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March 16, 1991

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The Trial of Antihypertensive Interventions and Management: 6 Month Changes in Diastolic Blood Pressure by Race-Sex and Age

Barry R. Davis, M. Donald Blaufox, Albert Oberman, Herbert G. Langford, Sylvia W. Smoller, Neal Zimbaldi, C. Morton Hawkins and Jeffrey Cutler for the TAIM Study Group. The University of Texas School of Public Health, Houston, TX.

We report 6 month diastolic blood pressure changes by race-sex and age (<55, ≥55 years) subgroups in the Trial of Antihypertensive Interventions and Management (TAIM), a randomized 3x3 factorial trial in 787 over-weight mild hypertensives. TAIM used 3 drugs [placebo, chlorthalidone, 25 mg, (C), and atenolol, 50 mg, (A)] and 3 diets [usual, weight loss (W), and low Na+high K+ (S)]. Differences (Δ) > 3.8 mm Hg in the overall analysis were considered significant at p < .05. Drug therapy was more effective than diet therapy in all subgroups except males where W and C were about equal. Additional benefit was obtained by adding W (but not S) to drug in all the subgroups. This benefit was more pronounced for C in black men (Δ=0.3 mm Hg) and black women (Δ=6.8 mm Hg) whereas the benefit was more pronounced for A in white men (Δ=2.1 mm Hg) and white women (Δ=4.9 mm Hg). The extra benefit of adding W to drug was similar in both age groups (Δ=2-4 mm Hg). These results are consistent with the previously reported overall 6 month results that weight loss plus drug is the most effective antihypertensive therapy.

Systolic Blood Pressure and Carotid Artery Disease in Elderly Adults.

Kim Sutton-Tyrrell, Hope G. Alcorn and Sidney K. Wolfson, Jr. University of Pittsburgh, Pittsburgh, PA

To evaluate the relationship between Systolic Blood Pressure (SBP) and carotid disease, 112 adults participating in the Systolic Hypertension in the Elderly Program and 67 normotensive control subjects underwent duplex scanning. Other than blood pressure, all participants were generally healthy. An Internal Carotid Artery (ICA) stenosis was defined as an internal to common carotid blood flow velocity ratio of 2.0 or greater. Extent of carotid plaque was scored based on the size and number of lesions. The mean age of hypertensive and normotensive subjects was 76 and 69, and mean blood pressure was 170/79 and 125/69 respectively. Men comprised 36% of the hypertensive and 40% of the normotensive group. History of smoking was positive for 37% (42/113) of hypertensive subjects and 57% (38/67) of normotensive subjects. p = .05. The prevalence of ICA stenosis was 0% (0/67) among those with a SBP of < 160, 10% (6/65) for those with a SBP between 160 and 169 and 22% (10/45) for those with a SBP of ≥ 170, p < .01. No subject had symptoms of cerebral ischemia. The prevalence of ICA stenosis increased with age and was slightly higher among men. Similar results were obtained when analyzing extent of carotid plaque. After adjustment for age, sex, smoking history and diastolic blood pressure, the relationship between SBP and ICA stenosis remained significant, p < .01. Both SBP (p < .01) and history of smoking (p < .05) were found to be independently predictive of extent of carotid plaque. In the elderly population, SBP appears to be strongly correlated with carotid disease.

All Cause Mortality and Blood Pressure Change in the Multiple Risk Factor Intervention Trial.

Steven M. Butler, James D. Neaton, Jerome D. Cohen for the MRFIT Research Group. Biostat Division, School of Public Health, University of MN

The 12866 MRFIT participants included 8012 baseline hypertensives, defined by a diastolic BP≥90 mmHg or having antihypertensive medication prescribed before entry. Of these, 6019 were treated for hypertension with a stepped care protocol (SI). The remaining participants were referred to community physicians (UC). With proportional hazards regression analysis, the relationship between diastolic BP change and mortality was studied in two ways: (1) Participants were classified by diastolic BP change through 6 years of follow-up, and mortality in the subsequent 4.8 years was determined; (2) BP change over the initial 7 years of follow-up was used as a time dependent covariate. In both analyses a U-shaped association between BP change and total mortality was observed. For the first 7 years of follow-up, regression coefficients for the quadratic terms in BP reduction were significant in SI and UC (p<.01). For CHD, BP decrease was associated with increased mortality in SI for both time periods. Linear coefficients were positive with p<.02. For UC, a U-shaped curve was observed for CHD. Possible reasons for these associations include the adverse effect of an antihypertensive treatment, increased mortality resulting from large BP reductions, and confounding due to preclinical disease which results in BP lowering.

The Effect of Treatment on Combined Trial Endpoints in the Hypertension Detection and Follow-up Program (HDFP)


Hypertension remains one of the most common adult chronic diseases in the world for which treatment is available. It affects millions of people, significantly impairs life expectancy, and is a major independent risk factor for common adult cardiovascular-renal diseases. The risk associated with hypertension includes both fatal and nonfatal sequelae. To examine the effect of antihypertensive drug treatment on combined mortality and morbidity, data from the 10,940 HDFP trial participants were analyzed. The adjusted 5-year all-cause mortality rate was 64.1/1000 in the Stepped Care (SC) cohort and 76.7/1000 in the Referred Care (RC) cohort (95% confidence limits for difference: 3.07 to 21.88). When mortality was combined with nonfatal outcomes of stroke, CHD, and LVH, the adjusted 5-year incidence rates were 204.7/1000 SC versus 261.7/1000 RC (95% confidence limits: 41.41 to 72.64). While the mortality rate was relatively low among younger hypertensives, women, and those with mild, uncomplicated hypertension—groups who generally have not been shown to greatly benefit in terms of reduced mortality—there was a considerable risk of combined fatal and nonfatal events in 5 years in these patients and the benefit of treatment was impressive. These findings contradict the viewpoint that persons with mild hypertension are at low risk and gain little from antihypertensive drug treatment.
Body Mass Index as a Predictor of 20-Year Mortality in Hypertensive White and Black Women in Evans County, Georgia.

Janet B. Croft, H.A. Tyroler, Curtis G. Hames, University of North Carolina, Chapel Hill NC.

Recent prospective studies of white men suggest that mortality risk among hypertensives may vary inversely with obesity level. The relationship of body mass index (BMI) to mortality was examined in a biracial cohort of hypertensive women in the Evans County, Georgia Heart Study. Elevated systolic blood pressure (160 mm Hg) was present in 1960 among 230 (35%) of 664 white women and 282 (62%) of black women, ages 40-74. By 1980, 79 (67%) of 118 deaths in hypertensive whites and 93 (66%) of 140 deaths in hypertensive blacks were from cardiovascular disease (CVD). There was no association of BMI level with total mortality in either group. BMI was a statistically significant positive predictor of CVD mortality among hypertensive white women. In contrast, BMI was not a predictor of CVD mortality in hypertensive black women, but an inverse relationship is suggested (Figure). The results suggest both gender and ethnic differences in the prognostic significance of obesity.

Interaction Between Body Mass Index and Dietary Cholesterol on Risk of Coronary Mortality in the Western Electric Study

David C. Goff, Richard B. Shekelle, Jeremiah Stamler. The University of Texas School of Public Health, Houston, TX.

The relationship between body mass index (BMI), dietary cholesterol (DCHOL) and 20-year coronary (CHD) mortality was examined among 1824 middle-aged men in the Western Electric Study. The table shows relative risks of CHD mortality by level of BMI and DCHOL after adjustment for age, cigarette smoking, alcohol ingestion, dietary fat and energy intake. Both BMI and DCHOL were positively associated with CHD mortality, but the relationship between DCHOL and CHD mortality was strongest among relatively lean men. Adjusted relative risks for CHD mortality associated with a 150 mg/1000 kcal increase in dietary cholesterol were 1.77, 1.22, and 1.15 for the three ascending BMI strata, respectively. Likewise, the relationship between BMI and CHD mortality was strongest among men in the lowest DCHOL stratum. Further adjustment for serum cholesterol and systolic blood pressure diminished the relative risks by 3% on average, but had no appreciable effect on the pattern. Thus, serum cholesterol and obesity interact with respect to effects on risk of CHD.

Adjusted Relative Risk of CHD Mortality by BMI and DCHOL

<table>
<thead>
<tr>
<th>DCHOL (mg/1000 kcal)</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 24</td>
<td>&lt; 24-24.9</td>
</tr>
<tr>
<td>200</td>
<td>1.00</td>
</tr>
<tr>
<td>200-259</td>
<td>1.25</td>
</tr>
<tr>
<td>≥ 260</td>
<td>1.81</td>
</tr>
</tbody>
</table>

Relationship of Waist-to-Hip Ratio (WHR) and Weight to Changes in CVD Risk Factors in the Treatment of Mild Hypertension Study (TOMHS)

Patricia J. Elmer, Richard H. Grimm, John Lagus, for the TOMHS Research Group, University of Minnesota, Minneapolis, MN.

TOMHS is a multicenter randomized trial of the treatment of mild hypertension, comparing non-drug nutrition treatment (placebo) with five groups receiving nutrition plus one of 5 active drugs. Patients include 902 Black and White men and women, age 45-69 with mild hypertension (DBP 90-99 mmHg). After controlling for BMI, alcohol, physical activity, smoking and diet, predicted baseline blood glucose, uric acid (UA) and HDL in both men and women (p<0.1), and triglycerides (TG) in women only. Neither WHR nor BMI were associated with baseline total (TC) or LDL cholesterol. Participants received intervention to lower wt, alcohol and dietary sodium and to increase exercise. Wt loss after 1 yr was 10.4 lbs and activity score increased by 85%. At 1 yr multivariate analyses were performed, for the placebo group (n=234), to determine the effect of change in WHR on change in CVD risk factors. Change in WHR was not related to changes in glucose TC, HDL, LDL or TG in men or women, but was related to change in UA in men. However, change in weight was related to changes in TC, LDL, and TG in both men and women, and change in HDL in men. Using this model, a reduction in TD of -11 mg/dl in women and -4.7 mg/dl in men could be expected with a 10 lb wt loss. Although cross sectional studies have found positive relationships between WHR and CVD risk factors, little prospective data on the effect of change in WHR and risk factors has been available. These data indicate that change in wt is a better predictor of risk factor change in men and women than change in body fat distribution.

