest additional reductions in major risk factors, as already seen in the healthiest groups, might prevent or postpone more than 300,000 CHD deaths in 2010.

P323

Favorable Cardiovascular Risk Profile and 10-Year Cardiovascular Disease Incidence in Women and Men: Results from the CUORE Project

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Purpose: Cardiovascular risk factor research has recently broadened its focus based on new data demonstrating benefits of favorable levels of all major risk factors - low risk (LRi). Aims are to assess relation of LRi to cardiovascular disease (CVD) risk of men and women, and to evaluate implications for prevention. **Methods:** Prospective population-based Italian study, 7,438 men and 13,009 women ages 35–69 years without previous cardiovascular disease, mean follow-up 10.3 years, validated first coronary and stroke events; baseline CVD risk classified in three categories: LRi – total cholesterol $<$200 mg/dl, SBP$\leq$120mmHg, DBP$\leq$80 mmHg, no antihypertensive medication, BMI $<$25.0 kg/m^2, no diabetes, no smoking; unfavorable but not high risk (U-NHRi); high risk (HRi) – any one or more of: total cholesterol $\geq$240 mg/dl, SBP$\geq$140mmHg, DBP$\geq$90 mmHg, need for antihypertensive medication, BMI $\geq$30.0 kg/m^2, diabetes, smoking. To analyze relation of the three risk profiles to CVD incidence, age-adjusted CVD incidence was calculated, stratified as baseline LRi, U-NHRi, or HRi. To assess independent relationship of individual risk factors to CVD incidence, multivariate proportional hazards models were computed for combinations of risk factors. Results: Only 1.4% of men and 3.4% of women met LRi criteria; 85.0% and 79.3% were HRi. No CVD events occurred in LRi men, only 2 in LRi women. Age-adjusted CVD incidence rates for men and women not high risk (LRi + U-NHRi) were 31.8/10,000 person-years and 16.9/10,000 person-years – 63% and 49% lower respectively than for HRi participants, 51% and 32% lower than for those with one only HRi factor. Blood pressure, need for antihypertensive medication, smoking, hyperglycemia, diabetes, total and HDL-cholesterol were independently related to CVD risk. **Conclusions:** Low risk is a rare condition; favorable levels of all risk factors assure low rates of cardiovascular disease. To make cardiovascular disease become endemic, not epidemic, preventive action strategy should aim to increase and to maintain during life the proportion of low risk people in the general population.

P324

Missing Indicator Method for Missing Confounder Data: Comparison with Complete Case Analysis and Multiple Imputation

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Introduction Values of one or more confounders are frequently missing in etiologic research. The missing indicator method (MIM) is often used to handle missing confounder data, despite ample evidence that this method gives biased results. In this study we aimed to demonstrate with empirical data the degree of bias in the effect estimate of exposure when using MIM for missing confounder data in comparison with complete case analysis (CC) and multiple imputation (MI). Methods From the PREDICT-NL study, a prospective cohort study on risk factors for depression, we identified an exposure (marital status), an outcome (depressive disorder), and three confounder variables (age, sex and income). We created missing values in the confounder variable 'income' according to different patterns of missingness: missing values were created completely at random and missing values depended on the exposure and outcome values. Percentages of missing values ranged from 2.5% to 30%. Results When missing values were created completely at random, MIM gave an overestimation of the odds ratio of exposure while CC and MI gave unbiased odds ratios. MIM and CC gave under- or overestimations of the odds ratio when missing values depended on the exposure and outcome values, i.e. were not completely random. The magnitude and direction of the bias depended on how the missing values were related to exposure and outcome. Bias increased with an increasing percentage of missing values. Conclusions MIM should not be used in handling missing confounder data, even when missing values are missing completely at random, because it gives an over- or underestimation of the odds ratio of exposure already with small percentages of missing values. CC should not be used when missing values are not completely random. MI gives unbiased effect estimates when missing values are completely random and when they depend on observed data, which is usually the case in medical research, and should therefore be used in most situations with missing confounder data.

P325

Prevalence of Congenital Heart Disease in Mongolia: Results and Lessons Learned from 5 Years of Large-Scale Screening

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BACKGROUND: The prevalence of congenital heart disease (CHD) in Mongolia is unknown and difficult to assess due to a vast nomadic lifestyle preventing true representative sampling. OBJECTIVE: To determine the prevalence of CHD in Mongolia. METHODS: Since 2003, large scale screenings for CHD have been carried out throughout 12 sites in 8 different provinces in Mongolia. Children from birth to 18 years were screened by American and Mongolian physicians and nurse practitioners who had been trained in basic evaluation for cardiac pathology. Information obtained included: name, age, HR, RR, pulse oximetry, past medical and family history, presence of a murmur and whether the murmur was pathologic. An echocardiogram by a pediatric cardiologist was performed on all children with pathologic murmurs. RESULTS: In 2007, a total of 948 children were screened over three days in the Southern Gobi region of Mongolia. One hundred and thirty responded that the child had a known heart problem, 154 responded that they had been advised that there was some type of problem, 123 were determined to have a murmur and 64 were thought to be pathologic. Of the 64 children who were thought to have a pathologic murmur, 63% had an abnormal echocardiogram. The defects were as follows: ventricular septal defects 14, atrial septal defects 10, patent ductus arteriosus 9, tetralogy of Fallot 6, sub aortic valve stenosis 1 and hypertrophic cardiomyopathy 1. Prevalence of congenital heart defects utilizing our screening methods was 4.3%. CONCLUSION: Our data suggest that the prevalence of CHD in Mongolia is higher than figures obtained in other countries, which may represent a genetic predisposition, a response to living at a higher altitude or a sample population that is heavily weighted in favor of disease. It appears that non-lethal congenital heart disease may be overrepresented and complex congenital heart disease that is usually lethal in the first year of life is likely underrepresented. Under or over representation of certain children with CHD has made estimating a true prevalence in nomadic cultural settings like Mongolia very difficult. In the future, new screening techniques will need to be incorporated to more accurately define the prevalence of CHD in nomadic peoples living in remote areas.

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P326

Positive Predictive Values of Name Lists to Identify Persons of Asian Descent in a Clinical Population in Northern California

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Background: We undertook a study to validate the Asian given and surname name lists (Asian Indian, Chinese, Filipino, Japanese, Korean, and Vietnamese) previously developed by Kestenbaum and Lauderdale in a clinical population. **Methods:** Surveys were administered by phone and mail to seek self identification of race/ethnicity in a San Francisco Bay Area clinical population. Patients were assigned an "Inferred Race/Ethnicity" if their first or last name was on either the given or surname list for each of the six Asian ethnic groups listed above. People with dissimilar inferred race/ethnicity by first and last names were excluded. Hispanics were identified using a Spanish surname list developed by the U.S. Census Bureau. The remaining group, whose names were non-Hispanic and non-Asian, were inferred as Non-Hispanic White (NHW), as the clinic and surrounding community includes relatively few African Americans. Hispanic and NHW name lists served as comparison groups. Positive predictive value = true positives (self identified race/ethnicity)/ all positives (inferred race/ethnicity). **Results:** The response rates and positive predictive values for each race/ethnic group are shown below (Table 1). In the telephone survey, 2,671 individuals were contacted, and the overall response rate was 31.4%. In the mail survey, 3,200 letters were mailed, and the overall response rate was 5.8%. **Conclusion:** Despite low response rates, Asian given and surname lists had high positive predictive value in this clinical population. Given and surname lists may offer a way method to study differences in Asian ethnic subgroups when self identified race/ethnicity is not available in clinical records.

TABLE: RESPONSE RATES AND POSITIVE PREDICTIVE VALUES OF GIVEN NAME AND SURNAME LISTS

	Telephone Survey		Mail Survey	
	Response Rate	PPV	Response Rate	PPV
Asian Indian	32.7%	0.77	3.3%	0.85
Chinese	29.7%	0.92	4.3%	1.00
Filipino	32.8%	0.81	8.8%	0.94
Japanese	30.6%	0.80	9.8%	0.85
Korean	32.7%	0.78	5.5%	0.86
Vietnamese	34.1%	0.74	6.5%	0.88
Non-Hispanic White	28.1%	0.83	8.0%	0.88
Spanish (Hispanic)	31.0%	0.67	3.8%	0.53

P327

Risk Factors for Chronic Obstructive Pulmonary Disease Mortality in Chinese Adults

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Background: Chronic obstructive pulmonary disease (COPD) mortality is increasing and becoming a leading cause of death worldwide. We studied COPD-related mortality and risk factors in Chinese adults. **Methods:** We conducted a prospective cohort study in a nationally representative sample of 169,871 Chinese men and women aged 40 years and older. Baseline data were collected in 1991 using a standard protocol and follow-up evaluation was conducted in 1999–2000, with a response rate of 93.4%. **Results:** The age-standardized mortality (per 100,000 person-years) was 179.9 in men and 141.3 in women. After adjusting for important risk factors, the relative risks (95% confidence interval) of COPD-related mortality in men and women were 2.80 (2.64, 2.98) and 2.71 (2.53, 2.89) for each 10-year increase in age, 0.84 (0.74, 0.95) and 1.44 (1.07, 1.95) for alcohol consumption, 1.18 (1.04, 1.35) and 1.77 (1.45, 2.15) for ≥20 pack-years of smoking, 2.37 (1.91, 2.94) and 2.47 (1.66, 3.67) for non high school graduates, 1.57 (1.38, 1.79) and 1.35 (1.17, 1.56) for physical inactivity, 2.66 (2.34, 3.02) and 2.60 (2.25, 3.00) for underweight, 1.39 (1.23, 1.57) and 1.73 (1.50, 2.00) for living in northern China, and 2.14 (1.86, 2.46) and 1.79 (1.55, 2.07) for living in rural China, respectively. **Conclusions:** We found that men have a higher COPD-related mortality than women. Furthermore, our study indicated that cigarette smoking, low education, physical inactivity, and underweight are important modifiable risk factors for COPD-related mortality in China.

P328

Neighborhood Socioeconomic Disparities and 1-Year Case Fatality After Incident Myocardial Infarction: The Atherosclerosis Risk in Communities (ARIC) Community Surveillance

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The role of sociodemographic disparities in case fatality (CF) following myocardial infarction (MI) is not well documented in the U.S., largely due to the lack of SES data in hospital records. We examined the association of neighborhood household income (nINC), grouped into tertiles [low (L-), medium (M-), high (H-)], with one-year CF in 8489 (weighted) incident hospitalized MI patients ages 35–74 years in 4 U.S. communities under epidemiologic surveillance by ARIC (1992–2001). Overall, 1033 (12%) of patients died within one year of their MI event; of these, 567 (55%) died within 28 days of their MI. We used weighted Poisson regression, implemented with generalized estimation equations, to estimate case fatality rate ratios (RR) and 95% confidence intervals (CI) taking into account the clustering of participants within census tracts. Overall, the age-adjusted one-year CF was 17% in L-nINC, 10% M-nINC, and 7% H-nINC areas. Because race modified the nINC-CF association, further estimates were calculated within race-SES strata in the two communities with a sufficient number of captured MI events in blacks. H-nINC whites served as the referent group. Results are presented in the Table below. In the ARIC surveillance communities, living in a less affluent neighborhood was associated with higher one-year case fatality in black MI patients. The magnitude of this association was stronger for deaths occurring after the first 28 days following an MI event.*

TABLE: MI CASE FATALITY RR AND 95% CI BY NINC-RACE GROUPS*

	28-Day	29 days to 1-year	One-Year
Black M-nINC	1.00	1.00	1.00
White H-nINC	0.9 (0.5, 1.7)	1.9 (0.3, 10.5)	1.3 (0.4, 3.9)
Black H-nINC	1.2 (0.8, 1.8)	1.3 (0.8, 2.0)	1.2 (0.9, 1.6)
White M-nINC	1.9 (1.2, 3.1)	3.0 (0.8, 5.1)	2.2 (1.5, 3.2)
White L-nINC	1.7 (0.9, 2.8)	1.0 (0.4, 2.5)	1.4 (0.8, 2.3)
Black L-nINC	1.8 (1.1, 3.0)	3.6 (2.3, 5.8)	2.4 (1.8, 3.4)

* Adjusted for age, gender, center, and year of MI.

P329

High Plasma Oxidized Low-Density Lipoprotein Levels Are Associated with Increased Arterial Stiffness: Is Physical Activity a Mediator?

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Background - Oxidized LDL (ox-LDL), a key player in the pathogenesis of atherosclerosis, has been implicated in the development of arterial stiffness. However, the association between ox-LDL and aortic pulse wave velocity (aPWV), a marker of arterial stiffness, has not been examined. Thus, we determined the association between ox-LDL and aPWV in a community-dwelling sample of older adults. We also examined whether physical activity explains this association, as regular physical activity has been shown to decrease both arterial stiffness and ox-LDL levels. **Methods** - Plasma ox-LDL levels and aPWV were measured in 2465 participants (mean age, 74 years; 52% female; 40% black) from the Health, Aging and Body Composition study. Walking endurance and fitness, as measured by a 400-meter walk test, and self-reported physical activity and exercise habits were also assessed. **Results** - Arterial stiffness increased across tertiles of ox-LDL (tertile 1, 871±381 cm/s; tertile 2, 901±388 cm/s; tertile 3, 938±412 cm/s; p=0.001). Total activity (tertile 1, 87±71 kcal/kg/week; tertile 2, 83±71 kcal/kg/week; tertile 3, 79±65 kcal/kg/week; p=0.05) and the proportion of fit individuals (tertile 1, 28.3%; tertile 2, 25.9%; tertile 3, 22.4%; p=0.03) decreased across tertiles of ox-LDL. Minutes and kilocalories per week of walking/exercise did not differ by ox-LDL tertile. There was a significant association between ox-LDL and aPWV after adjustment for age, sex, race, clinical site, smoking status, LDL cholesterol, blood pressure, heart rate, fasting glucose, hemoglobin A1c, abdominal visceral fat, diabetes, and hypertension (β=0.05±0.02, p=0.02). This association remained significant after further adjustment for min/week of walking (β=0.06±0.03, p=0.02), kcal/week of walking/exercise (β=0.05±0.02, p=0.02) and min/week of vigorous exercise (β=0.05±0.02, p=0.01). **Conclusion** - Among generally healthy, community-dwelling older adults, high plasma ox-LDL levels are associated with increased arterial stiffness, independent of physical activity and exercise habits.

P330

Long-Term Prediction of MRI Measures of Carotid Wall Thickness, Wall Volume, and Plaque: The Atherosclerosis Risk in Communities (ARIC) Study

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The composition of atherosclerotic plaque is critical to the occurrence of atherothrombotic events. Identifying the correlates of plaque vulnerability (e.g., large lipid core and thin fibrous cap) may help predict clinical outcomes. We obtained magnetic resonance imaging (MRI) exams of the carotid artery in a subset of participants at year 18 of the ARIC study, hypothesizing that baseline levels of traditional risk factors are predictors of carotid wall and plaque characteristics. A total of 2066 individuals were recruited by stratified sampling (by carotid intima-media thickness strata by previous ultrasound) for this substudy. A high-resolution contrast-enhanced MRI exam of the thickest 1.6 cm segment of the thicker carotid artery was performed in 1769 participants according to a standard protocol. Readings were performed at a central facility. Five risk factors obtained at the ARIC baseline examination and at year 18 (concurrent) were examined in relation to carotid wall volume and maximum thickness, lipid core volume and maximum area, and fibrous cap thickness. Statistical analyses applied sampling weights as appropriate. The average age of the substudy sample was 70 years, 57% female, 81% white, and 19% African American. Internal carotid artery wall volume

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and maximum thickness were greatest in white males (4.84 mm3, 2.5mm) and lowest in African American females (3.5 mm3, 1.8mm). Greater body mass index, total cholesterol, diabetes, hypertension and smoking at baseline were all significant predictors of increased wall volume and maximum wall thickness 18 years later. An analysis of lipid core was restricted to the 1180 participants (67% of 1769) with maximum wall thickness >=1.5mm. Lipid core was observed in 48% (569/1180). Greater plasma cholesterol predicted presence of lipid core but not its size (e.g. volume or area). None of the baseline variables predicted fibrous cap thickness. Concurrently measured risk factors showed weaker relationships with these MRI measures (with the exception of total cholesterol which was significantly related to total wall volume at baseline and at year 18). In summary, wall volume, wall thickness, and presence of lipid core can be predicted by risk factors measured two decades earlier.

P331

Carotid Remodeling by Magnetic Resonance Imaging: The ARIC Carotid MRI Study

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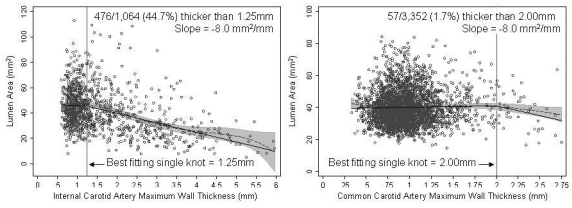
In coronary arteries, atherosclerotic thickening of the arterial wall may be accommodated by outward remodeling of the vessel. Beyond a threshold, however, compensation is incomplete and luminal narrowing occurs. It is unclear whether a similar process occurs in carotid arteries. The ARIC Carotid MRI Study enrolled adults aged 60–85 years, from individuals studied in the Atherosclerosis Risk in Communities (ARIC) Study. Maximum wall thickness and lumen area measurements were made using gadolinium-enhanced magnetic resonance imaging (MRI) in both common carotid arteries (CCA) and in one selected internal carotid artery (ICA) at 2mm above the flow divider. Complete data were available for 1,064 ICAs and 3,352 CCAs. In the ICA, lumen area was relatively constant across wall thickness values <1.25mm. Lumen area decreased linearly with greater wall thickness above 1.25mm. Wall area represented a median of 38% of the area circumscribed by the entire vessel at a maximum wall thickness of 1.25±0.05mm, 50% at 2.5±0.05mm, and 70% at 4.0±0.10mm. In the CCA, lumen area was preserved across wall thicknesses <2.00mm. Plaque growth in the internal carotid artery appears to be accommodated for vessels with maximum wall thickness below 1.25mm. Beyond this threshold, greater thickness is associated with a smaller lumen. The common carotid appears to accommodate wall thickness values below 2.0mm. As carotid luminal narrowing may be related to hypoperfusion and greater accommodation may be related to plaque vulnerability, identification of factors associated with carotid remodeling may help predict the atherosclerotic lesions which confer the highest risk of clinical events.



Fourth-order polynomial (dashed curve and shaded area) and single-knot linear splines (solid curve) models, adjusting for age, sex, height and height^2, were used to estimate the relationship between wall thickness and lumen area. Model fit was assessed by likelihoods.

P332

Red Blood Cell Omega-3 Fatty Acids Are Not Associated with Reduced Carotid Atherosclerosis: The Genetics of Coronary Artery Disease in Alaska Natives Study

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Eskimos were once thought to be immune to atherosclerosis because of high fish oil consumption. Dietary omega-3 fatty acids (FA) levels were inversely related to carotid intimal medial thickness (IMT) in middle aged Japanese, but effects of omega-3 fatty acids over a wide range of omega-3 FA consumption have not been studied. We have previously reported that Eskimos have a higher prevalence of carotid atherosclerotic plaque than other ethnic groups and that dietary intake of omega-3 FAs was not associated with plaque burden. Because dietary intake is not a direct measure of cellular FAs, we have analyzed red blood cell (RBC) FA composition and evaluated the relations with carotid ultrasound measures. From a population-based sample of 1241 Alaskan Eskimos ≥ age 18, FA composition was analyzed in RBC membranes by gas chromatography in all participants > age 35 (N = 718, omega-3 FA intake ranging from 0.8–13.8 g/day). The percentage of individuals with plaque and the plaque score (number of segments containing plaque) were assessed by ultrasound. Models evaluated relations among FAs and quartiles of carotid parameters adjusting for age, gender, diabetes, low-density lipoprotein cholesterol, hypertension, and smoking status. The extent of plaque, scored from 1–8, was not related to RBC total omega-3 FAs or to C20–22 omega-3 FAs (Table), nor did the percentage of participants with plaque vary by quartile of total or C20–22 omega-3 FAs (p = 0.89 for both). The RBC data reinforce the dietary data that diets high in omega-3 FAs do not prevent the development of atherosclerotic plaques and they suggest that the protective effect of omega-3 FA consumption on cardiovascular disease events observed in trials is mediated via mechanisms other than reductions in atherosclerotic plaque.

RELATION BETWEEN PLAQUE SCORE* AND RED BLOOD CELL FATTY ACIDS

Fatty Acid	N	Q1	Q2	Q3	Q4	P
Total omega-3	718	0.573	0.557	0.519	0.569	0.689
C20–22 omega-3	718	0.570	0.564	0.522	0.564	0.754

*mean (log plaque score + 1) adjusted for all covariates.

P333

Carotid Intima-Media Thickness and Cognitive Function in Middle-Aged Males

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Background: Common carotid artery intima-media thickness (CCIMT) is a non-invasive indicator of atherosclerotic cardiovascular disease (CVD), and a predictor of stroke and myocardial infarction. Recent evidence suggests that atherosclerosis and neurodegenerative conditions may share etiologies. **Methods:** We studied 325 apparently healthy male twins age 47–60 years without overt CVD, neurological disorders or cognitive impairment. CCIMT was measured by B-mode ultrasonography. Cognitive function was assessed with verbal and visual memory measures using the Wechsler Logical Memory (WLM) test, the Wechsler Visual Reproduction (WVR) test, and the Selective Reminding Test (SRT-Verbal and SRT-Visual). We also administered the Trail Making Test (TMT), assessing attention and executive function. For each domain, composite scores were derived by transforming individual test scores into standardized Z-scores and then averaging the indices comprising a specific measure. Generalized estimating equation modeling was used for analysis. **Results:** The mean age (± SD) of the twins was 54 ± 2.86 years, and mean CCIMT (± SD) was 0.74 ± 0.10 mm. Higher CCIMT was independently associated with lower Z-scores of WLM and WVR (Table). The adjusted Z-scores were 13% SD lower for WLM and 14% SD lower for WVR with each 0.1 mm positive difference in CCIMT. **Conclusion:** Higher CCIMT is associated with lower memory performance in middle-aged apparently healthy men. A common etiology may link atherosclerosis and cognitive decline prior to symptomatic CVD. Treatment of atherosclerosis to prevent cognitive decline should be further investigated. **Table** Relation between cognitive functions and CCIMT with covariates adjustment: Differences in cognitive Z-scores with each 0.1mm positive difference in CCIMT

	Adjusted* effect	
Cognitive tests	% SD	95% CI
Wechsler Logical Memory	-13.4	-27, -0.1
Wechsler Visual Reproduction	-13.5	-24, -2.8
Verbal Selective Reminding	-10.4	-22, 1.1
Visual Selective Reminding	-10.7	-22, 1.1
Trail Making	2.3	-11, 15

* Adjusted for age, education, body mass index, physical activity, systolic blood pressure, smoking, alcohol use, current depressive symptoms, and history of hypertension and diabetes

P334

Ethnic Differences for Calcified Atherosclerosis in the Thoracic and Abdominal Aorta

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The aims of this study were to 1) determine the association between ethnicity and both thoracic and abdominal aortic calcium (TAC and AAC) and 2) investigate associations between CVD risk factors and both TAC and AAC. Methods: Participants were 1,957 men and women enrolled in the Multi-Ethnic Study of Atherosclerosis who had computed tomography scans of both the chest and abdomen. These scans were obtained at the same clinic visit and calcium scores were computed using the Agatston method. Results: The mean age was 65 years and 50% were female. Forty percent were White, 26% Hispanic, 21% African American and 13% Chinese. Whites had the highest prevalence of AAC (80%) which was significantly higher than Hispanics (68%, p<0.001), African Americans (63%, p<0.001) and Chinese (74%, p=0.029). Similarly, Whites had the highest prevelance of TAC (42%) which was significantly higher than Hispanics (30%, p < 0.01) and African Americans (27%, p<0.001) but was not significantly different from that in Chinese (38%). Compared to Whites and in age- and sex-adjusted multivariable regression models, Hispanics, African Americans and Chinese had significantly lower risks for the presence of any AAC while Hispanics and African Americans, but not Chinese, had significantly lower risks for any TAC (Table, Model #1). Additional adjustment for body mass index, hypertension, diabetes, dyslipidemia, smoking and family history accentuated the lower risk for AAC in Hispanics and African Americans while the risk in Chinese became non-significant (Table, Model #2). The results were essentially the same for TAC. In these models, diabetes, smoking and dyslipidemia appear to have stronger associations with AAC while hypertension is stronger for TAC. Conclusions: Compared to Whites, African-Americans and Hispanics, but not Chinese, have evidence of less atherosclerosis in both the

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thoracic and abdominal aorta which does not appear to be accounted for by traditional CVD risk factors.

Variable	AAC RR	AAC 95% CI	AAC p-value	TAC RR	TAC 95% CI	TAC p-value
Model #1						
Age (per 10 yr)	3.93	3.31–4.67	<0.001	3.98	3.43–4.60	<0.001
Gender (M vs. F)	1.34	1.05–1.71	0.02	0.82	0.64–1.02	0.08
Ethnicity						
White	1.00 (ref)	–	–	1.00 (ref)	–	–
Chinese	0.70	0.48–1.00	0.05	0.82	0.57–1.16	0.26
Black	0.42	0.29–0.59	<0.001	0.37	0.26–0.54	<0.001
Hispanic	0.64	0.48–0.86	0.003	0.66	0.50–0.87	0.004
Model #2						
Age (per 10 yr)	4.25	3.47–5.21	<0.001	3.79	3.22–4.45	<0.001
Gender (M vs. F)	1.10	0.83–1.44	0.52	0.71	0.54–0.91	0.008
Ethnicity						
White	1.00 (ref)	–	–	1.00 (ref)	–	–
Chinese	1.10	0.83–1.45	0.52	1.04	0.66–1.65	0.85
Black	0.30	0.80–1.88	<0.001	0.34	0.23–0.52	<0.001
Hispanic	0.57	0.41–0.81	0.001	0.64	0.47–0.86	0.004
Body Mass Index	1.10	0.94–1.30	0.21	0.95	0.82–1.10	0.48
Hypertension	1.72	1.14–3.06	0.001	2.59	1.98–3.39	<0.001
Diabetes Mellitus	1.87	1.14–2.06	0.013	1.18	0.82–1.70	0.37
Smoking						
Never Smoker	1.00 (ref)	–	–	1.00 (ref)	–	–
Former Smoker	2.37	1.73–3.25	<0.001	1.71	1.30–2.26	<0.001
Current smoker	5.76	3.50–9.49	<0.001	2.44	1.56–3.84	<0.001
Dyslipidemia	2.10	1.56–2.81	<0.001	1.45	1.11–1.89	0.006
Family History of CHD	1.17	0.88–1.56	0.27	1.29	1.00–1.68	0.05

P335

Withdrawn

P336

Fitness, 20-Year Change in Fitness, and Carotid Intima-Medial Thickness: The Cardia Fitness Study

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Background: Cardiorespiratory fitness is protective against the development of cardiovascular disease (CVD) morbidity and mortality, but few studies document the relationship between fitness and subclinical CVD measures such as carotid intima medial thickness (IMT). **Methods:** We studied the association of baseline and 20-year change in fitness with carotid IMT in 2,157 black and white men and women participants (age 18–30 at baseline) in the CARDIA study who: 1) completed a symptom-limited graded exercise treadmill test (GXT) at both the baseline and 20 year follow-up exams; 2) achieved at least 85% age-predicted maximum heart rate, calculated as [208 - (0.7 x age in years)], on the GXT at each exam; and, 3) underwent carotid ultrasound assessment of IMT at the year 20 exam. **Results:** Baseline treadmill test duration was stratified by race-gender specific quartile, and 20-year change/decrease in duration was categorized as low (increase or <15% decrease), medium (15–35% decrease), and high (>35% decrease). Unadjusted baseline test duration was inversely associated, while 20-year change/decrease in duration was directly associated, with maximum IMT in each of the 3 carotid artery segments [common carotid (CCA), bulb, internal carotid (ICA)]. In a linear regression model adjusting for age, race-gender, and baseline and 20-year change in BMI, systolic blood pressure, and LDL cholesterol, baseline test duration was no longer associated with IMT but high duration decrease was associated with 0.027 mm greater IMT in the ICA than low change/decrease (p=0.03). Results for the CCA and bulb were consistent with the ICA findings. Race-gender specific findings were generally consistent with the overall model. **Conclusions:** 20-year decrease in fitness was a predictor of high carotid IMT independent of other CVD risk factors, while baseline fitness was not. Thus, decline in fitness from the level of young adulthood may be important in the development of subclinical CVD.

UNADJUSTED IMT AND MEAN DIFFERENCE IN IMT BY CAROTID ARTERY SEGMENT AND FITNESS CHANGE CATEGORY

	Unadjusted CCA IMT (mean, sd)	Adjusted mean difference in CCA IMT from low change group^	Unadjusted bulb IMT (mean, sd)	Adjusted mean difference in bulb IMT from low change group^	Unadjusted ICA IMT (mean, sd)	Adjusted mean difference in ICA IMT from low change group^
Low 20-year fitness change (<15%) N=461	0.75 (0.12)	ref.	0.98 (0.25)	ref.	0.76 (0.15)	ref.
Medium 20-year fitness change (15–35%) N=968	0.78 (0.12)**	0.007	1.01 (0.25)	0.013	0.80 (0.19)**	0.021
High 20-year fitness change (>35%) N=728	0.80 (0.12)**	0.009	1.02 (0.27)*	0.017	0.81 (0.21)**	0.027*

^adjusted for age, race-gender, baseline GXT duration, BMI, SBP, LDL; 20-year change in BMI, SBP, LDL. *p<0.05, **p<0.001 for comparison with low change.