Body Composition Relation to Blood Pressure and Lipids in 9-10 year old Black and White Girls: NHLBI Growth and Health Study (NGHS)

Sue Y.S. Kimm, Edward Lakatos, Frank Falkner, Frank M. Biro, George B. Schreiber, Bruce A. Barton, University of Pittsburgh, Pittsburgh, PA

Increased body mass index is known to adversely affect blood pressure (BP) and lipids. This study investigated relationships between adiposity, its regional patterning, and lean body mass (LBM) with BP and lipids in 2379 black (BG) and white girls (WG) enrolled in NGHS, a multicenter longitudinal study of obesity development. At baseline, BG had a higher quetelet index (QI), sum of skinfolds (SSF) at 3 sites, and lean body mass (LBM) than did WG. Systolic (S) and diastolic (D) blood pressure (BP), HDL-C, and Apo-A1 were also higher among BG, but triglycerides(trig) and LDL-C were lower. Multivariate analyses revealed that LBM was positively correlated with SBP, DBP, and trig, and negatively correlated with total-C (TC), LDL-C, HDL-C, and Apo-A1. SSF was negatively correlated with HDL-C, but positively correlated with TC, LDL-C, Apo-A1, DBP, and SBP. Multivariate analysis of the role of regional fat patterning in the relationship between SSF and DBP, by race, shows that the association is due entirely to iliac skinfold thickness (ISF) in BG, while midarm circumference (MAC) was the sole determinant for WG. A similar analysis for SSF and LDL shows that the association could be entirely explained by MAC, triceps SF for BG, and by ISF for WG. For HDL-C, it was explained completely by subscapular SF for WG and BG.
Relationship of Serum Testosterone Levels to High-Density Lipoprotein Cholesterol and Other Characteristics in Men

David S. Freedman, Thomas R. O’Brien, W. Dana Flanders, Frank DeStefano, Joseph J. Bartoriami. Centers for Disease Control, Atlanta, GA.

Although levels of high-density lipoprotein cholesterol (HDL-C) are 1) higher among women than men, and 2) decrease in boys during adolescence, several studies have reported a positive correlation between levels of HDL-C and testosterone in middle-aged men. Reasons for these apparently contradictory observations were examined in a cross-sectional analysis of 3,562 white and 500 black 31- to 45-year-old men. As compared with whites, blacks had higher mean levels of HDL-C (52 vs 44 mg/dL) and total testosterone (709 vs 676 mg/dL), and levels of testosterone and HDL-C were positively correlated (r = 0.22, whites; r = 0.26, blacks). The black/white difference in levels of HDL-C, however, was not altered by controlling for total testosterone. In addition, levels of testosterone were related positively to alcohol consumption (r = 0.11) and cigarette smoking (r = 0.22), and inversely to age (r = -0.18), Quetelet index (r = -0.34), and use of β-blockers. Stratification and regression analyses were used to determine if the association between levels of HDL-C and total testosterone was due to confounding. Controlling for most factors had little influence, but adjusting for Quetelet index reduced the strength of the association between HDL-C and testosterone levels by about 30%. These findings suggest that the positive association between testosterone and HDL-C may not be causal, and emphasize the importance of controlling for levels of HDL-C and obesity in assessing the relation of testosterone levels to CHD.

Serum Cholesterol Measured in Youth and Risk of Subsequent Violent Death

Michael J. Klag, Lucy A. Mead, Paul K. Whelton, David M. Levine. Johns Hopkins University, Baltimore, MD

Cholesterol-lowering therapy has been suggested to be associated with an increased risk of violent death. We studied the risk associated with serum cholesterol in a prospective study of 1,040 former male medical students (mean age, 26 years) who were followed for 24-42 years. Outcomes were assessed by annual questionnaire, review of medical records and death certificates. Serum cholesterol (mean 225 mg/dL) was measured in medical school. There were 87 deaths (26 due to accidents or suicide) and 157 CVD events (87 CHD). In Kaplan-Meier analysis, serum cholesterol level was not associated with accidental/suicide death (p = 0.98) but was associated with total mortality (p < 0.05) and CHD (p = 0.0001) and CVD (p = 0.01) incidence. In proportional hazards analysis adjusting for age, systolic blood pressure, body mass index, coffee intake, cigarette smoking, and parental history of CHD, a 10 mg/dL increase in serum cholesterol was associated with an elevated relative risk (RR; 95% CI) of CHD (1.12; 1.07, 1.17; p < 0.001) and CVD (1.06; 1.02, 1.10; p < 0.01) but not accidental/suicide death (0.98; 0.88, 1.11; p = 0.8) or total mortality (1.0: 1.0, 1.0; p = 1.0). These findings confirm the association of cholesterol, measured in youth, with CHD and CVD in later life but do not support an increased risk of violent death in persons with lower cholesterol levels.

A Case-Control Study of Antibody to Cytomegalovirus, Herpes Simplex Virus, Human Herpes Virus 6, and Coronary Artery Disease


We conducted a case-control study to examine the relation between coronary artery disease and antibody to cytomegalovirus (CMV), herpes simplex virus (HSV) and human herpes virus 6 (HHV6). Cases were 95 patients with coronary artery disease, defined as one or more lesions occupying 50% or more of luminal diameter on coronary angiography. Controls were 95 patients, matched with cases by gender and age, who had no demonstrable coronary artery disease on angiography. Enzyme-linked immunosorbent assays were used to measure HSV (types 1 and 2 combined) and HHV6 antibody. CMV antibody was measured with a latex agglutination assay. Antibody to CMV was present in 67% cases and 66% controls (age and sex adjusted relative risk = 0.9). HHV6 antibody was present in 86% of controls and 88% of cases (adjusted relative risk = 0.9). In contrast, HSV antibody was present in 91% of cases and 81% of controls (adjusted relative risk = 1.9; 95% confidence interval = 0.8-4.7). These preliminary results, interpreted with results of in vitro studies of HSV infection of human endothelial cells, suggest that HSV infection may be associated with the development of coronary artery disease.
Associations of CVD Risk Factors With Peripheral Vascular Disease in American Indians.
Richard R. Fabsitz for the Strong Heart Study Investigators, Bethesda, MD

Among the first 1632 American Indian men and women ages 45-74 participating in the Strong Heart Study, 481 were determined to have peripheral vascular disease (PVD), defined as the absence of posterior tibial or dorsalis pedis pulses, presence of femoral bruits, or an ankle/brachial blood pressure ratio less than 0.8. Prevalence rates of PVD were higher in women (29.6%) than men (24.5%) and increased with age. In addition, lower and middle rates were substantially higher among diabetics (DM) versus non-diabetics (NDM) for both men (33.3% vs 19.0%) and women (33.9% vs 25.5%). Analyses comparing CVD risk factors for PVD versus non-PVD by sex and diabetic status indicated several consistent findings. Prevalence of PVD was associated with higher levels of 2-hour glucose, fibrinogen, hemoglobin Alc, and urinary albumin in all groups. For men, PVD was associated with lower levels of LDL cholesterol for both DM and NDM. No other lipid or lipoprotein measurements were associated with PVD. Obesity was positively associated with PVD for all groups except DM men. Smoking was lower among men and women with PVD. In addition, among DM, PVD was associated with older ages, duration of diabetes and systolic blood pressure. From this cross-sectional analysis, the prevalence of PVD appears to be high among American Indians and is associated with diabetes but not with some of the major CVD risk factors.

Rapid Deterioration of West German Risk Factor Profile - Results of German National Health Examination Surveys
Eberhard M. Greiser, Ulrike Maschewsky-Schneider, Günter Tempel, Uwe Helmer. Bremen Institute for Prevention Research and Social Medicine (BIPS), Bremen, Germany

National Health Examination Surveys (NHES) were conducted in West Germany in 1984/86 and 1987/88 in conjunction with the German Cardiovascular Prevention Study, based on a representative sample of 4690 (NHES-1) and 3390 (NHES-2) men and women, aged 25-69 (multi-stage clustered sampling design), achieving response rates of 66% and 71%, respectively. Results show rapid changes in major cardiovascular risk factors. Total serum cholesterol population means increased from 232.4 to 254.7 mg/dl (m: 230.6 to 253.4; w: 234.0 to 252.1) with w: 250.0 mg/dl) from 33.6% to 35.6% (m: 31.4% to 36.0%; w: 35.6% to 35.3%). Systolic blood pressure increases from 131.1 mm Hg to 133.1 (m: 134.1 to 135.4; w: 128.3 to 131.0) with no change in diastolic bp. Prevalence of hypertension (WHO criteria) is unchanged in men (24.6% to 24.4%), but increases in women (19.6% to 21.0%). Awareness is unchanged in men (37.1% to 37.8%), but decreases in women from 54.5% to 50.9%. Rate of treatment increases in men from 34.3% to 39.8%, but decreases in women from 56.0% to 52.4%. Rates of control of hypertension are low in both surveys and in both gender (m: 17.3% and 20.2%; w: 28.0% and 29.0%). Prevalence of actual smoking increases in men from 41.6 to 44.3%, and in women from 27.0 to 27.6%. Increases in men affect all age groups, whereas in women sharp increases in younger age groups are balanced by decreases in older ages. Cardiovascular mortality risk (ICD-9:410-414, 430-438; age groups 40-69), as derived from US NHANES-2 Epidemiological Follow-up Study multivariate logistic coefficients, shows a 4.1% increase in men, and a 7.1% increase in women. Analyses with regard to social class indicators show an increase of risk factor prevalence and mortality risk in lower SES and concurrent decreases in high SES. Deterioration of risk factor profile has to be discussed in context of absence of national programs to combat any of the major cardiovascular risk factors and in the light of an economic policy which subsidizes both agricultural and tobacco industry.

Lipids Trends in South and North Chinese Cohorts
Zhendong Huang, Shou-chi Tao, Zhikui Xiao, Yiling Zhuo, Beifan Zhou, Yihe Li, Ying Li, Aaron Folsom, Russell Wallace, Barbara Dennis, O. Dale Williams, Jeremiah Stamler, Guangzhou Cardiovascular Institute, Guangzhou, PRC

As part of PRC-US collaborative study in cardiovascular epidemiology, baseline (BL: 1983-84) and 4-year follow-up (FU: 1987-88) surveys were done in urban and rural samples from Guangzhou, south China and Beijing, north China. Serum lipids (CDC standard) were measured in 6,825 persons aged 35-54 at BL. Three 24-hr dietary recalls were obtained in a subset. Mean serum total cholesterol (TC) and triglycerides (TG) increased markedly over 4 years in Guangzhou, but less in Beijing.

<table>
<thead>
<tr>
<th>Site</th>
<th>Sex</th>
<th>BL</th>
<th>TG (mg/dl)</th>
<th>FU</th>
<th>TG (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guangzhou</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Urban</td>
<td>M</td>
<td>182</td>
<td>196</td>
<td>8%</td>
<td>105</td>
</tr>
<tr>
<td>Rural</td>
<td>M</td>
<td>187</td>
<td>196</td>
<td>10%</td>
<td>127</td>
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<tr>
<td>Beijing</td>
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<tr>
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<td>M</td>
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<td>110</td>
</tr>
<tr>
<td>Rural</td>
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<td>2%</td>
<td>115</td>
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</table>

There were 1-2 kg increases in Guangzhou and Beijing in body weight; Keys score predicted 3 mg/dl of the TC increase was due to change in dietary fat and cholesterol. This study indicates unfavorable trends in lipid levels in China and points to an important prevention issue.