P337

Associations of Family History of Coronary Heart Disease, Stroke, and Diabetes with Subclinical Atherosclerosis: Multi-Ethnic Study of Atherosclerosis

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Background: Family history (FamHx) of premature coronary heart disease (CHD) is a well established risk factor for clinical and subclinical CHD. However, the relationship of overall FamHx of CHD and that of stroke and diabetes with CHD is not well defined. In this study we examined the possibility that aspects of FamHx beyond early onset CHD might contribute to CHD susceptibility. We investigated the association between the coronary artery calcium score (CACS) and history of CHD, stroke, and diabetes in first-degree relatives of non-diabetic participants in the Multi-Ethnic Study of Atherosclerosis. Methods: The probability of a positive CACS was modeled using logistic regression, adjusting for age, sex, education, income, marital status, ethnicity/race, study site, family size, current smoking, LDL and HDL cholesterol, triglycerides, systolic and diastolic blood pressure, and body mass index. Results: There were 5,264 eligible non-diabetic subjects (age range, 44–84 years, 47% (2,459) males and 57% (3,018) non-whites). Significant associations with a positive CACS were observed for FamHx of CHD only (OR, 1.91; 95% CI: 1.58, 2.31), CHD and diabetes (OR, 1.76; 95% CI: 1.38, 2.24), CHD and stroke (OR, 1.78; 95% CI: 1.40, 2.25), CHD, diabetes and stroke (OR, 1.73; 95% CI: 1.31, 2.27), and FamHx of diabetes only (OR, 1.34; 95% CI: 1.06, 1.70) compared to no FamHx of these conditions. In subgroup analyses, FamHx of diabetes only was significant in males (OR, 1.67, 95% CI: 1.19, 2.35) but not females, and in Hispanics (OR, 1.81, 95% CI: 1.12, 2.95) and no other racial group. In 1,619 subjects with FamHx of diabetes, associations with a positive CACS were observed when there were 3 or more relatives with CHD (OR, 2.72, 95% CI: 1.58, 4.69) and female relatives with CHD (OR, 1.5, 95% CI: 1.04, 2.15). Conclusion: We have identified significant family history characteristics in addition to premature CHD in a first-degree relative that are associated with a positive CACS. Of interest, FamHx of diabetes is a significant risk factor, particularly for males and Hispanics, and FamHx of both diabetes and CHD in relatives is associated with a high-risk familial pattern of CHD. These results have implications for improving familial risk stratification and overall risk assessment for CHD.

P338

Cystatin C Has Different Associations with Small and Large Arterial Elasticity: The Multi-Ethnic Study of Atherosclerosis (MESA)

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Cystatin C (a novel marker of kidney function) is independently associated with higher risk for adverse cardiovascular outcomes, but the mechanisms are unknown. One possible pathway is that mild impairments of kidney function lead to increased vascular stiffness. Using multivariable linear regression, we studied the association of cystatin C with small and large arterial elasticity and aortic distensibility among 6,282 participants without clinical cardiovascular disease in MESA. Small and large arterial elasticity were assessed by pulse wave contour analysis using the HDI PulseWave CR-2000, and aortic distensibility by MRI. Higher cystatin C quintiles were incrementally associated with lower small arterial elasticity in adjusted models in the 3rd, 4th, and 5th quintiles. Higher cystatin C was associated with lower large arterial elasticity only at highest quintile. There was no association between cystatin C and MRI aortic

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distensibility (p-values >0.12 for all). Mildly impaired kidney function is associated with arterial stiffness, particularly in small arteries. Future studies should focus on understanding whether these associations may explain the link between CKD and cardiovascular disease.

THE ASSOCIATION OF CYSTATIN C WITH SMALL (SAE) AND LARGE (LAE) ARTERIAL ELASTICITY

		SAE	SAE Adjusted**		LAE	LAE Adjusted**	
	N	Median [IQR]	β	p-value	Median [IQR]	β	p-value
Cystatin C quintiles							
<0.75	1344	4.11 [2.50, 6.21]	Ref		13.28 [10.31,16.76]	Ref	
0.75–0.82	1274	3.93 [2.49, 6.39]	-0.023	0.24	13.19 [10.30,16.63]	-0.005	0.70
0.83–0.90	1209	3.80 [2.48, 6.39]	**-0.055**	**0.01**	12.67 [9.55,16.47]	-0.008	0.55
0.91–1.02	1273	3.51 [2.30, 5.72]	**-0.102**	**<0.001**	12.16 [9.13,15.71]	-0.005	0.74
>1.02	1182	3.10 [2.10, 4.81]	**-0.175**	**<0.001**	11.04 [8.00,14.96]	**-0.032**	**0.04**

**adjusted for age, gender, race, income, education, smoking, BMI, SBP, HTN, DM, HDL, IL6, CRP, diuretics, ACE-I .

P339

Incidental Findings After Computed Tomography of the Chest and Abdomen for Coronary and Aortic Calcification in Asymptomatic Men and Women in the Community: The Framingham Heart Study

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Background: We systematically analyzed the prevalence and nature of incidental findings (IFs) on multidetector computed tomography (MDCT) exams of the chest and abdomen conducted in an asymptomatic community-based sample. **Methods:** We analyzed the reports for IFs, generated by board certified radiologists from 3429 participants (mean age: 55.7±11, 50.9% women) from the Offspring and Third Generation cohorts of the Framingham Heart Study, who underwent routine non-contrast enhanced MDCT of the chest and abdomen for the detection of coronary and aortic calcium. The radiologist, who was blinded to participant health history, reported the nature, location, and the potential significance (no follow-up necessary, follow-up necessary, or immediate follow-up necessary) of the IF. A standardized phone questionnaire was administered to all participants at least six months after the IF was reported to determine the final diagnosis and type of diagnostic tests and treatments administered in follow-up. **Results:** At least one IF was reported in 21% of participants (n=719/3429). The most commonly reported IF from the chest CT scan were pulmonary nodules (n=199), aneurysms of the thoracic aorta (n=53), esophageal hernia (n=36), and cystic liver lesions (n=126). The most common findings in the abdominal CT scan were cystic renal lesions (n=198), kidney stones (n=33) gastrointestinal diverticula (n=29) and aneurysms of the abdominal aorta (n=23). Overall, 661/1030 findings (64%) were regarded as potentially significant, among them seven, that required an urgent follow-up. IF reporting resulted in a physician visit in 55% of participants and 16% were referred to a specialist, and incurred financial costs in 11% of participants. After completion of follow-up, 7% of participants were still worried about the IF. **Conclusions:** While IFs requiring immediate follow-up are rare, IFs of potential significance are frequently identified on non-contrast enhanced chest and abdominal CT scans in an asymptomatic community-based sample. The subsequent follow-up is associated with significant economic and emotional burden for research participants. However, information on clinical outcomes is necessary to establish formal recommendations.

P340

Marine-Derived n-3 Fatty Acids and Atherosclerosis in Japanese, Japanese Americans, and Whites

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Background: Recent studies in Japan, where fish intake is very high, indicate that marine-derived n-3 fatty acids (FAs) are associated with reduced risk of nonfatal coronary events, suggesting that high intake of marine-derived n-3 FAs has anti-atherogenic effects. We studied the associations of serum marine-derived n-3 FAs with subclinical atherosclerosis in Japanese in Japan, Whites in the United States, and Japanese Americans. **Methods:** Subclinical atherosclerosis and serum n-3 FAs were evaluated in population-based samples of 281 Japanese, 306 White, and 281 Japanese American men aged 40–49 without clinical cardiovascular disease. Subclinical atherosclerosis was assessed as coronary artery calcification (CAC) and intima-media thickness of the common carotid artery (IMT). Serum FAs were analyzed by capillary-gas-liquid chromatography. **Results:** Japanese in Japan compared to Whites had a less favorable or similar profile of many traditional risk factors including blood pressure, LDL-C, triglycerides, diabetes, and smoking. Japanese in Japan had the lowest levels of subclinical atherosclerosis whereas Whites and Japanese Americans had similar levels (Prevalence of CAC(%), 9.3, 26.1, and 31.4 and IMT(mm) 0.614, 0.670, and 0.720 for Japanese, Whites and Japanese Americans respectively). Japanese in Japan had twofold higher levels of marine-derived n-3 FAs than Whites and Japanese Americans (9.20%, 3.85%, and 4.84%, respectively). Serum marine-derived n-3 FAs had significant and non-significant inverse associations with IMT and CAC prevalence, respectively, in Japanese in Japan and Whites. The inverse association in Japanese in Japan remained after adjusting for blood pressure, TG, HDL-C and other cardiovascular risk factors but not in Whites. Significant differences in multivariate-adjusted levels of CAC prevalence and IMT between Japanese in Japan and Whites were attenuated and became non-significant after further adjusting for serum marine-derived n-3 FAs. The significant differences between Japanese and Japanese Americans were attenuated but remained significant. **Conclusions:** Lifelong high levels of marine-derived n-3 FAs in Japanese in Japan may contribute to their lower burden of atherosclerosis in this population.

P341

Sleep Duration and Incident Coronary Artery Calcification: The CARDIA Sleep Study

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Among identified CAC risk factors are several recently found to be correlated with sleep duration: glucose regulation, blood pressure, sex, age, education and BMI. We tested whether sleep duration was associated with incident CAC over five years and whether CAC risk factors mediated the association. CAC was measured in 2000–1 and 2005–6 in the CARDIA cohort. For the sleep substudy, 6 days of sleep were measured with wrist actigraphy (2 waves of 3 consecutive days in 2003–5). Logistic regression models quantified the effect of average sleep duration on incident CAC, adjusting for potential confounders (age, sex, race, education, apnea risk, and smoking). We examined whether cholesterol, triglycerides, blood pressure, fasting glucose, BMI, fibrinogen, IL-6, CRP, alcohol, depression, hostility, type A personality, and income mediated the association. We also examined whether other sleep metrics (daytime sleepiness, sleep quality, fragmentation and self-reported duration) were associated with incident CAC. Of 535 persons aged 35–47, 494 had no baseline CAC. CAC incidence was lower among persons with longer average measured sleep duration (see table). There was a linear association between sleep hours and adjusted log odds of incident CAC (OR = 0.66 for each additional hour, p=.006). The association was stronger for women, but effect modification was not significant. Potential mediators had little effect on the magnitude or significance of sleep hours. Other sleep metrics were not significantly associated with CAC. Longer sleep is associated with lower CAC incidence independently of examined potential mediators and confounders. Further research is needed to confirm and to understand the mechanism.

UNADJUSTED ASSOCIATION BETWEEN SLEEP AND INCIDENT CAC

Average Sleep Hours	N	Unadjusted CAC Incidence
<4	17	.47
4 < 5	49	.20
5 < 6	148	.11
6 < 7	187	.11
7 < 8	88	.07
8+	5	0
ALL	494	.12

P342

Digital Thermal Monitoring of Vascular and Neurovascular Function Correlates with Framingham Risk Score in Asymptomatic Adults

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Background: Digital Thermal Monitoring (DTM) of vascular reactivity is a new test of vascular function that has been shown to correlate with Framingham Risk Score (FRS) and sub-clinical coronary artery disease measured by coronary calcium score. This study evaluates thermal reactivity in the non-occluded arm during DTM with FRS. **Methods**: 233 asymptomatic subjects (mean age 55±9 years, 62% male), without known ischemic heart disease, underwent DTM after a 5 minute supra systolic arm cuff occlusion. Thermal reactivity was studied in both occluded and non-occluded arms. Baseline temperature (TMP initial), temperature rebound (TR), delta of post-cuff deflation maximum temperature and TMP initial, were studied as indices of vascular reactivity. **Results:** TR was lower in FRS>20% than FRS<10% in both occluded and non-occluded arm respectively. After adjustment for age, gender and CHD risk factors, the odds ratio for TR in the non-occluded arm (lower tertile vs. upper 2 tertiles) was 3.5 (95% CI 1.7–7.2, p=0.001) in FRS>20% compared with FRS<10%. **Conclusion:** DTM based measurement of neurovascular dysfunction as identified by thermal changes in non-occluded hand is associated with increased burden of CHD risk as measured by FRS.

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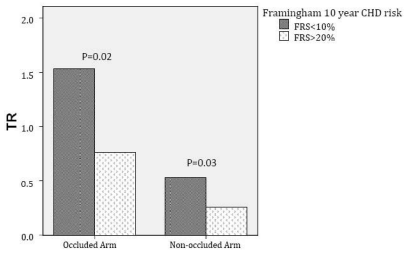

Thermal Vascular Function Decreased in both Occluded and Non-occluded Arm with increasing risk of CHD event

P343

Hormone Therapy Affects Adventitial Diameter in Early Postmenopausal Women

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The effect of estrogen on the peripheral vasculature is largely unknown. Recently it has been reported that as women transition the menopause, decreases in estrogen are accompanied by increases in common carotid artery adventitial diameter (AD). Larger AD is a marker of adverse vascular health as the vessels are less able to adapt to stressors. The effect of hormone therapy (HT) on AD is unknown. We wanted to determine whether there were differences in AD in early postmenopausal women based on baseline use or non-use of HT using the Women on the Move through Activity and Nutrition (WOMAN) cohort. Potential participants were 52 to 62 years of age, recent users of HT, waist circumference $\geq$ 80cm, BMI $>$25 kg/m^2, LDL 100 to 160mg/dL, not on lipid lowering drugs, not diabetic, $<$ 160/95mmHg for their blood pressure (anti-hypertensive medication use was allowed) and from Allegheny County, PA. AD, history of HT use and several cardiovascular risk factors were measured in 502 African American and Caucasian early postmenopausal women at baseline. AD was not normally distributed and was transformed by cubing the values. Linear regression was used to assess the association between AD and HT adjusting for age, race, SBP, BMI, and current smoking status. All final results were back transformed. The women were predominately on HT (60%), Caucasian (89%), not using anti-hypertensive medications (76%), and current non-smokers (93%); average age was 57, average BMI was 31 kg/m^2. Univariate analysis found women on HT had smaller mean AD than women not on HT (6.57mm vs. 6.89mm, respectively, $p < 0.001$). Using linear regression, factors significantly associated with AD were HT use (β= -3.31, $p<0.001$), SBP (β = 1.03, $p<0.001$), current smoking (β = 3.53, p=0.009), and BMI (β = 1.34, p=0.030); age and race were not significantly associated with AD. We found that early postmenopausal women on HT from the WOMAN trial had significantly smaller AD compared to women not on HT suggesting an acute vascular benefit of HT.

P344

Risk Factors for the Progression of Carotid Artery Intima-Media Thickness in Healthy Men and Women

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While the determinants for carotid artery intima-media thickness (CIMT), a measure of subclinical atherosclerosis are well known, the risk factors associated with progression of CIMT have not been well investigated. The Vitamin E Atherosclerosis Prevention Study (VEAPS) was a randomized, double-blind, placebo-controlled single-center trial that tested the effects of vitamin E on CIMT progression. Men and women $\geq$40 years old with LDL-cholesterol $\geq$ 130mg/dl and no cardiovascular disease were randomized. CIMT was measured at baseline and every 6 months. After 3 years, the CIMT progression rate did not differ between treatment groups. To determine the correlates of CIMT progression we evaluated the following VEAPS factors in this analysis: age, gender, weight, BMI, blood pressure, anti-hypertensive and lipid-lowering medication intake, serum lipids, glucose, urea, creatinine, a panel of antioxidants, oxidative lag time, percent of total calories from carbohydrate, protein, and fat, and total fiber intake. A total of 332 participants had a mean (SD) age of 56.2(8.9) years; 48% were male. A multivariate mixed effects analysis revealed that higher age, educational status and higher serum LDL-cholesterol levels were significant positive predictors of CIMT progression whereas higher fiber intake, lipid-lowering medication intake and higher serum ascorbic acid level had significant inverse associations with CIMT progression. Retinol was significantly inversely related to CIMT progression in females only (p for interaction= 0.05). At baseline, age, systolic blood pressure and serum urea levels were independently associated with CIMT. Longitudinal analysis identified factors related to atherosclerosis progression that were not identified in cross-sectional analysis.

P345

Characteristics and Prognosis of MESA Participants with Extensive Coronary Artery Calcium: The Multi-Ethnic Study of Atherosclerosis (MESA)

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Background: MESA is a prospective cohort study of cardiovascular disease (CVD) risk in individuals, age 45 to 84 years, free of clinical CVD at baseline. Coronary artery calcium (CAC) is associated with CVD risk; however, while the risk of a CAC score $>$400 is known, the characteristics and risk associated with extensive CAC ($>$1000) are less clear. We identified characteristics of participants with extensive compared with severe CAC (400–999) and examined risk for CVD events. Methods: CAC was measured in Agatston Units (AU) from fast CT at baseline. Multivariate logistic regression was used to compare CVD risk factors in subjects with severe CAC (AU 400–999, n=420, 6.2%) compared with extensive CAC (AU $\geq$ 1000, n=257, 3.8%). Hypertension was defined as BP 140/90 mm Hg or medication use. Dyslipidemia included total cholesterol/HDL ratio $>$5 or medication use. Chronic kidney disease (CKD) was defined as estimated GFR$<$60 ml/min/m^2 or albuminuria ($>$30 mg/g). Cox proportional hazard models were used to determine risk of CVD events during a median follow-up of 3 years. CVD events included myocardial infarction, angina, resuscitated cardiac arrest, coronary heart disease death, nonfatal or fatal stroke, and other atherosclerotic or CVD death. Results: Extensive CAC, compared to severe CAC, was associated with male gender (OR 2.9, $p<0.001$), older age (OR 1.7 per IQR of 66–77 years of age, $p<0.001$) and hypertension (OR 1.5, p= 0.05); there were no significant associations with race/ethnicity, dyslipidemia, smoking, or diabetes. CKD was associated with extensive CAC (OR 1.5, p=0.03) due to a greater prevalence of moderate CKD (GFR 30–59) in the extensive group (18% vs. 25%). No associations were seen with IL-6, homocysteine, or fibrinogen. There were 76 CVD events during follow-up (annualized event rate= 3% in severe and 4.6% in extensive CAC groups). Those with extensive CAC tended to have more CVD events in unadjusted analyses (HR 1.5, p=0.06). After adjusting for Framingham risk score, race/ethnicity, and CKD, the HR was 1.4 (p=0.15). Conclusions: Extensive CAC is associated with moderate CKD in the general population and a high CVD event rate. When compared to severe calcification, the rate is not significantly different during short term follow-up.

P346

Association Between ACE Pathway Genes and Coronary Artery Calcification in the Multi-ethnic Study of Atherosclerosis (MESA)

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Angiotensin I-converting enzyme (ACE) is a key factor involved in blood pressure (BP) regulation. Since hypertension is a risk factor for atherosclerosis, variations in ACE pathway genes (ACE, AGT, AGTR1, NOS3) may be associated with atherosclerosis development. We genotyped 2847 subjects in MESA, including 4 ethnic groups (712 African Americans, AA; 712 European Americans, EA; 718 Chinese Americans, CHN; and 705 Hispanic Americans, HA), to examine the association between 46 tag SNPs of 4 genes and coronary artery calcification (CAC). CAC was assessed by CT scanning and defined as present if the score was $>=1$ Agatston unit. Under the additive model, logistic regression was performed adjusted for age, gender, and BMI, and then additionally adjusted for BP and hypertension treatment only if BP was associated with SNPs. SNP-SNP interactions were first evaluated by the multifactor dimensionality reduction method, and then confirmed by logistic regression. To account for multiple testing, empirical p values were estimated by permutation of 10000 replicates. Among 2847 subjects, 1370 (48.1%) had CAC present. Significant associations were identified in the AGTR1 gene. In AA, 3 SNPs were associated with CAC (rs3772616, p=0.002; rs385338, p=0.006; rs2638363, p=0.041). In EA, 2 SNP-CAC associations were identified (rs4681443, p=0.002; rs718858, p=0.004). Since the direction of association was the same between AA and EA at rs3772616 and rs4681443, these SNP-CAC associations were stronger in the combined AA and EA (p=0.001 and p=0.0008 respectively). ACE and NOS3 did not yield any associations at the significance level of 0.05. Interestingly, 1 SNP-SNP interaction (AGTR1: rs3772616 and AGT: rs2478545) was identified with CAC in the combined AA, EA and CHN populations (p=0.014). No strong associations were identified in HA. Only rs3772616 was associated with BP (p=0.022 for SBP and p=0.006 for DBP) in the combined samples. In summary, two SNPs (rs3772616 and rs4681443) in the AGTR1 gene were associated with CAC in both AA and EA. Interaction between AGTR1 (rs3772616) and AGT (rs2478545) was identified with CAC in 3 of 4 ethnic groups. These data provide evidence that genes in the ACE pathway contribute, independently of BP, to the etiology of coronary atherosclerosis.

P347

Defining Normal Distributions of Coronary Artery Calcification in At-Risk Community-Based Women and Men: The Framingham Heart Study

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Background: Coronary artery calcification (CAC) may improve risk stratification for coronary heart disease (CHD) beyond traditional risk factors. However, there is a need to establish

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reference values of CAC. **Methods:** Participants from the Framingham Heart Study Offspring and Third Generation cohorts (48% women, mean age 53 years), underwent non-contrast ECG triggered cardiac multidetector (MD) CT. Distributions of CAC according to absolute (Agatston Score [AS] >0, >100, >400) and relative cutpoints (25th, 50th, 75th, 90th, 95th percentile stratified by age and sex) were derived from a healthy reference group free of cardiovascular disease (CVD) or CHD risk factors (n=1586), the overall sample free of CVD at risk (n=3238), and participants at intermediate Framingham CHD risk (n=1177). We compared absolute and relative cutpoints to identify subjects with elevated CAC using the 90th percentile of the healthy reference group versus an AS < 400. **Results:** CAC was detected in 30% of the healthy reference sample, 43% of the overall cohort, and 64% of subjects at intermediate Framingham risk. The prevalence and extent of CAC increased with age/risk strata, and was higher in men as compared to women. Less than half of the participants were identified as having elevated CAC by an absolute cutpoint of AS < 400 as compared to the 90th percentile of the healthy reference group (6.8% vs. 14.5%). The difference was even higher in women at intermediate Framingham risk (2% vs. 13.2, respectively). Among all subjects with any CAC, disagreement using absolute versus age-specific methods occurred in 29.3% of participants for an AS >400 vs. >90th percentile and in 40.9% for an AS >100 vs. >75th percentile, respectively. **Conclusions:** Using healthy reference values, we establish population-based normal distributions of absolute and relative CAC cutpoints. Agreement between these cutpoints to identify subjects with elevated CAC is poor. The use of absolute cutpoints renders a small effect size for further risk stratification, especially in women at intermediate FRS.

P348

The South Asian Paradox: High Risk Despite Favorable Lifestyle Factors

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Background: There are approximately 4 million people of South Asian origin (ie, Indian subcontinent) in the U.S., but no population-based studies of this ethnic group and cardiovascular disease in the United States. Objectives: To assess the prevalence and antecedents of subclinical atherosclerosis in South Asians (SA), and compare SA to other U.S. ethnic groups. Methods: We performed a population-based study of 130 South Asians using methods identical to the Multi-Ethnic Study of Atherosclerosis (MESA). MESA included four ethnic groups (Whites, African Americans (AA), Latinos and Chinese) between 45–84 years without known cardiovascular disease. We obtained demographic and lifestyle information, fasting blood tests, physical examination, carotid ultrasound for intima media thickness (IMT) and CT for coronary artery calcium (CAC). We compared prevalence of risk factors and atherosclerosis in SA to the MESA ethnic groups. Using adjusted linear regression models, we examined risk factors associated with common carotid IMT. Results: The mean age of SA was lower than the MESA subgroups (57 vs. 60–62 years, p<0.001). Approximately 98% were immigrants who had lived in the U.S. for a mean 24±11 years. SA had significantly higher socioeconomic attainment (education ≥Bachelor's degree: 75%; family income ≥$75,000: 65%) compared to each MESA ethnic group. The table below compares characteristics among all ethnic groups. In adjusted models, compared to Whites, South Asians (β= 0.11, p≤0.001) had higher common carotid IMT after adjusting for sex, age, smoking, blood pressure, HDL, LDL, glucose, and waist circumference. Conclusion: Despite low BMI and high socioeconomic status, South Asians have a higher prevalence of diabetes and hypertension than other ethnic groups, and high levels of carotid IMT but not CAC. Traditional risk factors do not explain the high levels of common carotid IMT in South Asians.

COMPARISON WITH MESA ETHNIC GROUPS

	SA n=130	Whites n=2,507	Chinese n=769	AA n=1,821	Latinos n=1,429
Current smoking	5%	12%†	6%	18%†	14%†
BMI, kg/m2	26 ± 5	28 ± 5†	24 ± 3†	30 ± 6†	29 ± 5†
Waist circ., cm	97 ± 12	98 ± 15	87 ±10†	101 ± 15†	101 ± 13†
LDL, mg/dl	113 ± 31	117 ± 30	115 ± 29	116 ± 33	120 ± 33*
HDL, mg/dl	48 ± 14	52 ±16*	49 ± 13	52 ± 15*	47 ± 13
Hypertension	46%	37%*	36%*	59%*	40%
Diabetes	26%	7%†	15%*	20%	19%
Common carotid IMT, mm	0.95±0.2	0.86±0.2†	0.82±0.2†	0.90±0.2*	0.85±0.2†
Ln (CAC + 1)	1.8 ± 2.3	2.5 ± 2.6*	2.1 ± 2.4	1.8 ± 2.4	1.9 ± 2.4

* comparing individual MESA ethnic groups to SA, p<0.05; † p<0.001

P349

Substantially Increased Mortality in Patients with Peripheral Arterial Disease and/or Diabetes Mellitus in Primary Care: 5-Year Outcomes of the getABI Study

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We aimed to assess the 5-year risk of death associated with peripheral arterial disease (PAD) and/or diabetes mellitus (DM) in elderly patients in primary care. Methods: In a monitored prospective cohort study (German epidemiological study on ankle brachial index, getABI), 6,880 unselected patients ≥65 years were followed up by 344 representative primary care physicians in Germany since November 2001. PAD was defined as ankle brachial index (ABI) <0.9 determined with standard Doppler sonography, or intermittent claudication, peripheral revascularisation or amputation due to PAD. DM comprised physician diagnosis, use of antidiabetic medication, or HbA1c > 7%. Results: At baseline, mean age of patients was 72.5 yrs, 58% were females, 46% (ever) smoker, 65% had hypertension, 52% lipid disorders, and 25% DM. The prevalence of PAD in the cohort was 20.8% (distal occlusions not included). Compared to patients without PAD or DM, 5-year mortality in patients with one or both diseases was substantially increased (Table). On multivariate analysis in the Cox model, with adjustment for age, gender and the known cardiovascular risk factors the hazard ratio (HR) for mortality, compared to patients without PAD and DM, was 1.6 [95% confidence interval 1.3–2.0] for patients with PAD alone, 1.6 [1.3–1.9] for patients with DM alone, and 3.0 [2.5–3.7] for patients with PAD + DM. Conclusions: Patients with PAD (as an indicator disease for generalized atherosclerosis) or DM, and particularly those with the two diseases concomitantly, carry a substantially increased risk for all-cause mortality. Our data confirm the necessity to screen for these patients at excess risk in the primary care setting to ensure timely treatment of the atherosclerotic risk factors and the metabolic condition.

INCIDENCE OF ALL-CAUSE DEATH AT 5-YEAR FOLLOW-UP IN PATIENTS WITH (+) OR WITHOUT (-) PAD OR DM

PAD	DM	N	Deaths (n)	Deaths (%)
-	-	4125	349	8.5
-	+	1218	153	12.6
+	-	904	154	17.0
+	+	513	144	28.1

n= 6760 (excluded were patients with missing data on survival or DM status; and patients with ABI >1.5 = media sclerosis)

P350

Ethnic Differences in the Relationship of Segment-Specific Carotid Intima-Media Thickness with Cardiovascular Risk Factors: The Multi-Ethnic Study of Atherosclerosis (MESA)

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Background: Evidence that the association of cardiovascular (CVD) risk factors with intima-media thickness (IMT) differs by carotid segment is mixed. However, few studies have evaluated the associations of CVD risk factors with segment-specific carotid atherosclerosis within various ethnic groups. **Objective and Methods:** We examined the baseline associations of CVD risk factors with mean maximal common (CCA) and internal (ICA) carotid artery IMT within four ethnic groups in a sample of 6479 adults (38% Non-Hispanic Whites, 28% African-Americans, 12% Chinese, 22% Hispanics) without clinical CVD aged 45–84 years from the MESA Study in 2000–02. IMT was assessed by B-mode carotid ultrasound. **Results:** Differences in associations of selected CVD risk factors with CCA and ICA IMT were found within ethnic groups (Table shows selected CVD risk factors for women). In general, higher age and SBP were significant risk factors for both higher CCA and ICA IMT in all ethnic groups except ICA IMT in Chinese. Different patterns of association were seen for smoking, weight, LDL, HDL, and glucose. For example, higher weight was a significant correlate for CCA IMT only (all ethnic groups) while higher LDL was significantly associated with ICA IMT. In men, the patterns of association were similar except that LDL and glucose were significant risk factors for both carotid segments. **Conclusion**: These findings suggest that associations of CVD risk factors with segment-specific carotid atherosclerosis may vary slightly among ethnic groups with higher glucose levels associated mainly with the carotid segments in Hispanics and lower HDL levels and smoking in Non-Hispanic Whites.