8.5-Year Cardiovascular Disease and Non-Cardiovascular Mortality ofMiddle-Aged Japanese National Railways Workers

In 1975-78, baseline data were collected on 7171 men ages 40, 45, 50 and 55 (mean 47.8 yrs), working in the Japanese National Railways. Mean body mass index was 22.7 kg/m²; serum total cholesterol (TC) 173.0 mg/dl; systolic blood pressure (SBP) and diastolic (DBP) 131.4/80.4; 71% were current cigarette smokers, mean 25 cigs/day; 75% reported current alcohol use, mean 53 gm/day. With follow-up of vital status complete through Mar. 31, 1985 (mean 8.5 yrs), 258 men (36.0/1000) were deceased--107 (14.9/1000) from malignant neoplasms, 90 (12.6/1000 from cardiovascular diseases (CV). The most common cancer was gastric (35 deaths). The most common CV cause was stroke (35 deaths. 26 of them hemorrhagic); deaths from coronary disease (CHD) numbered 18. Quantile and Cox regression analyses indicated the following significant independent relationships: all-cause mortality--age, SBP, post-load glucose, alcohol use; CVD mortality--age, SBP, TC, CHD--TC, stroke--SBP; gastric cancer--age, TC (inverse), alcohol use. These findings indicate both persistence into the 1980s in Japan of Far Eastern mortality patterns, and major risk factor relationships common to those around the world.
Smoking and Antihypertensive Medication are Determinants of HDL Cholesterol and Non-HDL Cholesterol - Results of German National Health Examination Surveys

Eberhard M. Greisler, Ulrike Maschewsky-Schneider, Günter Tempel, Uwe Helmert, Bremen Institute for Prevention Research and Social Medicine (BIPS), Bremen, Germany

To determine the impact of smoking and antihypertensive drugs, besides body mass index and age, on total serum cholesterol (TC), HDL serum cholesterol (HDL), and non-HDL serum cholesterol (NHD), data of 1st and 2nd National Health Examination Surveys, conducted in 1984/86 and 1987/88 in conjunction with the German Cardiovascular Prevention Study, were analysed. Data comprised cardiovascular risk factors on 4980 (1st survey) and 5330 (2nd survey) men and women, aged 25–69. Antihypertensive medication was a self-reported and b) assessed from packages of drugs brought to examination site and covered drugs taken 7 days prior to examination data. Weighted multiple linear regression analyses were done using TC, HDL and NHD as dependent and age, body mass index, amount of cigarettes smoked currently, date of survey, and reported antihypertensive drugs (RAH) / coded drugs in groups: diuretics (DIU); beta-blockers (BB); calcium channel blockers (CCB); other hypotensives / any antihypertensive drug (AAH) as independent variables. Means and coefficients were statistically significant at least at 0.05 level, are:

<table>
<thead>
<tr>
<th>Mf</th>
<th>mg/dl</th>
<th># 20 cig./day</th>
<th>RAH</th>
<th>AAH</th>
<th>Bu</th>
<th>CCB</th>
<th>DIU</th>
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<tr>
<td>TC</td>
<td>232</td>
<td>+ 6.5</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>HDL</td>
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<td>- 2.8</td>
<td>-3.5</td>
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<td>-9</td>
<td>+6</td>
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</tr>
<tr>
<td>NHD</td>
<td>182</td>
<td>+ 9.6</td>
<td>+6.8</td>
<td>+5.1</td>
<td>+12.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WOMEN</td>
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<tr>
<td>TC</td>
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<td></td>
</tr>
<tr>
<td>HDL</td>
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<td>-2.8</td>
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</tr>
<tr>
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Similar results are reached, when calculating partial correlation coefficients, controlling for age, body mass index, survey date and amounts of cigarettes smoked or antihypertensive medication, respectively. Conclusions: Both cigarette smoking and antihypertensive medication increase NHD and decrease HDL, cigarette smoking increases also TC. Results controlling impact of nutritional habits also will be presented.

Cross-Sectional and Longitudinal Associations between Women’s Employment and HDL-Cholesterol

Ursula Haertel, Gerardo Heiss, Birgit Filipiak, Angela Doering. GSF Medis-Institute, Dept. of Epidemiology, Munich-Neuherberg, West Germany

This study examined the effect of women’s employment on HDL-C. Subjects were 1998 women aged 25 to 64 sampled by the first MONICA Augsburg population survey in West Germany 1986/85 who were followed up for 3 years and reexamined in 1987/88. At baseline, the mean HDL-C of employed women was 3.4 mg/dl higher than that of full-time home makers (p=0.001). After multivariable adjustment, this difference decreased to 2.1 mg/dl (p=0.01). During followup, employed women who became home makers decreased their mean HDL-C, whereas home makers who became employed showed no significant change in HDL-C levels in 3 years. The change in mean HDL-C of employed women who had become home makers could be explained in part by changes in alcohol consumption and in the number of pregnancies. We conclude that giving up employment is related to lifestyle changes, which are associated with a decrease in HDL-C levels. Further, our findings suggest that employment may exert a beneficial influence on coronary risk in women, consistent with a positive association between employment and HDL-C.

Blood Lipid and Lipoprotein Levels in the Oldest Old: A Community-Based Study

Robert B. Wallace, Patricia L. Colsher, University of Iowa College of Medicine, Iowa City, IA

We examined serum lipid and lipoprotein cholesterol distributions and correlates in a cohort of 1950 persons 70 to 102 years of age living in a geographically-defined area. Total and HDL-Cholesterol levels declined with age, but were substantially higher in women than in men. HDL-Chol. levels were 10–12 mg/dl higher in women and were not age-related. Even in the tenth decade, a large proportion of subjects fell above NCEP screening guidelines. Mean lipid levels were lower among persons residing in long-term care institutions. HDL-Chol. levels were sensitive to hygienic behaviors (e.g., alcohol use, body mass) as in younger adults, and were positively correlated with physical performance measures such as stair-climbing and the timed walk, and negatively related to the presence of chronic illness. The high prevalence of abnormal blood biochemical values obscured the ability to determine the prevalence of secondary hyperlipidemia. Two-year all cause mortality was not clearly related to total Chol. but was inversely related to HDL-Chol. levels. HDL-Chol. levels were clear and sensitive markers of health and physical activity levels, even at very low levels of function and in the presence of clinical disability.
Apolipoprotein E: An Inherited Metabolic Risk Factor.

Sera frozen since 1975 from the Multiple Risk Factor Intervention Trial (MRFIT) were used to screen 207 coronary heart disease (CHD) cases and 412 matched controls for the apolipoprotein (apo) E polymorphism. Cases consisted of 93 CHD deaths and 114 non-fatal myocardial infarctions. This polymorphism occurs because of single amino acid substitutions in the apo E 3 polypeptide and is an important genetic determinant of low density lipoprotein cholesterol (LDLc) levels. There are 6 common phenotypes, apo E 2-2, 3-2, 3-3, 4-3, 4-4, and 4-2.

Logistic regression analysis of matched pairs gave the following results for the four most common phenotypes:

<table>
<thead>
<tr>
<th></th>
<th>N (cases,cont)</th>
<th>All Cases</th>
<th>N (cases,cont)</th>
<th>CHD Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>apo E 3-3</td>
<td>(110,276)</td>
<td>1.00</td>
<td>(43,126)</td>
<td>1.00</td>
</tr>
<tr>
<td>apo E 3-2</td>
<td>(24,354)</td>
<td>1.73</td>
<td>(8,141)</td>
<td>1.72</td>
</tr>
<tr>
<td>apo E 4-3</td>
<td>(61.85)</td>
<td>1.79</td>
<td>(31.42)</td>
<td>2.28</td>
</tr>
<tr>
<td>apo E 4-4</td>
<td>(6.5)</td>
<td>1.38</td>
<td>(5.2)</td>
<td>8.74</td>
</tr>
</tbody>
</table>

Relative risks were adjusted for age, cigarettes/day, diastolic blood pressure, body mass index and LDLc. Results indicate that apo E 4 and apo E 2 are independent risk factors for CHD.

Lipoprotein[a] as a Risk Factor for Preclinical Atherosclerosis
Pamela Schreiner, Wolfgang Patsch, Richey Sharrett, Joel Morrisett, Gerardo Heiss. University of North Carolina, Chapel Hill, NC.

Although lipoprotein[a] (Lp[a]) is a risk factor for clinically manifest atherosclerosis, its association with asymptomatic, preclinical disease has not been shown. The purpose of this study was to examine the association of Lp[a]—measured as apolipoprotein[a]—with prevalent asymptomatic atherosclerosis. The study population was derived from the Atherosclerosis Risk in Communities (ARIC) Study—a prospective, multi-center investigation of atherosclerotic clinical events and of non-invasively measured atherosclerosis in adults, ages 45-64, sampled from four U.S. communities.

Atherosclerosis was identified from measurements of carotid artery intimal-medial wall thickness with B-mode ultrasound. Cases were defined as exceeding 2.5 mm wall thickness, or having a bilateral wall thickening above the 90th percentile value of wall thickness at the carotid artery (common, internal, or its bifurcation). Controls were chosen from below the 75th percentile of wall thickness distribution and pair-matched to cases by race, gender, study center, 10-year age group, and time of examination to yield 378 matched pairs.

Mean apo[a] concentrations in cases and controls were 105.0 μg/dL and 74.2 μg/dL, respectively (p<0.0001). The adjusted odds ratio for the apo[a] and atherosclerosis association was 1.60, based on one standard deviation difference in apo[a] concentration. This odds ratio is of comparable magnitude to that of total and LDL cholesterol, and remained constant with adjustments for age, total cholesterol, hypertension, apoA1, apoB, triglyceride, waist-to-hip ratio, fibrinogen, ethanol intake, and smoking behavior. No statistically significant effect modification of apo[a] by gender, cholesterol, apoB or fibrinogen was observed.

In this predominantly white sample, Lp[a] is independently associated with prevalent atherosclerosis in asymptomatic individuals. Further evidence based on phenotypic diversity exhibited by apo[a], the protein unique to Lp[a], may reveal even stronger associations.

Hopelessness and Mortality from Ischemic Heart Disease in the NHANES I Epidemiologic Followup Study.
Robert F. Anda, Diane H. Jones, Carol A. Macera, David F. Williamson, Elaine D. Eaker, James S. Marks. Centers for Disease Control, Atlanta, GA

Psychological factors such as stress, Type A personality, and hostility have been explored as risk factors for cardiovascular disease. More recently, depression and hopelessness (HL) have been explored as determinants of mortality. To assess the relationship between HL and ischemic heart disease mortality (IHD), we used data from a cohort of 2918 adults aged 45-74 years from the NHANES I Epidemiologic Followup Study (mean length of follow-up = 12.4 years) who had no history of heart disease or serious illness at baseline. HL, assessed at baseline using an item from the General Well Being Schedule, was more common among women, blacks, and persons with less education; 11% reported moderate HL, while 3% reported high levels of HL. During the follow-up period, 201 IHD deaths occurred. After adjusting for age, sex, race, education, blood pressure, cholesterol, smoking, physical activity, and body mass index, HL was independently related to the risk of IHD. The relative risks of IHD for moderate and high levels of HL were 1.5 (95% CI=1.0-2.3) and 2.0 (95% CI=1.1-3.6), respectively. Hopelessness may be a psychobiologic factor that affects IHD.

Relation of Social Networks to Incidence of, and Survival after, Ischemic Heart Disease

Three measures of social network—breadth of the network (scope), total number of contacts (frequency), and number of persons in the network (size)—and one of social support (work support)—were assessed in a random sample of 2603 adult members of a large HMO. Over the following 15 years, incidence, survival after incidence, and total mortality from IHD were related to these measures. After 15 years, the relative risks of lowest/highest tertile of network scope for all death and IHD incidence were 2.3 (CI=1.8-4.0) and 1.5 (CI=1.0-2.3), respectively. Among persons who suffered an incident case of IHD, an increase of network scope of 1 SD was associated with a decline in RR of IHD death (RR=0.68, CI=0.54-0.72) and total mortality (RR=0.72, CI=0.60-0.87). The other network measures predicted RR of death but not IHD incidence. All network measures were strong predictors of survival among those who suffered incident IHD. These data are the first to our knowledge which indicate that social networks may reduce susceptibility to IHD, but are more strongly associated with survival after it has occurred.
Cynical Distrust and Anger Control Associate with Accelerated Progression of Carotid Atherosclerosis


We investigated the association of cynical distrust (a component of hostility) and anger control with progression of common carotid artery (CCA) atherosclerosis in 114 42-60 years old men examined in the Kuopio Ischaemic Heart Disease Risk Factor Study (KIHDS) in 1987. High-resolution B-mode ultrasonography was repeated in 24 months. Cynical distrust was assessed with a Cook-Medley subscale (8 items, Chronbach's α=0.81, re-test r=0.82) and anger control with the Spielberger Anger Expression scale (8 items, α=0.88, r=0.76). The mean age, S-LDL-Chol and cigarette-years -adjusted mean 2-year increase of maximal CCA intim-media thickness (IMT) was 2.5-fold (p=0.005 in 2-way ANCOVA) in men with cynical distrust over median compared to others, 0.18 mm in men with both high cynicism and high anger control and 0.04 mm in those with low cynicism and low anger control. These data suggest that hostility and anger are risk factors for atherosclerosis progression.

Emotional Arousalability Predicts Sudden Cardiac Death in Post-MI Men

Lynda H. Powell, Steven R. Simon, Thomas Bartzokis, Jerry R. Pattillo, Carl E. Thoresen, Yale School of Medicine, New Haven, CT.

Lown has suggested that sudden cardiac death (SCD) is an electrical accident triggered by a transient factor that momentarily alters cardiac excitability. Stress--in the lab or as a major life event--has been implicated as this transient factor, but this reveals little about those persons predisposed to this risk.

We studied 929 post-MI men living in the San Francisco Bay Area, to determine the relation between Emotional Arousalability, as measured during a casual interview, and SCD over 8.5 years. Results from multivariate analyses, controlling for major risk factors, indicated that Emotional Arousalability was an independent predictor of SCD (RR=2.13, p=0.01). It was more predictive in men $<54$ (RR=3.19, p=0.04) than in older men, in men with cholesterol $<250$ (RR=2.94, p=0.01) than cholesterol $>250$, and as men drank increasing amounts of alcohol (RR abstain=0.85; kevwk=1.89; kev/day=3.81, p=0.01). This concept of stress is a behavioral trait which predisposes to emotional upset, can trigger electrical malfunction in men with coronary disease, and is particularly lethal in younger men and men with elevations in other risk factors.

A Prospective Study of Aspirin Use and Primary Prevention of Cardiovascular Disease in Women

JoAnn E. Manson, Meir J. Stampfer, Graham A. Colditz, Walter C. Willett, Bernard Rosner, Frank E. Speizer, Charles H. Hennekens. Channing Laboratory, Harvard University, Boston, MA

We examined aspirin use and the risk of a first cardiovascular event in a prospective cohort study (the Nurses' Health Study) of 87,678 U.S. women aged 34 to 59 years in 1980. Participants were free of diagnosed cardiovascular disease (CVD) at baseline and were followed for six years. During 475,266 person-years of follow-up, we documented 240 nonfatal myocardial infarctions (MI), 146 nonfatal strokes, and 130 deaths due to CVD. Among women reporting the use of 1-6 aspirin per week, the age-adjusted relative risk (RR) of a first MI was 0.68 (95% CI, 0.52-0.89, P=0.005), as compared with nonusers of aspirin. After simultaneous adjustment for CVD risk factors, the RR was 0.73 (95% CI, 0.55-0.93, P=0.02). We observed no influence on the risk of stroke (multivariate RR=0.96, P=0.79). The multivariate RR of CVD death was 0.84 (P=0.36). When examined separately, the results were nearly identical for the subgroups using 1-3 and 4-6 aspirin per week. Among women taking 7 or more aspirin per week, there were no apparent reductions in risk. Our results indicate that the use of 1-6 aspirin per week is associated with a substantial reduction in the risk of a first myocardial infarction among women.

Menopause and Serum Cholesterol: Differences Between Blacks and Whites

Jasenka Demirovic, J. Michael Spratka, Aaron R. Folsom, David Laitinen, Henry Blackburn. School of Public Health, University of Minnesota, Minneapolis, MN

To test the hypothesis that menopause (natural and surgical) increases total serum cholesterol (TC) and decreases HDL cholesterol (HDL-C) in both black and white women, we carried out an analysis of 384 black and 537 white women aged 35-54 who participated in the population-based Minnesota Heart Survey in 1985-1986. A linear regression model was used for black and white women separately, and included potential confounders: age, education, body mass index, cigarette smoking, physical exercise, alcohol consumption, diabetes mellitus, and sex hormones, beta-blockers and diuretics use. After controlling for the confounders, white postmenopausal women had significantly higher TC compared to premenopausal women (204.6 versus 191.6 mg/dl, p < 0.002). This effect was mainly due to natural menopause (p < 0.0003) whereas the effect of surgical menopause on TC in white women was of borderline significance (p < 0.06). In black women, neither natural nor surgical menopause significantly affected TC (estimated difference of 5 mg/dl, p >0.2). No significant relationship of natural or surgical menopause to HDL-C was found in both blacks and whites. The results concerning TC may reflect a true physiologic difference between black and white women. The absence of any significant menopausal change in HDL-C indicates that estrogen deprivation due to menopause may not substantially affect atherosclerosis risk mediated through HDL-C, in both blacks and whites.
Black-White Differences in Serum Estrogens and Lipids in Elderly Women.
Jane A. Cauley, James P. Gutai, Lewis H. Kuller, Dennis M. Black. University of Pittsburgh, Pittsburgh, PA.

In an attempt to understand racial disparities in coronary heart disease, we analyzed differences in serum estrogens (estrone/estradiol) and serum lipids in 272 white women (mean age 73.7 ± 5.8 years), and 87 black women (mean age 71.4 ± 4.9 years). None of the women were on estrogen replacement therapy. Data are complete for whites and for sex hormones, but lipid data in blacks is limited to 72 women. Both serum estrogens were significantly higher in blacks, even after adjusting for age, body mass index (BMI), and waist-to-hip ratio. The unadjusted mean estrone in whites was 36.8 ± 44.6 pg/ml in blacks, p < 0.0001. For estradiol, the mean for whites was 3.2 ± 9.5 pg/ml in blacks, p < 0.0001. There were no differences in total cholesterol by race. Both total high density lipoprotein cholesterol (HDL-TC) and HDL-2C were significantly higher in blacks vs. whites: HDL-TC, 57.3 ± 55.8 mg/dl; HDL-2C, 20.9 ± 15.9 mg/dl. Differences in HDL-TC and HDL-2C became more marked once we adjusted for BMI. Unadjusted HDL-3C levels were slightly higher in blacks. Once we controlled for BMI, whites actually had significantly higher HDL-3C. Serum sex hormones were not related to lipids in whites. For blacks, a positive relationship between HDL-TC and estrone and estradiol was present, but not significant once we controlled for BMI. Stratification by BMI (kg/m²) ("low" < 30.0 vs. "high" ≥ 30.0) revealed little difference in lipids by race in the "high" BMI group. In the "low" BMI group, blacks had significantly higher HDL-2C, but lower HDL-3C than whites. In conclusion: 1) racial differences in sex hormones do not appear to contribute to racial differences in lipids; and 2) the degree of obesity is an important modifier of racial differences in lipids.

Gender and In-Hospital Mortality Associated With Coronary Artery Bypass Grafting

Increased risk of in-hospital mortality experienced by women undergoing CABG has been attributed to the presence of more severe cardiovascular disease at the time of referral. In a prospective regional study of 3,371 patients (26% female) undergoing CABG at 5 medical centers, the in-hospital mortality rates for women (7.0%) and men (3.1%) differed; odds ratio (OR)=2.3; p<0.0001. Adjusting for demographic data, cardiac catheterization results, priority at surgery, intensity of therapy, and co-morbidity did not substantially change these results: adjusted OR=2.0; p<0.0002. Body surface area (BSA) differed between women and men (means 1.69 vs. 1.96; p=0.0001) and was inversely related to mortality (p=0.003) among both genders. In multivariate analysis, BSA was an independent predictor of mortality (p=0.014). After adjustment for BSA, gender no longer significantly predicted in-hospital mortality (p=0.09). Intra-operative measurements of coronary artery diameters were made on 955 patients. Significant positive correlations (p=0.02 to <0.0001) were found between BSA and coronary artery diameter. In these data, BSA may be a proxy for myocardial vessel size. The observed gender related differences in in-hospital mortality associated with CABG may be a consequence of anatomical differences associated with gender rather than severity of disease. In these data, small men are also at increased risk of mortality.

Use of Lower Dose Oral Contraceptives and Risk of Myocardial Infarction
Lynn Rosenberg, Julie R. Palmer, Samuel Shapiro. Stone Epidemiology Unit, Brookline, MA.