β-COEFFICIENTS§ (STANDARD ERRORS) FOR THE ASSOCIATIONS OF SELECTED CVD RISK FACTORS WITH SEGMENT-SPECIFIC CAROTID IMT BY ETHNICITY IN WOMEN

Table of Contents
oVariable

	CCA IMT				ICA IMT			
Variable	Non-Hispanic Whites (N=1307)	Chinese (N=401)	African-Americans (N=984)	Hispanics (N=729)	Non-Hispanic Whites (N=1307)	Chinese (N=401)	African-Americans (N=984)	Hispanics (N=729)
Age	0.08 (0.01) ‡	0.05 (0.01) ‡	0.06 (0.01) ‡	0.06 (0.01) ‡	0.12 (0.01) ‡	-0.004 (0.02)	0.11 (0.02) ‡	0.07 (0.02) ‡
Current Smoking	0.03 (0.01) **	-0.002 (0.05)	-0.03 (0.02)	0.01 (0.02)	0.14 (0.03) ‡	-0.06 (0.27)	0.06 (0.04)	0.08 (0.04) **
Weight	0.01 (0.01) **	0.03 (0.01) †	0.02 (0.01) ‡	0.02 (0.01) **	0.004 (0.01)	-0.01 (0.02)	0.01 (0.02)	-0.004 (0.01)
SBP	0.03 (0.01) ‡	0.02 (0.01) **	0.03 (0.01) ‡	0.02 (0.01) ‡	0.05 (0.01) ‡	0.01 (0.01)	0.06 (0.01) ‡	0.04 (0.02) **
LDL	0.004 (0.01)	0.01 (0.01)	0.01 (0.01)	0.01 (0.01)	0.03 (0.01) ‡	-0.01 (0.01)	0.03 (0.01) **	0.03 (0.01) **
HDL	-0.01 (0.004) ‡	0.002 (0.01)	-0.01 (0.01)	-0.005 (0.01)	-0.03 (0.01) ‡	-0.004 (0.02)	-0.01 (0.01)	0.01 (0.01)
Glucose	0.01 (0.01)	0.02 (0.01)	0.001 (0.01)	0.01 (0.01) **	0.02 (0.02)	0.04 (0.03)	0.01 (0.02)	0.04 (0.02)

§Regression coefficients were expressed for each CVD risk factor higher by one gender-ethnic specific standard deviation. Education, former smoking, and height were also included in the median regression models. **p ≤ 0.05 †p ≤ 0.01 ‡p ≤ 0.001

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P351

Sex Differences in the Risk of Carotid Atherosclerosis in the Elderly: Impact of Lifetime Active-Smoking Exposure. The 3-City Study

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Population-based studies have shown that carotid atheroma at any age is more prevalent in men than in women. The reasons for this gender-related disparity are currently unclear. We investigated the contribution of each of the traditional risk factors of carotid atherosclerosis across genders in a large population-based cross-sectional study of 6519 subjects (3993 women and 2526 men) aged 65 or older and recruited from 3 French cities. Cigarette smoking was assessed by a standardized questionnaire. Ultrasound examination of the extra cranial carotid arteries included assessment of atherosclerotic plaque and measurements (at sites free of plaque) of intima-media thickness (IMT) at the common carotid arteries (CCA). Age, blood pressure, cigarette smoking, cholesterol, body mass index and diabetes were significantly associated with carotid plaque in both men and women. Similar patterns of association were observed with IMT although less pronounced. Smoking exposure (number of pack-years) showed a consistent dose-response relation with carotid plaque ($p<0,001$ for linear trend) in both sexes and it was higher in men than in women. Lifetime smoking accounted for 51% of the gender differences in carotid plaque while other traditional risk factors explained 5% only. Regarding IMT, 12% were explained by tobacco and 4% by the other risk factors. Our study provides evidence that smoking lifetime exposure may account for an important part of the gender differences in carotid atherosclerosis. These findings may have important public health implications in terms of prevention and treatment of ischemic arterial disease.

P352

Menopause Status Modifies the Contribution of Lipid Levels to Subclinical Vascular Disease in SWAN Heart Women

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Lipid levels are known risk factors for cardiovascular disease (CVD). Changes in lipid levels are also associated with the menopausal transition. The way in which the menopausal transition modifies the contribution of HDL and LDL to subclinical CVD is unknown. To evaluate this, aortic calcification (AC), carotid plaque index (PI) and intima media thickness (IMT) were measured in 587 women enrolled in an ancillary study to the Study of Women's Health Across the Nation (SWAN). Women were stratified into two menopause groups; premenopausal or early perimenopausal (Pre/EP) and late perimenopausal or postmenopausal (LP/Post). Multinomial logistic regression was used to analyze AC categorized into zero, low and high AC, comparing high to zero. PI, dichotomized into no plaque and any plaque, was evaluated using binary logistic regression. Linear regression examined associations with the log of IMT. Final models were adjusted for age, race, site and other potential confounders. On average Pre/EP women were 49 years of age and LP/Post women were 52 years of age. LP/Post women had higher HDL and LDL levels compared to Pre/EP women (59 vs. 56 mg/dL, $p = 0.06$ and 127 vs. 114mg/dL, $p < 0.01$). Across all women, HDL was negatively associated with AC, PI and log of IMT while LDL was positively associated in univariate models. In multivariate models, Pre/EP women demonstrated a negative association between HDL levels and AC (OR = 0.97, 95%CI 0.94, 1.00), PI (OR = 0.97, 95%CI 0.94, 1.00) and log of IMT (β = -0.002, 95%CI -0.003, -0.000), however only IMT showed a significant association. In LP/Post women, a positive association between HDL levels and AC (OR = 1.05, 95%CI 1.00, 1.09), PI (OR = 1.01, 95%CI 0.99, 1.04) and log of IMT (β = 0.001, 95%CI -0.000, 0.003) was observed, but was only significant for AC. Interactions were tested in all three outcomes for both HDL and LDL with menopause status. The interaction between menopause status and HDL was statistically significant for AC and log of IMT ($p = 0.01, 0.01$). In conclusion, menopause status modifies the contribution of HDL to subclinical CVD. The protective effects of HDL diminish in LP/Post women compared to Pre/EP women. Future analyses will examine the differential contribution of small and large HDL lipoprotein subclasses to subclinical CVD.

P353

Cross-Sectional Association of Cardiovascular Risk Factors with Subclinical Atherosclerosis in Different Vascular Beds: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Background: Cardiovascular disease (CVD) risk factors are associated with intima-media thickness (IMT) and coronary artery calcium (CAC). However, few studies have compared these associations among both imaging modalities at the same time. **Methods:** We assessed the cross-sectional associations of CVD risk factors with mean maximal IMT (including common and internal carotid arteries) and positive CAC (CAC>0) in a sample of 2905 adults (45% African-Americans, 57% women) aged 38–50 years from the CARDIA Study (yr 20) in 2005–06. Participants were stratified into four groups based on IMT percentiles and prevalence of CAC>0 (CAC+). IMT and CAC were assessed by B-mode carotid ultrasound and computed tomography respectively. Overall, 10% of the women and 28% of the men were CAC+. To make the IMT groups comparable with CAC+ prevalence, we used gender-specific percentiles for IMT (90th in women, 70th in men) (IMT+). **Results:** In this cohort, 71% were IMT-/CAC-, 11% were IMT+/CAC-, 12% were IMT-/ CAC+, and 6% had IMT+/CAC+. Individuals with IMT+/CAC- were significantly older with higher BMI, LDL, and SBP compared to those with IMT-/CAC- in both genders (Table). Women with IMT-/CAC+ and men with IMT+/CAC+ had similar CVD risk factor profile as seen in individuals with IMT+/CAC-. In addition, those with IMT+/CAC+ had significantly higher glucose levels compared to those with IMT-/CAC- or IMT+/CAC-. **Conclusion**: In general, individuals with evidence of subclinical atherosclerosis in two vascular beds have a worse CVD risk profile compared to those with either thicker carotid IMT or positive CAC. #

VARIABLE CARDIA YR 20 PARTICIPANT CHARACTERISTICS BY MEAN MAXIMAL IMT, CAC STATUS AND GENDER (N=2,905)

Women (n=1666) **Mean** (SD)	**IMT-/ CAC- Group¶ (n=1370)**	**IMT+/ CAC- Group¶ (n=127)**	**IMT-/ CAC+ Group¶ (n=144)**	**IMT+/ CAC+ Group¶ (n=25)**
Age (yrs)	45 (3.7)[1,2]	47 (3.2) [1]	46 (3.3) [2]	46 (3.7)
BMI (kg/m^2)	29.0 (7.0) [1,2]	32.4 (7.5) [1]	31.3 (8.3) [2]	29.0 (6.9)
Fasting Glucose (mg/dl)	94.2 (22.2) [3]	96.9 (23.7) [5]	97.4 (24.1)	111.8 (77.1) [3,5]
Current Smokers (%,n)	13 (181) [1,2,3]	24 (31) [1,5]	31 (44) [2,6]	60 (15) [3,5,6]
SBP (mm Hg)	112.4 (15.2) [1,2,3]	120.1 (15.7)[1]	118.4 (16.7)[2]	124.6 (20.9) [3]
LDL (mg/dl)	106.1 (29.9) [1,2]	117.3 (28.6)[1]	118.0 (32.6)[2]	118.9 (47.1)
Men (n=1239) Mean (SD)	**IMT-/ CAC- Group¶ (n=687)**	**IMT+/ CAC- Group¶ (n=202)**	**IMT-/ CAC+ Group¶ (n=211)**	**IMT+/ CAC+ Group¶ (n=139)**
Age (yrs)	44 (3.5) [1,2,3]	46 (3.3) [1,5]	46 (3.6) [2,6]	47 (2.7) [3,5]
BMI (kg/m^2)	27.8 (4.6) [1,3]	29.5 (5.0) [1]	28.8 (5.5) [6]	30.5 (5.4) [3,6]
Current Smokers (%,n)	20 (140) [3]	18 (36) [5]	23 (48) [6]	29 (40) [3,5,6]
Fasting Glucose (mg/ dl)	98.4 (21.2) [3]	100.5 (19.5) [5]	100.1 (21.5)	105.7 (27.4)[3,5]
SBP (mm Hg)	118.2 (11.9) [1,3]	121.9 (15.7) [1]	119.4 (11.5) [6]	123.7 (17.3)[3,6]
LDL (mg/dl)	110.0 (32.4) [1,3]	120.6 (32.3) [1]	114.1 (36.6)	120.7 (35.3) [3]

¶ IMT- defined as: **Women**: < than the 90th percentile **Men**: < than the 70th percentile IMT + defined as: **Women**: ≥ than the 90th percentile **Men**: ≥ than the 70th percentile Scheffe Pairwise 1- **IMT-/CAC-** vs. **IMT+/CAC-** group 2- **IMT-/CAC-** vs. **IMT-/CAC+** group Comparisons 3- **IMT-/CAC-** vs. **IMT+/CAC+** group 4- **IMT+/CAC-** vs. **IMT-/CAC+** group ($p < 0.05$) 5- **IMT+/CAC-** vs. **IMT+/CAC+** group 6- **IMT-/CAC+** vs. **IMT+/CAC+** group

P354

Various Approaches to Measure Carotid Intima-Media Thickness in Clinical Trials: What Is the Best Protocol?

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Background: Ultrasound protocols to measure CIMT differ considerably in number of carotid segments, angles and walls measured. High reproducibility, high ratio between progression rates and precision and high ratio between treatment effect and its precision are key requirements. We studied these aspects across various ultrasound protocols with data from the Osteoporosis Prevention and Arterial effects of tiboLone (OPAL) study, a randomized controlled trial among 866 healthy postmenopausal women. Methods: In the OPAL-study CIMT information was collected from 3 segments (common carotid, bifurcation and internal carotid artery), 5 angles, near wall and far wall of the left and right carotid artery. Based on all measurements, we built 66 different ultrasound protocols to estimate a CIMT for each individual. In the OPAL study ultrasound examinations were performed in duplicate at start of the study and at end of the study 3 years later. For each protocol we assessed reproducibility (intra-class correlation(ICC), mean and mean absolute difference of the duplicate scan), 3-year progressionrate and relation with blood pressure. Results: Of 675 women CIMT information was available from both baseline and end of study visits. The ICC obtained from duplicate baseline examinations ranged from 0.59 to 0.84 between the CIMT ultrasound protocols. The CIMT progression rates ranged from -0.85 μm/yr to 12.71 μm/yr. The variance in systolic blood pressure distribution explained by CIMT measurements ranged from 6 % to 12 % Overall, multiple-segment and multiple-angle approaches showed highest reproducibility, best balance between magnitude of CIMT progression and its corresponding precision and strongest riskfactor relation with systolic blood pressure. Conclusion: In a population of healthy post menopausal women, multiple-segment and multiple-angle ultrasound protocol to measure CIMT perform better than single segment and single angle CIMT protocols.

P355

Independent Predictors of Death Among Patients with Newly Diagnosed Atrial Flutter: A Population-Based Study from the Marshfield Epidemiologic Study Area

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BACKGROUND: Second only to atrial fibrillation (Afib), atrial flutter (Afltr) is the cardiac rhythm disturbance most frequently encountered in clinical practice. Scant epidemiologic data regarding its clinical course limits the use of radiofrequency ablation (RFA) predominantly to

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patients with symptomatic disease, as opposed to those at highest risk of adverse outcomes. The purpose of this study was to identify independent predictors of death among patients with newly diagnosed Afltr in a general population. METHODS: The Marshfield Epidemiologic Study Area (MESA), a database that captures nearly all medical care among its 58,820 residents was used to ascertain all new cases of Afltr diagnosed in the region from 7/1/91 to 6/30/95. Eleven pre-existing risk factors of potential prognostic significance in Afltr were evaluated including age, gender, concurrent Afib, stroke, myocardial infarction, heart failure (CHF), hypertension, rheumatic heart disease, hyperlipidemia, COPD, diabetes and thyroid abnormality. Multivariate Cox models were fitted to obtain hazard ratios (HR) and 95% confidence intervals (CI). RESULTS: During the 1,329 person-years of follow-up (mean duration 7.3 years), 134 (74%) of the 181 incident cases of Afltr died. At increased risk of death were those with advancing age (HR 1.06, 95% CI 1.04–1.08; P < 0.0001), CHF (HR 1.88, 95% CI, 1.21–2.91; P = 0.005), and COPD (HR 1.85, 95% CI 1.23–2.80; P = 0.003). Hyperlipidemia (HR 0.60, 95% CI 0.41–0.88; P = 0.009) and Afltr without coexisting Afib (HR 0.65, 95% CI 0.46–0.94; P = 0.020) were associated with a decreased mortality risk. In a subset analysis of those with Afltr without coexisting Afib, independent predictors of increased mortality were advancing age (HR 1.06, 95% CI, 1.02–1.09; P = 0.0012), CHF (HR 3.06, 95% CI, 1.52–6.19; P = 0.0018), and COPD (HR 2.97, 95% CI 1.46–6.05; P = 0.003). CONCLUSIONS: 1) This study represents the first report of independent predictors of death among patients with newly diagnosed Afltr in a general population. 2) Our data suggest advancing age, CHF, COPD and concurrent Afib are all associated with an increased mortality risk. 3) Further research is needed to determine the optimal utilization of RFA as a curative technique in Afltr.

P356

High Prevalence of Peripheral Arterial Disease in Asymptomatic US Adults Aged ≥40 with the Metabolic Syndrome: Results from the National Health and Nutrition Examination Survey, 1999–2004

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Background: Peripheral arterial disease (PAD) is a subclinical marker of coronary artery disease and identifies asymptomatic individuals at high risk for future cardiovascular disease (CVD) events. The Metabolic syndrome (MetSyn) is a constellation of clinical factors the presence of which increases the risk of developing diabetes and CVD. The goal of this study was to determine the prevalence of MetSyn in the population of asymptomatic U.S adult population with PAD. Methods: We analyzed data from three National Health and Nutrition Examination Surveys (NHANES) between the years 1999–2004. The prevalence of the MetSyn as defined by ATP III criteria and the prevalence of associated cardiac risk factors was determined in 5,376 asymptomatic participants aged 40 years and older. The presence of PAD was defined as an ankle-brachial index < 0.9. All estimates were weighted with the sample weights accounting for the unequal selection probability of the complex NHANES sampling and the over sampling of selected population subgroups. Results: The prevalence of the PAD in asymptomatic US adults age 40 and older was 4.2%. Thirty eight percent of the population with PAD also had MetSyn. An individual with MetSyn is twice as likely to also have PAD (OR=2.20, 95% CI: 2.15 - 2.22). The remarkably high rates of abdominal obesity, hypertension and HDL cholesterol are significant contributors to both the MetSyn and PAD.

	PAD (-)		PAD (+)			
NHANES Survey	1999–2000	2001–2002	2003–2004	1999–2000	2001–2002	2003–2004
MetSyn	22.9%	20.8%	23.3%	38.3%	39.3%	31.4%
[1]Abdominal Obesity Male Female	52.3%	52.9%	60.1%	53.6%	64.4%	72.7%
	42.6%	45.1%	53.6%	29.3%	58.9%	46.6%
	61.1%	60.6%	66.5%	71.5%	67.3%	84.4%
[2]Hypertension	55.1%	60.2%	43.0%	63.6%	69.4%	68.2%
Triglycerides > 150 mg/dl	46.0%	43.3%	46.9%	54.2%	50.2%	65.5%
HDL cholesterol < 40 mg/dl (male)	34.3%	29.3%	25.3%	45.6%	34.9%	37.8%
< 50 mg/dl (female)	32.6%	29.8%	24.7%	33.4%	42.4%	26.3%
	35.8%	28.8%	25.8%	54.6%	30.6%	42.7%
[3]Fasting glucose	16.0%	19.3%	18.2%	33.2%	33.9%	33.8%

[1]Abdominal obesity: Waist circumference ≥ 102 cm (male) or ≥ 88 cm (female) [2]Hypertension: Blood pressure 130/85 or treatment for hypertension [3]Fasting plasma glucose > 110 mg/dl Conclusions: This data provides a nationally representative sample of PAD prevalence stratified by MetSyn. Persons with the MetSyn have a twofold increase risk of having PAD. Of those persons with PAD, almost 40% have MetSyn. The presence of either PAD or the MetSyn should warrant screening for both conditions and aggressive treatment of the factors contributing to the metabolic syndrome.

P357

Long-Term Prognosis for Men with Claudicatio Intermittens Is Much Poorer than for Men with AMI or Stroke

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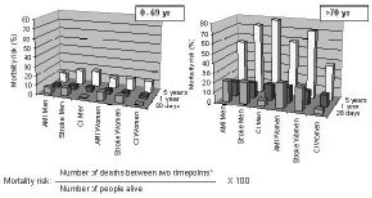
Objective Comparison of mortality risk of patients after a first hospital admission with the diagnosis of acute myocardial infarction (AMI), stroke or claudicatio intermittens (CI) by age group (0–69 yr and >70 yr) and gender. **Methods** Three nationwide cohorts (first hospitalized AMI patients, stroke patients, CI patients) were identified through linkage of the national hospital discharge register and the Dutch population register. Patients were followed through linkage of the Dutch population register and the Dutch cause of death register. Follow-up for mortality lasted 5 years. **Results** The AMI cohort, stroke cohort and CI cohort consisted of 21.656, 17.031 and 2.534 patients, respectively. Details about the different groups and their mortality risks at 28 days, 1 year and 5 years are presented in table 1 and figure 1. **Conclusion:** Patients who survive the first 28 days after their hospital admission have a 'relative' low mortality risk after one year, however those patients who are still alive after one year have a dramatically increased mortality risk after 5 years, especially male CI patients.

Figure 1: Mortality risk (%) at 28 days, 1 year and 5 years after a first hospital admission with the diagnosis of acute myocardial infarction (AMI), Stroke or Claudicatio Intermittens (CI), by gender and age group (0-69 yr, >70 yr). In The Netherlands



Mortality risk: $\frac{\text{Number of deaths between two timepoints*}}{\text{Number of people alive}} \times 100$

*The number of deaths between: timepoint 0 (hospital admission) and timepoint 28 days, timepoint day 28 and timepoint 1 year, timepoint 1 year and timepoint 5 years

Table 1: Baseline characteristics of patients after a first hospital admission with the diagnosis of acute myocardial infarction (AMI), Stroke or Claudicatio Intermittens (CI), by gender and age group (0-69 yr, >70 yr).

	AMI				Stroke				CI			
	0-69 yr		>70 yr		0-69 yr		>70 yr		0-65 yr		>70 yr	
	M	W	M	W	M	W	M	W	M	W	M	W
N	9.365	2.726	5.898	4.376	4.129	2.557	4.571	5.774	914	474	638	508
Age (yr)	57	60	77	79	59	57	78	81	59	56	77	78
Number of deaths during follow-up	1.825	603	3.044	2.675	1.251	658	3.366	4.159	257	91	406	281

P358

The Impact of Warfarin Therapy in Elderly Atrial Fibrillation Patients with No Additional Stroke Risk Factors: The ATRIA Study

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Background: The risk of stroke increases with age in patients with atrial fibrillation (AF). However, guidelines allow aspirin, instead of warfarin, therapy for AF patients > 75 years with no other stroke risk factors (RF). We explored stroke risk and warfarin effect in ATRIA cohort AF patients age 75–84 and 85+ years without other stroke risk factors to assess the validity of AF guidelines for the elderly. **Methods:** The ATRIA cohort consists of 13,559 patients with nonvalvular AF enrolled in Kaiser Permanente of Northern California (1996–2003). Warfarin exposure was determined using validated algorithms based on prescriptions and international normalized ratio tests. Patient characteristics and thromboembolism (TE) events (ischemic stroke and systemic embolism) were ascertained from health plan databases. TE were validated by chart review. We include diabetes mellitus, hypertension, heart failure and history of prior stroke as other RF for stroke. **Results:** At baseline, 4330 ATRIA patients had no stroke RF other than AF. These patients accumulated 15,999 person years (PY) of follow up with no RF: 9,763 PY off warfarin and 6,236 PY on warfarin. Annual event rates for age <75 were very similar on warfarin (0.38%; 95% CI: 0.23%–0.66%) versus off warfarin (0.37%; 95% CI: 0.25%–0.57%). However, those age 75–84 with no RF, were almost 3 times more likely to have an event off warfarin (1.41%, 95% CI: 1.02%–1.96%) as on warfarin (0.53%; 95% CI: 0.30%–0.95%), p=0.004. Among the small group of patients (n=643) who contributed to age >=85 with no RF, the annual TE rate off warfarin increased to 3.31% (95% CI: 2.35–4.68%) and was 0.86% (95% CI: 0.35–2.40%) on warfarin, p=0.01, reflecting a greater absolute warfarin effect in these oldest AF patients. **Conclusions:** Risk of TE among AF patients increases with age, even among those without other RFs. While the expected absolute benefit of warfarin is small in AF patients age 75–84 years with no other RFs, the absolute benefit in those >=85 years (with no other RFs) is large enough for guidelines to recommend warfarin for this small but growing age group. AF risk schemes need to account for the high risk of stroke faced by the oldest old.

P359

Cerebrovascular Disease Incidence, Characteristics, and Outcomes in Patients Initiating Dialysis: The Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study

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Background: Stroke is the third leading cause of death for patients on dialysis; however, stroke has not been well characterized in this population. **Methods:** We explored cerebrovascular disease event (CVE) characteristics among an incident dialysis cohort of 1,041 patients enrolled from 10/95 to 7/98 in the CHOICE study and followed a median of 2.9 years. CVEs were defined as both nonfatal (hospitalized stroke, carotid endarterectomy) and fatal (stroke death) events after dialysis initiation. Participants were censored for transplant, death, or on 12/31/04. Stroke subtypes were abstracted from medical records by two abstractors using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification system. Cox proportional hazard regression analysis was used to assess the risk of death after CVE compared to other atherosclerotic vascular disease (ASCVD). **Results:** A total of 163 participants experienced a CVE with an overall incidence of 4.6 per 100 person-years; 112 events from 98 of these participants were available for chart abstraction. The median time from onset of symptoms to first evaluation was 10 hours (IQR 1–42 hours). All subtypes of stroke were common, with cardioaortic embolism being the most common (Table). In time to event analyses from dialysis initiation, multiple etiologies, small artery occlusion, and hemorrhagic stroke had the longest time until onset (p=0.02 for this group vs rest of subtypes), suggesting CVE etiology may change over time. Compared to other ASCVD, CVE was a significant risk factor for death with a hazard ratio of 1.45 (95% CI [1.13–1.84], p=0.004). **Conclusions:** All types of CVEs are common in dialysis patients, and cerebrovascular disease carries a significant risk of mortality.

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Further studies are needed to understand the prevention and treatment of cerebrovascular disease in patients with ESRD.

CVE SUBTYPE CHARACTERISTICS IN INCIDENT DIALYSIS PATIENTS

CVE Subtype	Number of Events	Median Time in Months to CVE Subtype (IQR)
Ischemic Stroke	91	
Large Artery Atherosclerosis	9	12.4 (6.3–20.1)
Cardioaortic Embolism	26	16.8 (9.5–31.1)
Small Artery Occlusion	18	**27.3 (10.8–38.8)***
Multiple Ischemic Etiologies	17	**24.5 (17.7–33.1)***
Other/Unknown	21	15.2 (8.1–23.6)
Carotid Endarterectomy	11	10.5 (4.6–26.3)
Hemorrhagic Stroke	10	**30.1 (5.6–34.9)***
Total Events	112	17.8 (8.2–33.2)

*p=0.02 vs rest of subtypes

P360

Fasting Serum Glucose Level and Risk of Stroke Subtypes: Korea Medical Insurance Corporation Study

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Objective: Diabetes is a well-known risk factor for cardiovascular disease. However, the blood glucose levels below diabetic range are not fully studied in relation with the risk of stroke subtypes in general population. We investigated the relation between fasting serum glucose levels and the incidence of stroke subtypes in Korean men. **Methods:** We measured fasting serum glucose levels and other cardiovascular risk factors in 100,144 men without any diagnosed disease, aged 35–59 years in 1990 and 1992. Our primary outcomes were hospital admissions and deaths from stroke in 11 year follow-up from 1993 to 2003. Using the Cox proportional hazard model, we estimated the hazard ratios of stroke according to the baseline fasting serum glucose level, after adjustment for age, body mass index, blood pressure, total cholesterol level, cigarette smoking and alcohol consumption. **Results:** During the 11 years, 2,984 stroke events occurred. Relative risk of stroke was increased from impaired fasting glucose level (110–125mg/dL). In the analysis of stroke subtypes, the association of fasting serum glucose ≥110 mg/dL with increased relative risk of stroke was observed only in ischemic stroke, but not in hemorrhagic stroke. Neither intracerebral hemorrhage nor subarachnoid hemorrhage was associated with fasting serum glucose level. **Conclusions:** Risk of stroke was increased from impaired fasting glucose level (110–125mg/dL) in Korean men. The association of fasting glucose levels ≥110mg/dL with stroke was ascribed to increased occurrence of ischemic stroke.

HAZARD RATIOS(HRS) FOR STROKE SUBTYPES BY FASTING SER UM GLUCOSE LEVELS IN 100,144 MEN

	All Stroke		Ischemic Stroke		Intrac		Subar	
Fasting Glucose (mg/dL)	No. of events	HR* (95% CI)	No. of events	HR* (95% CI)	No. of events	HR* (95% CI)	No. of events	HR* (95% CI)
< 80	400	1.00	231	1.00	88	1.00	44	1.00
80–89	902	1.01 (0.90–1.14)	512	0.99 (0.85–1.16)	210	1.07 (0.83–1.37)	70	0.75 (0.51–1.09)
90–99	826	1.01 (0.90–1.14)	465	0.98 (0.83–1.15)	197	1.07 (0.83–1.37)	66	0.82 (0.56–1.20)
100–109	392	1.01 (0.87–1.16)	222	0.98 (0.81–1.18)	100	1.10 (0.82–1.47)	25	0.69 (0.42–1.14)
110–125	220	1.21 (1.03–1.43)	134	1.26 (1.02–1.57)	54	1.26 (0.89–1.77)	7	0.45 (0.20–1.00)
≥ 126	244	1.83 (1.56–2.15)	174	2.19 (1.79–2.67)	41	1.33 (0.91–1.94)	10	0.95 (0.47–1.91)
All	2,984-	1,738-	690	222	-			

*Adjusted for age, body mass index, blood pressure, total cholesterol, cigarette smoking and alcohol consumption.

P361

Tooth Loss, Systemic Inflammation, and Prevalent Stroke Among Participants in the Reasons for Geographic and Racial Difference in Stroke Study

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Background: Periodontal disease results in tooth loss and systemic inflammation and pathogenesis of atherosclerosis. Thus, regional and racial differences in periodontal disease may contribute to corresponding disparities in stroke. We examined associations of tooth loss with inflammation markers, region of residence, race and stroke status in the REasons for Geographic And Racial Differences in Stroke (REGARDS) Study. **Methods:** We studied 22175 participants enrolled between January 2003 and May 2007. REGARDS is a national cohort of whites and blacks ≥45 years. Linear regression was used to examine associations between tooth loss due to tooth decay or gum disease (categorized as none, 1–16 or 17–32 teeth lost) and the inflammatory markers C-reactive protein (CRP) and white blood cell count (WBC). Logistic regression was used to examine associations between tooth loss and stroke status. **Results:** 85.7%, 7.7%, and 6.5% of the participants had none, 1–16, and 17–32 teeth lost, respectively. Tooth loss was more common in the stroke belt and in participants who were black, older, female, had lower socioeconomic status, were past or current smokers, and had prevalent CHD, stroke/TIA, diabetes, hyperlipidemia, and hypertension. In multivariable analysis the odds ratio (OR) of having a higher category of tooth loss for blacks compared with whites was 1.5 (95% CI: 1.4–1.7), but geographic differences in tooth loss were attenuated ($p > 0.05$). Compared to those with no tooth loss, in those with 17–32 teeth lost CRP was 1.15 g/dL higher ($p<0.0001$), WBC was 0.138×10^9/L higher ($p=0.05$). Those with 17–32 teeth lost had a 1.3-fold increased odds of prevalent stroke (95% CI: 1.1–1.7) than those with no tooth loss, but there was no increased risk among those with 1–16 teeth lost. The odds of prevalent stroke by tooth loss were identical after adjustment for either CRP or WBC. **Conclusions:** Tooth loss, as a measure of periodontal disease, was more common in blacks than whites and was associated with inflammation markers and stroke status. Disparities in periodontal disease may contribute to racial, but not geographic, disparities in stroke. These data suggest that inflammation may not mediate the association of periodontal disease with stroke, but longitudinal data are needed.