Studies conducted in the 1970s indicated that women who were using oral contraceptives had a 3-4 fold greater risk of myocardial infarction (MI) than nonusers; the increase in risk was much greater for pill users who smoked heavily. In a hospital-based case-control study conducted from 1985 to the present among premenopausal women aged 25-44, we assessed the effect on MI risk of the newer lower dose preparations currently in use. Among 153 cases of first MI and 641 hospital controls, 10 cases and 48 controls were current users of oral contraceptives; the age-adjusted relative risk estimate was 1.5 (95% CI 0.8-3.7). For women who smoked 25 or more cigarettes a day and used oral contraceptives relative to those who did not smoke or use oral contraceptives, the estimate was 3.1 (95% CI 1.8-5.1); this estimate did not differ significantly from that for heavy smoking alone (RR = 1.1, 95% CI 6.7-17). The results suggest that, overall, the newer oral contraceptives are safer than the older higher dose pills. When the study is completed the sample size will be almost doubled, and it should be possible to determine whether they are also safer for use by heavy smokers.

Insulin and Sodium-sensitivity: Preliminary Findings of a Clinical Trial
Maurizio Trevisan, Alma Blake, Vittorio Krogh, Steven Gutai, Thomas Rosenthal, Teresa Quattrin, Joan Dorn, State University of New York at Buffalo, Buffalo, NY.

We present the preliminary findings of a nutritional trial aimed at investigating the role of a number of hormonal and metabolic factors in predicting the blood pressure response to sodium restriction in a group of normotensive individuals (n=50). Volunteers were randomly assigned to either the control (n=23) or low sodium group (n=27). At the end of six weeks of intervention, participants in the low sodium group experienced a larger decrease in systolic blood pressure (SBP) (Δ = -5.7 mm Hg) compared to participants in the control group (Δ = -1.3 mm Hg). In the sodium restricted group, baseline SBP and plasma insulin were both independently associated with SBP changes over the six weeks of the nutritional intervention (r = -0.65 and r = -0.27 respectively). These associations were not present in the control group. These preliminary findings indicate that blood pressure and plasma insulin could be important indicators of sodium sensitivity in normotensive individuals. Insulin, because of its hypothesized effects on renal sodium retention, could play an important role in determining blood pressure response to dietary sodium restriction.
Low plasma high density lipoprotein (HDL)-cholesterol concentration is a risk factor for coronary heart disease (CHD), and is frequently associated with high triglyceride (TG) concentration. Both abnormalities have been related to insulin resistance as estimated by plasma insulin concentrations, and to obesity, regional adiposity and physical fitness. To determine which of these variables, fasting plasma insulin, obesity estimated by body mass index (BMI), or abdominal adiposity measured by waist-to-hip ratio (WHR) best identifies men with low HDL-cholesterol and high TG concentrations, we divided 83 men ages 50-65, free of CHD or diabetes, into tertiles based on BMI, WHR or fasting plasma insulin. Only for plasma insulin tertiles were there statistically significant differences in HDL-cholesterol (tertile I, mean ± SE, 1.34 ± 0.08 mmol/L; II, 1.16 ± 0.05 mmol/L; III, 1.11 ± 0.06 mmol/L, p<0.03) and TG (tertile I, 1.05 ± 0.08 mmol/L; II, 1.48 ± 0.12 mmol/L; III, 1.82 ± 0.17 mmol/L, p<0.005) concentrations. In forward stepwise regressions with HDL-cholesterol and TG as dependent variables, fasting insulin concentration but not BMI, WHR or V0max, a measure of physical fitness, predicted HDL-cholesterol (R²=0.07, p<0.02) and TG concentrations (R²=0.20, p<0.001). The data suggest that plasma insulin concentration is an important predictor of HDL-cholesterol and TG concentrations independent of BMI, WHR or V0max.

Cross sectional studies have found a positive correlation between insulin and blood pressure. However, prospective data showing that insulin predicts blood pressure change (BPs) are lacking. We studied a biracial group of young adults aged 18 to 30 years at the first CARDIA examination to determine whether a single baseline (BL) insulin predicted 2 year BPa. A race-specific multivariate analysis was performed to determine the effect of BL insulin on BPa independent of potential confounders. Potential confounders included in these models were BL sum of triops and subcutaneous skinfolds, Δ in sum of skinfolds, family history of hypertension, BL pulse, BL blood pressure, BP medication status, physical activity (PA) score, Δ in PA score, age, time to reach heart rate 130 on the treadmill, SBP alone during treadmill testing, and gender. These models predicted approximately 30% of the variability in BPa and DBPa in both races. In whites, BL insulin (uU/ml) was positively related to DBPa (beta =0.063, p=0.037); the relation with SBP was in the same direction (b=0.054, p=0.07). In blacks, BL insulin was not predicted DBPa (b=0.09, p=0.24) or SBPa (b=0.041, p=0.11). These data provide new prospective evidence that insulin predicts DBPa independent of fatness, at least in whites. Furthermore, our data suggest that, in whites, insulin may also predict SBPa.

Vitamin D and Calcium Intake and Subsequent Risk of Stroke in a Cohort of Iowa Women
Ronald Munger, Aaron Folsom, Lawrence Kushi, Ronald Prineas, Paul Romiti, Yuki-Kun Li, Robert Wallace. University of Iowa, Iowa City, IA

Nutrient intake at baseline in January 1986 and subsequent risk of stroke were examined in a cohort of 41,837 Iowa women. Stroke occurrence over the next 2 years was ascertained by self-report and death certificate review, yielding 58 cases free of hypertension and heart disease at baseline. In a nested case-control study, 290 controls were randomly selected and age-matched to cases; the mean age was 64 years. Mean intakes of calories, fat, carbohydrate, fiber, sodium, and potassium did not differ significantly between cases and controls. Cases, compared to controls, had lower mean calorie-adjusted intakes of vitamin D (193 IU, SD 153, vs. 255 IU, SD 197, p<0.01) and calcium (574 mg, SD 305. vs. 658 mg, SD 329, p<0.07). Comparing the lowest with the highest tertile of intake, stroke risk was 2.5 times greater among those with low vitamin D intake (95% CI 1.2-5.6) and 2.2 times greater among those with low calcium intake (95% CI 1.1-4.5). After adjustment for smoking, estrogen use, and waist/hip ratio, the odds ratio estimate of stroke risk was 3.2 for low vitamin D intake (95% CI 1.4-7.4) and 2.1 for low calcium intake (95% CI 1.0-4.3). Low vitamin D and calcium intake may be a cause of stroke in postmenopausal women.
Advantages of Quantitative Imaging in the Study of Atherosclerosis

Thomas A. Pearson. M. I. Bassett Research Institute, Cooperstown, NY

Methods to quantitatively image atherosclerosis provide several opportunities to better understand the epidemiology and natural history of coronary heart disease, stroke, and peripheral arterial disease. First, atherosclerosis is studied rather than clinical manifestations. Risk factor-disease associations verify that a specific risk factor is not only related to subjective clinical events, but objective pathologic events as well. Second, studies of risk factors for clinical manifestations can adjust for the amount of atherosclerosis, allowing identification of risk factors which act after atherosclerotic plaque formation to cause clinical events. Third, serial measures of disease can be used to describe the natural history of atherosclerotic disease, including the role of risk factors. Finally, interventions can lower risk factors to determine the efficacy of the intervention in slowing or even reversing the disease process. Since the endpoints for such serial measures are often continuous progression or regressions scores, the sample sizes and study durations are vastly smaller than for those studies using clinical endpoints. The aforementioned advantages assure that, in the foreseeable future, many epidemiologic studies and most clinical trials of risk factor interventions will be employing quantitative imaging of atherosclerosis as their primary endpoints.

Current Methods to Measure Atherosclerosis

John R. Crouse. Bowman Gray School of Medicine, Winston-Salem, NC

Methods for quantifying atherosclerosis that focus on lumen diameter are most useful to define disease severity, while those that focus on the artery wall are somewhat better suited to define extent and characteristics of disease.

Angiography and Doppler Ultrasound both quantitate lumen diameter. Use of computerized information processing has improved these methods’ precision and reliability, but they are inherently limited in their ability to quantitate extent of disease. These methods are most useful to identify determinants of clinical outcome. Doppler ultrasound is non-invasive and thus has an added advantage for epidemiologic studies. B-Mode Ultrasound of peripheral vessels is another recently validated non-invasive technique that has gained acceptance. It is advantageous for studies of early disease because it images the artery wall. Intra-arterial ultrasound and magnetic resonance imaging, two other methods for imaging the artery wall, are under development.

It is not yet known whether other methods now on the horizon (such as those for quantifying wall stiffness) will possess the ability to define disease at a yet earlier stage.

Different methods complement each other and may be more or less appropriate depending on study design and research question.

Progression and Regression of Coronary Atherosclerosis: A Prospective, Quantitative Angiographic Analysis

David Waters, Jacques Lespérance, Gilles Hudon, Lucien Campeau. Montreal Heart Institute, Montreal, Canada

The evolution of coronary atherosclerosis was prospectively assessed by repeat arteriography after 24 months in a series of 335 pts aged 56 years with 5 to 75% stenoses in 24 coronary segments. A radiologist, blinded to the order of the films, viewed them together to select frames for quantitative measurement, done using the CAAS system of Reiber et al. Coronary occlusion developed in 2.4% (49/2,085) of stenoses ≤ 80% on the first arteriogram; the risk of occlusion increased from 0.5% for lesions ≤30% to 21% for lesions 70–79% (p<0.001). Progression ≥10% in stenosis severity occurred in an additional 13% of lesions (263/2,085) and was independent of the degree of stenosis at baseline. Regression by ≥10% was seen in 12% (114/942) of stenoses ≥40% on the first angiogram. For lesions initially between 40 and 70%, regression was usually (54/69, 78%) minor, between 10 and 20%. For lesions initially ≥70%, most regression (38/45, 84%) was by ≥20% and thus could have been due to thrombus remodelling. Correlations between clinical features, including risk factors, and these angiographic findings will be presented.