P362

Prospective Study of Cardiac Arrhythmias and Risk of Stroke Among Japanese

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Background and Purpose: With the exception of atrial fibrillation, the association between cardiac arrhythmias and stroke incidence has not been well elucidated. We sought to examine the association of atrial and ventricular arrhythmias with the incidence of stroke among Japanese men and women. **Methods**: A 20.9-year prospective study was conducted with 10,211 men and women aged 40 to 69 years and free of clinical cardiovascular disease or major electrocardiogram abnormalities (atrial fibrillation, major ST-T abnormalities, etc.) in 4 Japanese communities. Electrocardiograms were taken at baseline. The incidence of stroke was ascertained using systematic surveillance. **Results**: The prevalence of cardiac (atrial and ventricular) arrhythmias in men and women was 5.5 % (n=224) and 5.5% (n=338), respectively. During the 20.9-year follow-up, 749 strokes (358 non-cardioembolic ischemic strokes, 74 cardioembolic strokes, 235 hemorrhagic strokes, and 82 unclassified strokes) occurred. Men with a high frequency of cardiac arrhythmias (≥10% of total beats) had a 2-fold higher age-adjusted rate ratio (RR) of total stroke than did those without cardiac arrhythmias. After we adjusted for confounding variables (age, alcohol intake, smoking status, body mass index, cholesterol levels, hypertension category, and diabetes status), the RR for cardiac arrhythmias was reduced to 1.81 (95% CI, 1.11 to 2.94) but remained statistically significant ($p=0.02$). The associations of cardiac arrhythmias with stroke incidence were confined to cardioembolic and hemorrhagic strokes. The multivariate-adjusted RRs for non-cardioembolic ischemic strokes, cardioembolic strokes, and hemorrhagic strokes were 1.41 (95% CI, 0.71 to 2.79), 3.95 (95% CI, 1.13 to 13.7), and 2.59 (95% CI, 1.10 to 6.06), respectively. For women, however, there was no association of cardiac arrhythmias with stroke incidence. **Conclusions**: A high frequency of cardiac arrhythmias has predictive value for the risk of total stroke, especially cardioembolic and hemorrhagic strokes, among middle-aged Japanese men.

P363

A Prospective Study of Elevated Plasma Homocysteine and Risk of Recurrent Stroke Among Patients with Ischemic and Hemorrhagic Stroke

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Background and objective: Observational studies have demonstrated that elevated levels of plasma homocysteine independently increase risk of stroke, but its relevance to recurrent episodes among patients with ischemic or hemorrhagic stroke remains uncertain. We, therefore, assessed the relation of plasma homocysteine levels and methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism to risk of stroke recurrence among patients with stroke. **Methods:** The Multicenter Chinese Stroke Study, a longitudinal cohort of 1823 stroke patients (807 cerebral atherothrombosis, 513 lacunar infarction, and 503 intracerebral hemorrhage) who were followed for a median of 4.5 years. Total plasma homocysteine was determined by high-performance liquid chromatography, and C677T polymorphism was genotyped. **Results:** During follow-up (median, 4.5 years), 347 recurrent strokes and 323 deaths for all causes were recorded. Patients in the highest quartile of homocysteine levels had a significantly higher risk of recurrent strokes or mortality than those in the bottom quartile in Cox proportional-hazards models adjusted for conventional risk factors. Among thrombotic stroke patients, the multivariate relative risk (RR) was 2.07 (95% confidence interval [CI], 1.3–3.3) for recurrence and 1.82 (95% CI, 1.2–2.9) for mortality; among hemorrhagic stroke patients, the multivariate RR was 1.78 (95% CI, 1.1–3.0) for recurrence and 2.02(95% CI, 1.1–3.6) for mortality. Further, spline linearity analyses demonstrated a threshold level at 16 μmol/L. By dichotomized homocysteine levels, the multivariate RRs for stroke patients with ≥16 μmol/L compared with those with <16 μmol/L were 1.31 (95% CI, 1.10–1.61) for stroke recurrence and 1.47 (95% CI, 1.15–1.88) for mortality. The positive association between

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homocysteine and stroke recurrence or mortality was not significantly modified by MTHFR polymorphism. No significant association was found between MTHFR 677TT genotype and risk of stroke recurrence or mortality. **Conclusion:** Our findings suggest that moderately elevated homocysteine levels (≥16 μmol/L) are independently associated with increased risk of stroke recurrence or mortality among patients with stroke irrespective of MTHFR C677T polymorphism.

P364

Differential Association of Increased Serum Leptin Level with History of Coronary Heart Disease and Stroke: Jackson Heart Study

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Background: Leptin, an important adipose tissue-derived hormone, has been linked to cardiovascular diseases associated with obesity. However, data are limited in the African American populations. In this study, we assessed the association of increased leptin level with history of stroke and coronary heart diseases (CHD) in the Jackson Heart Study cohort. **Methods:** We analyzed data from 5302 participants aged ≥ 21 years who underwent a baseline exam with measurement of serum leptin and cardiovascular risk factors during 2000–2004. Odds ratios (OR) of prevalent stroke, CHD and combined stroke with CHD (Stroke/CHD) were calculated for sex-specific leptin quartiles using logistic regression model and adjusted for age, blood pressure, BMI and waist circumference. Data are presented as sex-stratified analyses **Results:** BMI and waist circumference (WC) are highly correlated with serum leptin levels (r = 0.7 for BMI and WC). The prevalence of stroke, CHD and stroke/CHD was 3%, 4% and 0.7% in women, and 2%, 3% and 0.6% in men, respectively. In multivariate analysis stratified by sex, high leptin level (highest quartile versus lowest quartile) was significantly associated with stroke (OR = 1.8 95% CI 1.1–2.9) in women even after adjustment for age, blood pressure and BMI. However in men, high leptin level was significantly associated with CHD (OR = 1.6 95% CI 1.02–2.43) after adjustment for age. **Conclusion:** Increased serum leptin concentration may be a significant risk marker for cerebrovascular disease in women and for coronary heart diseases in men. These associations, especially in women, are independent of traditional cardiovascular risk factors.

P365

Is Obesity a Risk Factor for Venous Disorders? Results of a Multifactorial Polytomic Regression Analysis of 15,743 Patients with Venous Disorders

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Aim: Identification of a possible independent effect of the BMI on the international CEAP classification of patients consulting for venous disorders. **Methods**: Application of the statistical data mining techniques to a large data warehouse devoted to venous disorders and their treatment and containing thousands of standardized observations issued from clinical trials as well as from observational studies. Use of a new polytomic logistic model able to analyse multifactorial effects on a polytomic variable such as CEAP with 6 classification levels in contrast to existing classic logistic model which requires to reduce artificially these 6 levels of answer to a dichotomic answers like varicose or not. **Results**: Among the 15.743 patients included in the study, 87,0% were female, patients were classified in C0s (symptomatic with no physical signs): 70.3%, C1(telangiectasis): 21.0%, C2 (varicose veins): 24.3%, C3 (Edema): 33.2%, C4 (skin changes): 11.1%, C5 (Healed venous ulcer): 2.2% and C6 (active venous ulcer): 1.1%. Age distribution: 19.8% were ≤35 years old, 24.2%]35–45], 24.9%]45–55], 16.1%]55–65], 15.1% >65. According to the BMI, 31,8% were overweight ([25<BMI<30[) and12,0% obese (BMI ≥30). Univariate analysis shows that CEAP classification level significantly increases with BMI as well in male as in female patients and after age adjustment. Polytomic regression including age, sex, family history of venous disease and BMI confirms the independent role of each of these four elements on the level of CEAP classification. Odds ratio are respectively 3,3 and 1,75 for obesity and overweight for all patients. A high Odds ratio of 3.5 respectively 1.9 was found for women, so for males being 2.6 respectively 1.4. These results suggest that many studies probably have not identified the link between BMI and venous disorders by male due to a too small sample size. For the stronger link in women the conjunction of BMI and sexual hormone could be discussed. **Conclusion:** Overweight and obesity appear, - as well in male as in female patients, to be a promoting factor of venous disorders inducing their quicker evolution to the high level of CEAP classification (C4-C6) and thus independently of the other well known risk factors such as age and family history.

P366

Soluble Endothelial Protein C Receptor, A3 Haplotype of the EPCR Gene, and Risk of Venous Thromboembolism in the LITE Study

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BACKGROUND The endothelial protein C receptor (EPCR) is involved in the protein C system, an anticoagulation system that operates to inactivate factors V and VIII to reduce thrombin formation. Prior case-control studies reported that levels of the soluble form EPCR (sEPCR) were strongly controlled by the A3 haplotype of EPCR and higher levels were a risk factor for venous thromboembolism (VTE). However, no prospective study exists on this association. We conducted a nested case-control study to examine the association of prospectively-measured sEPCR and A3 haplotype with incident VTE. Our hypothesis was that sEPCR and the A3 haplotype would be positively associated with incident VTE. **METHODS** LITE pooled data from CHS (with 10 years of follow-up) and ARIC (with 13 years of follow-up) on men and women aged ≥45. A nested case-control study was done excluding those taking warfarin at baseline, those without valid data for sEPCR or A3 haplotype, or without DNA consent. Controls were matched on age, sex, race, cohort, and follow-up time. There were 458 cases and 1,038 controls for sEPCR analysis and 496 cases and 1,016 controls for haplotype analysis. The odds ratios and 95% confidence interval (OR [95%CI]) for VTE were calculated according to quartiles of sEPCR and the A3 haplotype using unconditional logistic regression. **RESULTS** sEPCR levels were distributed trimodally according to A3 haplotypes. After adjustment for age, sex and race, no overall association was observed between sEPCR level and VTE (OR for highest vs lowest quartile =1.17 [0.86–1.59]). There were modest positive associations of sEPCR level with VTE in non-whites (OR =1.84 [1.05–3.22], p for interaction =0.07) and women (OR =1.51 [1.01–2.26], p for interaction =0.08). Further adjustment for body mass index, prevalence of diabetes and ABO blood type slightly attenuated these associations. The A3 haplotype was not associated with VTE risk (OR =0.93 [0.70–1.25]). **CONCLUSIONS** Contrary to our hypothesis, sEPCR and A3 haplotype were not associated overall with increased risk of VTE, although there was some evidence of an association in non-whites and women. At best, sEPCR seems to be only a weak risk factor for VTE.

P367

Metabolic Syndrome and Risk of Venous Thromboembolism: The LITE Study

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Background: In a recent case-control study, prevalence of the metabolic syndrome (MetSyn) was almost 2 times more likely in deep vein thrombosis cases than controls. Given the limitations of cross-sectional studies, we tested the hypothesis that the incidence of venous thromboembolism (VTE) is higher among adults with the MetSyn compared to those without MetSyn and further, that associations are stronger for idiopathic than other non-cancer related VTE. **Methods:** 21,688 middle-aged and elderly adults were followed for over 12 years for incident VTE in the Longitudinal Study of Thromboembolism Etiology (LITE). All hospitalizations were identified and VTEs were validated by chart review. Baseline MetSyn was defined according to the ATP3 guidelines including ≥3 of the following components: abdominal obesity, elevated blood pressure, low HDL-cholesterol, high triglycerides, and high glucose. Cox proportional hazards regression analyses assessed the relations of the MetSyn and each of the MetSyn components with risk of VTE, adjusting for potential confounders. Incident VTE included 195 idiopathic and 358 other non-cancer related VTE events. **Results:** In the table model 1, MetSyn (≥3 components) did not predict incident non-cancer related VTE, but abdominal obesity did (model 2). In parallel, no relation was observed between the metabolic syndrome and incident idiopathic VTE, but abdominal obesity was significantly related to increased idiopathic VTE risk (HR 1.80; 95% CI 1.29, 2.50). Lipid medication use did not affect study findings. **Conclusion:** Metabolic syndrome was unrelated to incident VTE in middle-aged and elderly adults, but abdominal obesity, one of its components, predicted greater risk of both idiopathic and other non-cancer related incident VTE.

HR (95% CI) OF VTE INCIDENCE (N=358) WITH METABOLIC SYNDROME AND ITS COMPONENTS*

MetSyn Component	Hazard Ratio	95% CI
Model 1: MetSyn (≥3 components)	1.10	(0.88,1.38)
Model 2		
Abdominal obesity	1.66	(1.30,2.11)
Elevated blood pressure	1.19	(0.93,1.52)
Low HLD-c	0.95	(0.74,1.22)
High triglycerides	0.80	(0.61,1.04)
High glucose	1.01	(0.78,1.30)

*Adjusted for age, gender, race, field center, education, and factors VIIc and VIIIc

P368

High-Density Lipoprotein Cholesterol and Venous Thromboembolism in the Longitudinal Investigation of Thromboembolism Etiology

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Venous thromboembolism (VTE), comprising deep vein thrombosis and pulmonary embolism, affects approximately 1 per 1000 individuals annually. Most atheroslcerosis risk factors do not increase risk of VTE; however, the relationship between high-density lipoprotein cholesterol (HDL-c) and VTE is controversial. We determined prospectively the risk of VTE in relation to baseline HDL-c levels, subfractions of HDL (HDL_2 and HDL_3) and apolipoprotein A-I (apoA-I) level, in the Longitudinal Investigation of Thromboembolism Etiology (LITE). The LITE pooled the Atherosclerosis Risk in Communities (ARIC) study and the Cardiovascular Health Study (CHS). After excluding participants who were not of white or black race, who had prevalent VTE at baseline, or who were taking warfarin at baseline, 20,828 participants were at risk for VTE. VTE events were assessed through annual or bi-annual participant contact, hospital surveillance and record searches, and were validated by medical record review. Incident VTE was defined as the first occurrence of validated deep vein thrombosis or pulmonary embolism from baseline through December 31, 2001. There were 199 and 244 VTE events in men and women, respectively. Age-adjusted incidence rates of VTE by HDL-c quartile ranged from 1.71 to 1.99 per 1000 person-years in men and 1.41 to 2.00 per 1000 person-years in women; however, there was no apparent trend of VTE incidence rates across HDL-c quartiles for either sex. Multivariate adjusted hazard ratios of VTE by HDL-c quartile (with quartile 4 as the referent

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group) ranged between 0.91 and 0.99 for men and 0.80 and 1.23 for women, but all confidence intervals included 1.0 for both genders. Hazard ratios for idiopathic and secondary VTE in both sexes were also very close to 1.0 with confidence intervals overlapping 1.0. Likewise, there was no association between HDL-c and VTE for ARIC and CHS analyzed separately. In the ARIC study, there was no trend of increased VTE risk across quartiles of HDL_2, HDL_3, or apoA-I, and all hazard ratios for both men and women were also nonsignificant. Low levels of HDL-c, HDL subfractions, and apoA-I did not increase the risk of VTE in this population.

P369

Vascular Disease Burden and Risk of Cardiovascular Events in Older Community Dwellers

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Older adults with minimal vascular disease have a high level of function and may have unique characteristics and longevity. Previous composite measures of subclinical disease defined high risk, but did not distinguish between low and modest levels of disease. We developed a new composite vascular burden index and assessed whether it could more fully define the spectrum from low to high risk. This index was based on non-invasive measures from the 1992–93 exam of the Cardiovascular Health Study (ankle-arm index, ECG, common carotid intima-media thickness, abdominal aortic aneurysms and MRI brain infarcts). For each measure, a score of 0, 1 or 2 (no, mild or severe abnormalities) was assigned based on clinical cut-offs for normal, intermediate and high values. Summing of the individual scores, we obtained the index (range 0–10, absent to severe disease). Incident cardiovascular events (MI, angina, stroke, TIA, peripheral arterial disease or cardiovascular death) were identified through July 2003. Excluding people with history of clinical cardiovascular disease, 2394 participants (age 74.3±4.9, mean±SD, 62.1% women, 15.2% African-Americans) had complete data. The index was skewed to low values (Table). Event rates increased across index grades. Compared with the absence of vascular disease (grade=0) and adjusted for age, sex and race, each grade of vascular disease, even low, was associated with a significantly higher risk of incident cardiovascular events. In summary, the vascular burden varied widely, identifying very low to high risk. Such an approach may be useful for more fully accounting for vascular burden in clinical studies and identifying exceptionally low disease risk.

Vascular IndexGrades	N	N Events	Rate/ 100 p-y	Adjusted Hazard Ratio(95% Confidence Interval)
0	164	47	3.0	referent
1	541	209	4.4	1.4 (1.1–1.9)
2	585	299	6.4	2.0 (1.5–2.7)
3	562	342	8.4	2.5 (1.9–3.4)
4	284	179	8.9	2.4 (1.7–3.3)
5	157	117	12.6	3.6 (2.5–5.1)
6	67	55	16.9	4.3 (2.9–6.5)
7+	34	32	25.3	7.0 (4.4–11.1)

Test for trend, p<0.001

P370

Age-Related Differences in Costs and Effectiveness of Coronary Computed Tomographic Angiography Using Medicare Category III Transaction Codes (T-Codes): A Matched Comparison to Myocardial Perfusion SPECT

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Background: Coronary computed tomography angiography (CCT) identifies coronary artery disease (CAD) by visualization of coronary plaque, while myocardial perfusion imaging (MPI) identifies CAD by assessment of myocardial perfusion defects. To date, no cost effective analysis has been done comparing these tests in different age groups. Using the Centers for Medicare recently-assigned for CT dedicated to coronary angiography, we examined CAD-related costs and clinical effectiveness for younger and older patients (pts) undergoing CCT, compared to matched pts undergoing MPI testing. Methods: ICD-9 codes were used to identify 142,535 pts who underwent CCT or MPI, with data collected for 9 months before and after the test. MPI pts were matched to CCT pts by multilevel modeling of 11 demographic and clinical states. Cost and clinical effectiveness was assessed as: 1) downstream CAD costs (2006 US dollars), and 2) clinical events including myocardial infarction (MI) and CAD-related hospitalization. Age was stratified by younger (age≤55) and older (age>55) cohorts. Results: Younger and older CCT pts (n=1,285; n=1,028) were matched 1:4 to younger and older MPI pts (n=5,140; n=4,112), respectively for age (47 v 47 yr; 61 v 61 yr), female gender (39.7% v 39.7%; 43.8 v. 43.8%), diabetes (7.8% v 7.8%; 14.2% v 14.2%), hypertension (32.2% v 32.2%; 49.8% v 49.8%), hyperlipidemia (45.5% v 45.5%; 61.3% v 61.3%), known CAD (11.1% v. 11.1%; 22.6% v 22.6) and 5 additional variables (p=NS for all). In multivariable analysis, 9-month CAD costs were lower for younger pts undergoing CCT compared to MPI by $542 (95% CI $141–1762) [p<0.001]; for older pts, 9-month CAD costs were lower for MPI compared to CCT by $607 (95% CI $202–1637) [p=0.01]. Despite cost differences, rates of MI (0.7% vs. 0.8%, p=NS), and CAD-related hospitalization (0.2 vs. 0.2, p=NS) were the same between CCT and MPI pts for both younger and older pts. Conclusion: Younger pts who undergo CCT incur lower CAD healthcare costs compared to MPI with equal clinical outcomes, while older pts who undergo MPI incur lower costs compared to CCT with equal clinical outcomes. These results suggest that CCT may be more cost-effective in younger pts with suspected CAD, while MPI may be more cost-effective in older pts with suspected CAD.

P371

Clinical Features and Impact of Successful Percutaneous Coronary Intervention on In-Hospital Mortality in Elderly Patients with Acute Myocardial Infarction

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Background: Aging is associated with an increased risk of mortality in patients with acute myocardial infarction (AMI). Achievement of successful reperfusion is considered to be more important in high risk patients. However, little is known about the impact of successful reperfusion on mortality in elderly patients with AMI. **Methods:** We studieded 7731 patients with AMI registered in the Osaka Acute Coronary Insufficiency Study (OACIS) database, which is a multicenter prospective observational AMI registry. We compared the risk ratio of 30-day mortality in successful PCI, defined as achieving final TIMI grade 3 flow, in elderly patients over 80 year-old (n=1034) and younger patients in each decades lower than 80 year-old (n=6697). **Results:** Patients over 80 years had more classical risk factors than those lower than 80 years. All cause death rate in 80s was 20.5 % and was significantly higher than 10.6% in the 70s, 6.0% in the 60s 3.3% in the 50s. Although reperfusion therapy was less frequently performed (75.9%) in the 80s, however, rate of angioplasty (PCI) and success rate of PCI(final TIMI grade 3) were equivalent to the other decades. After adjustment for clinical variables, the risk reduction for the in-hospital mortality by the successful PCI was significant in the 80s (risk ratio [RR], 0.48: 95% CI; 0.29–0.80, P<0.01) and was similar to those in the younger decades (RR; 0.26: 95% CI; 0.23–0.42, P<0.01), suggesting that successful PCI is useful for survival irrespective of age. Interestingly, frequencies of mechanical complications (free wall rupture, ventricular septal perforation, and mitral regurgitation with abrupt onset) was high in the 80s, the beneficial effect of successful PCI on the mechanical complication was also seen in the 80s (RR; 0.78 95% CI; 0.41–0.92, P<0.05). However, frequency of major bleeding during hospitalization was high (9.4%) in the 80s compared with 6.4% in the 70s, 6.1% in the 60s 2.4% in the 50s. **Conclusion:** Survival rate was low in the 80s in patients with AMI. The beneficial effect of successful PCI on in-hospital mortality is also seen in elderly patients with AMI. Therefore, a strategy to achieve TIMI grade 3 flow is important and crucial in elderly patients with AMI in case the risk of bleeding complication could be well controlled.

P372

Menopausal Complaints Are Associated with Cardiovascular Risk Factors

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Objective: We previously reported that the presence of menopausal complaints may be an indicator of estrogen sensitivity of several end-organs. Whether vasomotor menopausal complaints are associated with cardiovascular disease (CVD) risk is unknown. The aim of the present study was to examine whether menopausal complaints, as a proxy for estrogenic effects are associated with cardiovascular risk profile in a large community-based sample of perimenopausal women. **Methods:** We used data from a population-based sample of 5,648 women, aged 46 to 57 years, who were enrolled in the Eindhoven Perimenopausal Osteoporosis Study between 1994 and 1995. Validated questionnaires were used to collect data on menopausal complaints and potential confounders. Total cholesterol, systolic and diastolic blood pressures, BMI, and Framingham risk score were determined. Linear regression analysis was used to analyse the data. **Results:** Night sweats were present in 38% and flushing in 39% of all women. The mean age of the study group was 50.3 ± 2.3 y (range 46 to 57 y). After multivariate adjustment, women with complaints of flushing had a 0.28 mmol/L [95% CI 0.16, 0.40] higher cholesterol level compared to asymptomatic women. Having complaints of flushing was also associated with a 1.29 mm/Hg [95% CI 0.23, 2.35] higher systolic blood pressure, and a 0.98 mm/Hg [95% CI 0.39, 1.57] higher diastolic blood pressure. In addition, these women had a 0.46 kg/m^2 [95% CI 0.23, 0.68] higher BMI, as well as a 1.09% [95% CI 0.82, 1.35] higher chance of developing CHD over 10 years. All results were comparable for complaints of night sweating. **Conclusions:** Our results support the view that menopausal complaints are associated with reduced estrogenic effects on the cardiovascular risk profile. These findings may imply that symptomatic women might be more susceptible to the preventive effects of HT.

P373

Temporal Trends in Myocardial Infarction Case Fatality Rates Among US Medicare Beneficiaries

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Case fatality rates following acute myocardial infarction (AMI) have decreased markedly over the last three decades. We describe the temporal trends in case fatality rates among 4.9 million Medicare beneficiaries hospitalized for AMI between 1984 and 2003, and report age-adjusted trends by gender and race in this nationally-representative cohort. **Methods:** We obtained data on all hospitalizations among Medicare beneficiaries ≥65 years for AMI (ICD-9: 410) and

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calculated the proportion of patients that died within 30 days and within 1 year of hospitalization. We used multivariable risk models to estimate relative changes in case fatality rate for specific groups. Analyses were restricted to the >95% of patients that identified their race as either black or white. **Results:** There were >5.9 million hospitalizations for AMI among Medicare beneficiaries during the 20 year observation period. After adjustment for age, gender, and race, between 1984 and 2003 there was a 39.7% (40.3, 39.1%) and 23.0% (22.5, 23.5) reduction in the risk of 30-day and 1-year mortality, respectively. While improvements in 30-day mortality were relatively similar in blacks and whites, improvements in 1-year mortality were most pronounced in white men and women (Table). Only small and inconsistent differences were seen comparing men versus women after stratifying by race. **Conclusion:** Among Medicare beneficiaries in the US, AMI case fatality rates have decreased significantly in all groups, but the most pronounced long-term improvements have been observed among white versus black men and women. Additional work is needed to determine if these differences are due to differential risk factor profiles, comorbid conditions, or access to quality health care.

AGE-ADJUSTED RELATIVE REDUCTIONS IN 30-DAY AND 1-YEAR MORTALITY

	30-Day Mortality			1-Year Mortality		
	1984 Rate (%)*	2003 Rate (%)*	Relative Reduction (%)	1984 Rate (%)*	2003 Rate (%)*	Relative Reduction (%)
White Men	25.2	14.3	41.9 (41.0, 42.8)	40.3	28.7	26.2 (25.5, 26.9)
White Women	25.2	14.4	39.0 † (38.1, 39.9)	39.3	28.8	21.6 † (20.8, 22.3)
Black Men	20.9	15.5	25.2 † (20.1, 30.0)	37.2	34.8	5.0 † (1.1, 8.8)
Black Women	21.6	15.1	27.1 †‡ (23.0, 31.0)	38.5	33.8	8.0 †‡ (4.9, 11.1)

*:Age-standardized; †:p<0.05 vs white men; ‡:p<0.05 vs white women.

P374

Kaplan-Meier Analysis Indexed to Time of Study Entry Markedly Underestimates the Risk of Incident Cardiovascular Events During Middle Age in Families with Premature Coronary Artery Disease

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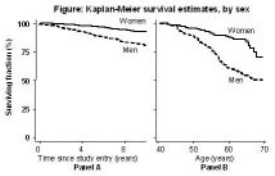
Recently, it was shown that cardiovascular survival analysis indexed to the time from study entry underestimates risk compared to analysis based on the actual age of subjects. However, the salience of this in high risk families is not known. We analyzed the coronary artery disease (CAD) events in healthy siblings of persons with premature CAD events, comparing the results using the two different time scales. Methods: We recruited 404 apparently healthy brothers and 380 sisters (30–59 years) of 449 probands with premature CAD (<60 years) and followed them for 10 years for incident first CAD events (sudden cardiac death, myocardial infarction, unstable angina, or coronary revascularization). We compared Kaplan Meier survival functions by sex from time on study with those modeled with the person's age as the underlying scale. Results: Incident CAD events occurred in 80 men (19.8%) and 27 women (7.1%). Panel A (Figure) shows the survival function since study entry, with cumulative incidence being 20% (95% CI: 17 to 24%) in men and 7% (95% CI: 5% to 10%) in women. However, using age as the time scale in panel B provides a much more accurate picture of the occurrence of events over time: there were no events before 40 years of age, but by the age of 70 years, the incidence of first CAD events was 49% (95% CI: 41 to 59%) in men and 30% (95% CI: 19 to 46%) in women. Conclusion: By 70 years of age about half of the male and a third of female siblings experienced a CAD event. Analyzing data by age, the natural scale for vascular disease, reveals the high disease incidence among persons with sibling history of premature CAD during the middle age years that might be missed had survival been modeled by time of follow-up.



P375

Hormone Therapy and Venous Thromboembolism: Early Results from the E3N Prospective Study

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Oral estrogen therapy increases the risk of venous thromboembolism (VTE) among postmenopausal women. Although recent data have shown that transdermal estrogen may be safe with respect to thrombotic risk, the impact of the route of estrogen administration is not fully established. In addition, data on the role of combined progestogens are scarce. We used the data from the E3N Study, a French prospective cohort of 85943 postmenopausal women born between 1925 and 1950 and followed by biannually questionnaires sent from 1990 (mean duration: 10.4 years). We identified 984 women with a first documented VTE (199 pulmonary embolisms and 785 deep vein thrombosis). The relative risks (RR) and 95% confidence intervals (CI) were estimated using a multivariate Cox proportional hazards models after adjustment for obesity, parity, education level and time-period. Compared with non-users, the RR for VTE in current users of oral and transdermal estrogen therapy was 1.6 (95% CI: 1.3–2.0) and 1.0 (95%CI: 0.8–1.2), respectively. Among oral estrogens users, there was no significant difference in VTE risk across all progestogen subgroups. Transdermal estrogen alone or combined with either micronised progesterone or pregnane derivatives was not significantly associated with VTE risk (RR=0.9; 95%CI: 0.6–1.3, RR=0.9; 95%CI: 0.7–1.1 and RR=1.0; 95% CI: 0.7–1.3, respectively) whereas transdermal estrogen combined with either norpregnane derivatives or nortestosterone derivatives significantly increased VTE risk (RR=1.4; 95%CI: 1.1–1.8 and RR=3.0; 95%CI: 1.3–7.3, respectively). In conclusion, these data confirm that the route of estrogen administration as well as the type of progestogen may be important determinants of the VTE risk among postmenopausal women who use hormone therapy. Transdermal estrogen alone or combined with either micronised progesterone or pregnane derivatives may be safe with respect to VTE risk.

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