Risk Factor Studies Using Noninvasive Methods

G. Heiss, University of North Carolina, Chapel Hill, N.C.

Several reports provide evidence of a relation between age, male gender, cigarette smoking, hypertension, and hyperlipidemia with atherosclerotic lesions or stenosis of the extracranial carotid arteries measured by ultrasound. Even in the absence of discrete plaque or stenosis, an association can be found between risk factors and the combined thickness of the arterial intima and media. Using this B-mode ultrasound technique to identify 386 cases of carotid atherosclerosis and their matched controls, investigators of the Atherosclerosis Risk in Communities (ARIC) Study observed the following:

<table>
<thead>
<tr>
<th>Multivariable</th>
<th>Adjusted (#)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds Ratio</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Smoker vs. Never Smokers</td>
<td>3.90</td>
<td>(2.56, 5.93)</td>
</tr>
<tr>
<td>Hypertensive vs. Normotensive</td>
<td>2.89</td>
<td>(1.94, 4.31)</td>
</tr>
<tr>
<td>Total Cholesterol ≥240 vs. &lt;200 mg/dL</td>
<td>2.15</td>
<td>(1.44, 3.23)</td>
</tr>
<tr>
<td>LDL-Cholesterol ≥160 vs. &lt;100 mg/dL</td>
<td>1.55</td>
<td>(1.05, 2.28)</td>
</tr>
<tr>
<td>HDL-Cholesterol ≥35 vs. ≥35 mg/dL</td>
<td>1.71</td>
<td>(0.99, 2.94)</td>
</tr>
<tr>
<td>Total Triglyceride ≥170 vs. &lt; 170 mg/dL</td>
<td>1.74</td>
<td>(1.15, 2.64)</td>
</tr>
</tbody>
</table>
Invasive vs Noninvasive Studies of Risk Factors and Atherosclerosis
A Richey Sharrett. National Heart Lung and Blood Institute, Bethesda MD

Atherosclerosis may be assessed invasively (e.g. coronary angiography) or non-invasively (e.g. ultrasound imaging of extracranial carotid arteries, performed either in clinical settings or in representative population samples). Studies of risk factor associations using these two methods differ in their intrinsic potential for bias. Non-differential misclassification of cases and controls occurs with each method as a result of its particular limits of precision. This biases associations toward the null. Biases in either direction occur with differential misclassification, which is more likely in clinical studies. Some such biases (e.g. medication use) can be recognized and controlled for in analyses. Others, unrecognized or inaccurately measured, produce residual confounding. Both lipid and blood pressure associations may be affected. If biases were minimized, studies by invasive and non-invasive methods would reveal different risk-factor associations if coronary and extracranial atherosclerosis differed etiologically. Limited available evidence suggests, however, that these differences are slight. There may be pathogenetic differences between early intra-mural lesions detectible by ultrasound and lumen-encroaching lesions seen on angiography.

Observational Studies of Atherosclerotic Progression
Jukka T. Salonen, Riitta Salonen. University of Kuopio, Kuopio, Finland

We have investigated biological and psychosocial determinants of the progression of atherosclerosis in 128 randomly sampled Eastern Finnish men examined in 1987 and 1989 in the Kuopio Ischaemic Heart disease Risk Factor Study (KIHDS). The maximal thickness of the intima-media complex of common carotid artery far wall was assessed with high resolution (10 MHz) B-mode ultrasonography by one observer (RS) twice with an interval of exactly 24 months. The strongest baseline risk factors for atherosclerosis progression were age, cigarette pack-years and S-LDL-cholesterol. S-LDL-C was a risk factor only when serum copper above median, and this synergism was stronger in men with low serum selenium. Also serum copper and selenium (inv), plasma vitamin C (inv), platelet aggregability and blood leukocyte count were independent, although weaker, determinants of atherogenesis. Of the psychosocial factors studied, cynical distrust-hostility and anger had residual associations with atherosclerosis progression.

The Progression/Regression of Atherosclerosis And Randomized Trials. The FATS example.
B. Greg Brown, Qiao Zhao, John J. Albers, University of Washington, Seattle, WA

The FATS trial is a randomized, fully blinded, quantitative arteriographic comparison of 3 lipid-altering strategies. Men, age ≤ 62 yrs, with disease, a family history of premature cardiovascular events (CVE), and with apolipoprotein B ≥ 125 mg/dl were counseled in diet and assigned to niacin (N) 4 gm/d, plus colestipol (C) 30 gm/d, or to lovastatin (L) 40 mg/d plus C, or to conventional therapy (CON=placebo + C). Bimonthly visits spanned 2.5 years between coronary arteriograms. Stenosis change (Δ%S) was averaged over the same 9 proximal segments in each patient. Lesion Δ%S was "progression" (PR) if ≥ 10% or "regression" (RE) if ≤ -10%. CVE were death, proven MI, or newly refractory ischemic symptoms requiring bypass surgery or angioplasty. Results are expressed in patient-based measures:

<table>
<thead>
<tr>
<th>Rx</th>
<th>N</th>
<th>LDL</th>
<th>HDL</th>
<th>CVE</th>
<th>Δ%S</th>
<th>PR</th>
<th>RE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON</td>
<td>36</td>
<td>-7</td>
<td>5</td>
<td>11</td>
<td>2.7±3</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td>L+C</td>
<td>38</td>
<td>-6**</td>
<td>6**</td>
<td>15**</td>
<td>-0.7±4*</td>
<td>8</td>
<td>12*</td>
</tr>
<tr>
<td>N+C</td>
<td>36</td>
<td>-32**</td>
<td>43**</td>
<td>2</td>
<td>2.9±4**</td>
<td>9</td>
<td>14**</td>
</tr>
</tbody>
</table>

Versus CON: *p<.05; **p<.01
Favorable changes in clinical course and lesion severity appear mediated by change in both LDL and HDL.

Methodologic Issues Facing Studies of Atherosclerotic Change. Jeffrey L. Probstfield, Susan E. Marpiscic, Curt D. Furberg, NHLBI, Bethesda, MD

Studies that assess risk factor modification and atherosclerotic change must measure arterial wall lesions. Endpoint selection and ascertainment methods are important. But, quantifying disease and evaluating subsequent change remain the key issues. Measurements must be valid, precise and reliable, and require appropriate a priori definitions of lesions and their change. Consistent methodology across and throughout the study is crucial. Multiple measurements are essential and data reduction methods merit consideration. Problems include imputing values for those with missing data and the attendant validity. Identifying predictors of atherosclerotic change and appropriate interventions mandate monitoring biochemical, physiologic and/or clinical variables and making inferences from these. Key research objectives include observing clinical outcomes to validate arterial wall changes and optimizing the risk and cost/benefit ratios. Several current epidemiological studies and clinical trials are addressing these issues.
Poster Presentations

Precursors of Hypertension. Steven Haffner, Michael Stern. UTHSC, San Antonio, TX.
While several studies have shown that insulin (INS) resistance is characteristic even of non-obese hypertensive (HBP) subjects, few data are available on the metabolic precursors of HBP. We examined the development of HBP (diastolic BP >95 mmHg or current use of anti HBP meds) in 1089 subjects who were free of HBP at baseline. Subjects were studied in the 8-year follow-up of the San Antonio Heart Study cohort. One hundred incident cases of HBP were identified.

<table>
<thead>
<tr>
<th>Age</th>
<th>BMI</th>
<th>Insulin</th>
<th>LDLc</th>
<th>HDLc</th>
<th>TG</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBP</td>
<td>46.7</td>
<td>27.4</td>
<td>14.5</td>
<td>135</td>
<td>49.3</td>
</tr>
<tr>
<td>N1</td>
<td>44.0</td>
<td>25.5</td>
<td>11.4</td>
<td>113</td>
<td>54.1</td>
</tr>
<tr>
<td>p-values</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.19</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Thus, the metabolic precursors of HBP include increased overall adiposity, increased INS, TG, LDLc and decreased HDLc concentrations. After age and BMI adjustment, the TG and LDLc and HDLc differences remained statistically significant, though the INS differences did not. However, when only normoglycemic (2-hr glucose ≤140 mg/dl), non-obese subjects (BMI ≤25) were considered, the 25 converters to HBP had higher baseline INS concentrations (U/ml) than the 438 subjects who remained normal (16.2 vs. 10.1, p=0.02). Thus, converters to HBP may have increased LDLc and TG and decreased HDLc (even after adjustment for obesity) suggesting the occurrence of multiple lipoprotein abnormalities prior to the onset of HBP or anti HBP meds. Moreover, in a subset of normoglycemic, non-obese subjects (25% of pre HBP subjects), INS was also elevated.

Low Plasma Cholesterol and Mortality: The Lipid Research Clinics Follow-Up Study.
Jacques E. Rossouw, Shrikant I. Bangdiwala, Basil M. Rifkind. Lipid Metabolism-Atherosclerosis Branch, National Heart, Lung, and Blood Institute, Bethesda, MD
Participants aged 35-69 at baseline (3730 males, 3222 females) were followed for a mean of 12.2 years. Mortality from all causes numbered 569, from cardiovascular disease (CVD) 254, from cancer 222 and from other causes 113. Hazard rate ratios (HRR) relative to a cholesterol of 160-199 mg/dl were calculated, adjusting for age, DBP, cigs/day, alcohol intake, and BMI. In males, all-cause mortality showed a U-shaped relationship to cholesterol due to increased CVD at higher cholesterol levels (HRR 2.62, P<0.001 at cholesterol >240 mg/dl) and increased cancer mortality at low cholesterol levels (HRR 1.50, NS at cholesterol <160 mg/dl). In females, there was no clear trend for all-cause mortality; increased CVD at increasing cholesterol levels was countered by an opposite trend in non-CVD, non-cancer mortality. Excluding early deaths altered these relationships only marginally. Individuals with low levels of cholesterol had lower HDL cholesterol, alcohol intake, and educational levels; they had more weight loss and abnormal liver functions. These and other baseline characteristics may confound the associations of low cholesterol with mortality.

Serum Sterol Changes Suggesting Increased Synthesis and Decreased Absorption of Cholesterol With Increasing Blood Glucose in Middle-Aged Men
Timo E. Strandberg, Veilko V. Salomaa, Hannu T. Vanhanen, Vesa Naukkarinen, Seppo Sarna, Tatu A. Miettinen. Second Department of Medicine, University of Helsinki, SF-00290 Helsinki, Finland.
Lipid abnormalities probably contribute to the increased cardiovascular risk in diabetic patients. We studied associations between serum lipids and tertiles of fasting blood glucose (I ≤4.45, II 4.45 - 5.05, III >5.05 mmol/l; range 3.7-12.5 mmol/l) in 221 middle-aged men participating in a follow-up study of cardiovascular diseases. Only six men were on antidiabetic drugs. We used analysis of variance and covariance. Special emphasis was put on serum cholesterol precursors (lathosterol and desmosterol) which reflect hepatic cholesterol synthesis, and serum plant sterols (campesterol and sitosterol) which reflect intestinal cholesterol absorption. Serum concentrations of cholesterol, HDL-cholesterol, triglycerides and apoproteins B and A-I were not significantly different between the three groups, whereas body mass index (BMI) was significantly (p<0.05) increased in III compared to I. The serum concentrations of lathosterol and desmosterol were significantly (p<0.05) increased and those of plant sterols decreased in III as compared to I. The plant sterol differences persisted after adjustment of the values for serum linoleic acid (used to reflect dietary intake of plant sterols), as well as for serum triglyceride level and BMI. Factors also related to serum contents of plant sterols. The results suggest increased hepatic cholesterol synthesis and decreased intestinal cholesterol absorption even at moderately elevated blood glucose. The findings may have implications in choosing hypcholesterolemic treatment for hyperglycemic patients.
Long Term Effect of Estrogen Use on Cardiovascular Death in Women. Results from the Lipid Research Clinics (LRC) Follow-Up Study.

Trudy L. Bush for the LRC Estrogen-CVD Working Group, Johns Hopkins University, Baltimore, MD.

We previously reported from the LRC Program that after 8 years of follow-up, women using estrogen at baseline had a 66% reduction in CVD mortality compared to non-users. We now report on 14 years of follow-up in the same cohort, which was identified in 1972-1974. Currently, there are 20,333 person years of follow-up (FYUP) among non-users (N=1677) & 7,372 FYUP among users (N=593). After 14 years, women using estrogen had significantly lower total (47%) and CVD mortality (65%). Cancer mortality also was lower in users (19%). Estrogen protected women with & without CVD risk factors, & protected at each level of each risk factor examined. For example, estrogen was protective in non-smokers (relative risk [RR]=0.13, ex-smokers [RR=0.50] and current smokers [RR=0.36]. Further, estrogen appears to negate the effect of the risk factors on CVD death, i.e., users who smoked had the same CVD risk as non-smoking, non-users; users with hypertension had the same risk as normotensive non-users, & obese users had the same risk as non-obese non-users. Adjustment (Cox model) for smoking, hypertension, HDL & LDL did not alter the significant protective effect of estrogen use on CVD risk. These results suggest that estrogen use has long term beneficial effects on CVD risk. Also, estrogen may protect through mechanisms in addition to changes in lipoproteins.

Children's Pressor Reactivity and Subsequent Blood Pressure. Joseph K. Murphy, Bruce S. Alpert, and Sammie S. Walker, Miriam Hospital, Providence, RI.

This longitudinal study sought to determine if BP reactivity to a psychologic stressor (a television video game; VG) was associated with subsequent resting (R) BP. In Year 1, children enrolled in 3rd grade of the public schools of an entire county were eligible: 481 of 484 (99.3%) were studied. Measures included height, weight (Quetelet = weight [kg]/height [m]²), activity level, salt intake, and both BP and HR both at R and during the VG. R and VG measurements were each performed 3 times. In Year 3, R measurements were performed on 400 of the 481 (83.2%) of the children studied in Year 1. Stepwise regression analysis of Year 1 data on Year 3 R-BP (Table; entries represent % of variance in Year 3 R-BP)

<table>
<thead>
<tr>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-BP</td>
<td>0.28</td>
</tr>
<tr>
<td>VG-BP</td>
<td>0.06</td>
</tr>
<tr>
<td>Quetelet</td>
<td>0.03</td>
</tr>
<tr>
<td>R-HR</td>
<td>0.01</td>
</tr>
</tbody>
</table>

indicated that pressor reactivity was significantly associated with later SBP and DBP (both p<0.0001).

Results indicate that assessments of pressor reactivity may aid the detection of children whose BP will rise over time; longer follow-up is needed to determine the clinical importance of these data.

Age, Body Size, and Blood Pressure Affect Children's Left Ventricular Mass (LVM): The Muscatine Study

Donald D. Malcolm, Trudy L. Burns, Larry T. Mahoney, Ronald M. Lauer, University of Iowa, Iowa City, Iowa

LVM was measured using M-mode echocardiography in 906 children, 6-16 years, in Muscatine, Iowa. Age, gender, height, weight, and weight-gender specific Z-scores were determined for LVM, weight (Wt), height (Ht), and systolic blood pressure (SBP).

<table>
<thead>
<tr>
<th>LVM Quintile</th>
<th>Age-Ht-Wt</th>
<th>Mean Z-Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-Gender</td>
<td>SBP</td>
<td>Wt</td>
</tr>
<tr>
<td>Ht-Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wt-Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72-75</td>
<td>5-5</td>
<td>0.16*</td>
</tr>
<tr>
<td>21-23</td>
<td>5-4</td>
<td>-0.20</td>
</tr>
<tr>
<td>44-47</td>
<td>5-1-4</td>
<td>1.50</td>
</tr>
<tr>
<td>44-50</td>
<td>5-5</td>
<td>0.67*</td>
</tr>
</tbody>
</table>

* p < 0.0001; t p < 0.005; * p < 0.05

Children with LVM high for age, Ht, and Wt were heavier suggesting an independent correlation between Wt and LVM. Those with high LVM for age and Wt, but not Ht, were taller and had lower Wt and SBP for their Ht consistent with an independent association between Ht and LVM. Children with high LVM for age only, were taller, heavier and had higher SBP, with SBP higher for Ht and Wt, suggesting SBP may be independent of body size in its association to LVM. When LVM was high for Ht and Wt but not age, the children were shorter and thinner and had appropriate blood pressure for age, Ht, and Wt. Therefore age may exert an independent influence on LVM. Thus relationships of body size, age, and blood pressure must be considered when evaluating high LVM in childhood. This is particularly important when studying the affects of BP on LVM in childhood.

Prevalence of Left Ventricular Hypertrophy by Electrocardiogram in Blacks and Whites: Are Racial Differences Overestimated?

Dara K. Lee, Paul R. Marantz, Hillel Cohen, Richard B. Devereux, Michael H. Alderman. Albert Einstein College of Medicine, Bronx, NY.

Compared with echocardiogram (echo), the ECG has a low sensitivity for detection of left ventricular hypertrophy (LVH). Because of the increased prevalence of ECG-LVH in blacks, the impact of race on the ability of ECG to identify patients with echo-LVH was studied in members of a worksite hypertension program (159 blacks and 185 whites). ECGs were coded by program physicians. M-mode echos were read in blinded fashion, with echo-LVH defined as LV mass index ≥ 311 g/m² in men and ≥ 231 g/m² in women. Blacks had a higher prevalence of ECG-LVH than whites (13.2% vs 3.2%, p<0.01). However, the prevalence of echo-LVH was similar in blacks and whites (26.4% vs 20.3%, p>0.2). The ECG had a sensitivity of 22.5% in blacks compared to 8.6% in whites. Specificity was lower in blacks (89.9%) than in whites (97.9%). Black race remained a significant independent predictor of increased sensitivity and diminished specificity after logistic regression adjusting for age, gender, BMI, and smoking. The ECG is a significantly more sensitive measure of LVH in blacks than in whites, and thus may exaggerate racial differences in LVH prevalence.
Years of Education and Blood Pressure: Findings of the INTERSALT Study

Rose Stamler, Martin Shipley, Paul Elliott, Alan Dyer, Susana Sans for the INTERSALT Collaborative Group. Northwestern University Medical School, Chicago, IL

Inverse association between social class and disease has been reported; education, an indicator of social class, is negatively related to blood pressure (BP) in many studies, although reasons are not fully clear. INTERSALT, an international study on electrolytes and BP, obtained data on years of education for 10,000 persons in 52 centers in 32 countries. Data here are for 47 centers, omitting 5 with no education or differences in education level. Regression coefficients were calculated for the education-BP association in each center. For systolic BP (SBP), adjusted only for age-sex, 39 centers had negative coefficients, with 5 significant. However, with adjustment also for 4 lifestyle factors (sodium, potassium, body mass, alcohol), there were 34 negative coefficients, 1 significant. Study-wide estimate was for a 2.3 mmHg lower SBP (95% CI 1.5-3.0) for 8 years' more education, when adjusted for age-sex; the estimate was reduced to 1.4 mmHg (95% CI 0.6-2.1) when the other 4 lifestyle factors were included. While INTERSALT confirmed the negative education-BP association, several lifestyle factors related to both education and BP confounded the association, and accounting for them reduced its magnitude.

Coffee Intake and Coronary Heart Disease (CHD)

Michael J. Klag, Lucy A. Mead, Andrea Z. LaCroix, Kung-Yee Liang, David M. Levine. Johns Hopkins University, Baltimore, MD

Coffee use is a prevalent habit that has been linked to CHD in some, but not all, studies. We examined this issue in 1,040 former male medical students (mean age 26 years) follow-up for 24 to 40 years. Coffee use was assessed in medical school and at 5-year intervals. CHD incidence was assessed by yearly questionnaires, review of medical records, resting ECG and death certificates; 94 CHD events (57 MI, 30 angina) occurred. Coffee intake measured in medical school (p<0.001) and averaged over the duration of follow-up (p<0.03) was associated with CHD in Kaplan-Meier analysis. The increased risk associated with baseline coffee intake was present in both non-smokers (p<0.05) and smokers (p<0.2). In proportional hazards analyses adjusting for age, serum cholesterol in medical school and the time-dependent covariates cigarette smoking and incident hypertension, the relative risks (95% CI) associated with 5 cups of coffee/day were 1.86 (1.03, 3.28) for baseline, 2.72 (1.35, 5.49) for average and 2.01 (1.13, 3.56) for most recent intake. These risks were stronger when MI was used as the outcome. These results confirm an independent, dose-response relationship between coffee intake and CHD in this cohort and support the recommendation that men should limit their intake of coffee.

Self-Esteem and Obesity in Black and White Girls: the NHLBI Growth and Health Study (NGHS)

Sue Y.S.Kimm, Bruce A. Barton, John Morrison, Zak Sabry, George B. Schreiber. University of Pittsburgh, Pittsburgh, PA

It is believed that obesity impacts self-esteem negatively and that self-esteem is impaired when there is lack of congruence between our perception of self and of how others see us. Since obesity is much more prevalent in adult black (B) women than white (W) women, B girls (BG) may suffer less in self-esteem from obesity. This study assesses correlates of self-concept in 9-10 year old B and W girls (G) enrolled in NGHS, a longitudinal study of obesity development. The Harter Scale of Self-Perception was administered to 1180 B and 1144 W. Overall, B and W scored the same on Self Worth (SW) and Social Acceptance (SA) subscales, but obese [-75th %ile Quetelet Index (QI)], BG scored higher than obese W on Physical Appearance (PA) and SA. Multivariate analyses revealed that among B, obesity was negatively(-) correlated with SW, Scholastic Competence (SC) and PA. For W, obesity was (-) correlated with SA. When obesity was defined as >90th %ile QI, it was correlated (-) to SW for W and BG. For W, obesity(-) and income(+) were related to SA while age (+) was also related for BG. For PA, obesity(-) for W, and obesity(-) and age (+) for BG were correlated. Though BG in the upper decile of QI scored lower on PA than other BG, they found it more socially acceptable than did W in the upper decile.

Multiple Measurements Enhance Blood Pressure Tracking from Childhood to Early Adulthood.

Matthew W. Gillman, Nancy R. Cook, Bernard Rosner, Denis A. Evans, Mary E. Keough, James O. Taylor, Charles H. Hennekens. Boston University and Harvard Medical Schools, Boston, MA.

Blood pressure (BP) tracking correlations (r) within childhood can be raised by averaging BP over several weekly visits in each year. "True r" can be calculated by fully correcting for within-person variability, the statistical equivalent of measuring BP on an infinite number (∞) of visits.

To extend these findings to a longer interval covering the important crossover period from childhood to early adulthood, we re-examined, at age 18-26 years, 318 (94%) of 337 former school children whose BP was ascertained 8-12 years previously. In both childhood and adulthood, we obtained 3 BP readings on each of 3 visits, one week apart, with a random-zero sphygmomanometer.

Age- and sex-adjusted r for the 8-12 year follow-up interval, based on mean BP from 1, 2, and 3 visits at each time, were 0.33, 0.37, 0.41, and 0.47, respectively, for systolic BP and 0.19, 0.29, 0.32, and 0.44, respectively, for diastolic BP.

The use of "true r" allows determination of the maximal extent to which childhood BP can predict adult levels, and therefore the usefulness of screening children for those at high risk of developing hypertension.
Hospital Discharge Surveillance for Stroke in Young Adults

Karen J. Mason, Mary Jane Seipp, Steven J. Kittner, Constance J. Meyd, David Buchholz, Barney J. Stern, Michael Sloan, Thomas E. Price, University of Maryland, Baltimore, Maryland

In order to evaluate the efficiency of the hospital discharge surveillance procedures in our registry of ischemic stroke in young adults, we examined the yield of the various ICD-9 codes. Charts having ICD-9 codes 431-438, 671.50-671.54 and 674.00-674.04 were abstracted by a trained nurse and reviewed by a panel of neurologists using written criteria. Out of 148 charts with only one ICD-9 code in the range of interest, 44 (30%) were found to be ischemic strokes. The yield for the different ICD-9 codes are as follows: 431 (1/14, 75%); 432.0-432.9 (0/4); 433.0-433.9 (5/12, 42%); 434.0-434.9 (29/46, 63%); 435.0-435.9 (1/18, 6%); 436 (3/6, 50%); 437.0-437.9 (0/14); 438 (1/11, 9%); 671.50-671.54 (1/2, 50%); 674.00-674.04 (1/2, 50%). Forty-one percent fewer charts could have been abstracted, with a loss of 7% of the cases, by excluding charts having code 431, 432.0-432.9, 435.0-435.9, 437.0-437.9, and 438 only. These results may be useful in developing surveillance strategies for ischemic stroke in young adults based on hospital discharge codes. Charts with code 430 only were not reviewed on the basis of results from the literature and our own experience.


Paul G. McGovern, Gregory L. Burke, Katherine M. Doliszny, J. Michael Sprafka, and Henry Blackburn, University of Minnesota, School of Public Health, Minneapolis, MN

While coronary heart disease (CHD) mortality has steadily declined between 1970 and 1985 in both men and women in Minneapolis-St. Paul (MSP), in-hospital acute myocardial infarction (MI) rates have remained stable. The relationship between improved survival of hospitalized MI patients and the reduction in CHD mortality was assessed. Four-year survival of a 50% sample of MSP residents hospitalized in 1970 (n=749), 1980 (n=794), and 1985 (n=825) with validated definite MI was examined.

After adjustment for multiple severity indicators (e.g., previous MI, and heart rate and systolic blood pressure on admission), four-year survival improved from 1970 to 1985 for both men (RR=0.67; 95% CI: 0.54, 0.83) and women (RR=0.74; 95% CI: 0.54, 1.00) but there was no change from 1980 to 1985 (p>0.25). After adjustment for severity factors, short-term (28-day) mortality declined significantly from 1970 to 1980 in men (OR=0.61; 95% CI: 0.41, 0.91), but not in women (OR=0.64, 95% CI: 0.38, 1.00); no change occurred from 1980 to 1985 (p>0.25). Four-year survival among short-term survivors between 1970 and 1980 improved significantly in men (RR=0.67; CI: 0.51, 0.89) but not in women (RR=0.70; CI: 0.46, 1.00); there was no change from 1980 to 1985 (p>0.25).

These results point to improvements in survival among hospitalized MI patients between 1970 and 1980 but not between 1980 and 1985, and suggest that medical care contributed to the decline in CHD mortality only in the 1970 to 1980 time period.


Diane H. Jones and Earl Ford, Centers for Disease Control, Atlanta GA

Knowledge of risk precursors for cardiovascular disease (CVD) is a key component of health decisions and a common feature of intervention programs. National data have only recently been available to assess CVD knowledge and identify populations at risk. We examined CVD knowledge among Whites, Hispanics and Blacks (n=25,518) with data from the 1985 Health Promotion Disease Prevention Supplement. Knowledge of CVD risk associated with hypertension, smoking and obesity was twice as high the knowledge of diabetes, history of heart disease and dietary fat as risk factors. The effects of socioeconomic factors, type of medical care, region and 7 self-reported risk factors on levels of CVD knowledge by race and sex were estimated using multivariate analyses. Education was the strongest predictor in all groups. Those with self-reported risk factors requiring physician diagnosis and those with regular health care showed greatest knowledge. Studies have shown Blacks have a higher recognition of hypertension as a CVD risk factor than Whites; this was not found. Results suggest population segments where education efforts could be best directed, e.g., those not completing high school, the elderly and minority populations, those with self-reported risk factors or those without health care.
Ability of NCEP Guidelines to Identify Young Adults With High LDL Cholesterol: The CARDIA Study

Samuel Gidding, Kiang Liu, Julius Cardin, John Flack, Stephen Hulley, Northwestern University Medical School, Chicago, IL

The NCEP has recommended measurement of total cholesterol (TC) in all adults over the age of 20 yrs. We examined 4,446 men and women, blacks and whites, aged 18-30 yrs at study entry, to assess how well the average of two TC performed 2 yrs apart identified those with elevated LDL. LDL cholesterol values were defined according to NCEP guidelines (low = <130 mg/dl; borderline-high = 130-159 mg/dl; high = ≥160 mg/dl). LDL < 130 mg/dl was found in 3381/4446 (76.0%), with TC ≥ 200 mg/dl. LDL of 130-159 mg/dl was found in 775 (17.4%) and LDL ≥ 160 was found in 209 (6.5%). Of those with LDL between 130-159 mg/dl, 585/775 (75.3%) had average TC ≥ 200 mg/dl. Of those with LDL ≥ 160 mg/dl, all had TC ≥ 200 mg/dl. Overall, 1071/4446 (24.1%) had TC ≥ 200 mg/dl and 875/1071 (81.7%) had LDL ≥ 130 mg/dl. We conclude that when 2 specimens are drawn two years apart, average TC ≥ 200 mg/dl is excellent for detecting young adults with LDL ≥ 160 mg/dl and reasonably good for detecting those with LDL 130-159 mg/dl.

Grandparental History of High Cholesterol Enriches the Identification of Children at Risk: The MUSCARE Study

Linda E. Muhonen, Trudy L. Burns, Ronald M. Lauer. University of Iowa, Iowa City, IA.

During childhood, a parental history of coronary heart disease (CHD) is rare. In Muscatine, Iowa High School students (9th - 12th grade) completed the Utah Health Family Tree regarding medical history of their first and second degree relatives and had measurement of their height, weight, blood pressure, lipids, lipoproteins and apolipoprotein levels. Those who provided information about at least one grandfather were described in the table below. A history of early CHD in either the paternal or maternal grandfather was myocardial infarction, bypass or death from a heart attack between 40 and 55 years of age. History of high cholesterol (HiCH) was also determined.

<table>
<thead>
<tr>
<th>Grandfather History</th>
<th>Mean for Grandchild of CHD</th>
<th>n</th>
<th>CHO</th>
<th>LDL-C</th>
<th>HDL-C</th>
<th>QUETLET</th>
</tr>
</thead>
<tbody>
<tr>
<td>HiCH +</td>
<td>135</td>
<td>162.0*</td>
<td>86.1</td>
<td>46.4*</td>
<td>2.3*</td>
<td></td>
</tr>
<tr>
<td>HiCH -</td>
<td>194</td>
<td>152.0</td>
<td>87.1</td>
<td>49.2*</td>
<td>2.3*</td>
<td></td>
</tr>
<tr>
<td>CHD +</td>
<td>81</td>
<td>152.2</td>
<td>88.1</td>
<td>46.4#</td>
<td>2.3#</td>
<td></td>
</tr>
<tr>
<td>CHD -</td>
<td>198</td>
<td>154.5</td>
<td>88.9</td>
<td>50.0</td>
<td>2.3</td>
<td></td>
</tr>
</tbody>
</table>

* p<0.01; # p<0.05; + in either CHD - vs - in both.

Grandfathers with CHD identify children with higher QT and lower HDL-C. Children with grandfathers with HiCH have twice the risk of having LDL-C ≥ 90th percentile than those without such a history, and those with CHD history have twice the risk of having LDL-C ≤ 10th percentile. Thus in childhood, positive histories in grandfathers enrich the identification of those at risk.

Alcohol and Coronary Heart Disease Mortality in the Multiple Risk Factor Intervention Trial: The Role of High Density Lipoprotein Cholesterol

II Suh, Jessica Shaten, Jeffrey A. Cutler, Lewis H. Kuller. National Heart, Lung, and Blood Institute, Bethesda, MD

We analyzed coronary heart disease (CHD) death rates in the Multiple Risk Factor Intervention Trial (MRFIT) for associations with baseline alcohol intake (alc), and the extent to which this could be explained by high density lipoprotein cholesterol (HDL-C), in 12,866 men age 35-57 yrs followed for 10.5 yrs. Alc was measured by self-reported number of drinks per week (DRWK), and plasma HDL-C, by CDC-standardized central laboratory. Correlations between plasma HDL-C and DRWK were 0.21 for nonsmokers and 0.25 for smokers (p<0.01). With either but not both variables in multivariate Cox models, DRWK and HDL-C had strong inverse associations with CHD death (p<0.01). The relative risk of CHD death for 22 or more DRWK vs nondrinkers was 0.66, and for highest quintile of HDL-C (≥51 mg/dl) vs lowest quintile (<33 mg/dl) was 0.44. When HDL-C was added to Cox model in which DRWK was a predictor, the coefficient for DRWK changed from -0.0115 (p=0.01) to -0.0065 (p=0.16). This suggests that HDLC mediated a large part of the association between alc and CHD death. We plan to discuss these relationships further by analyzing changes in alc, HDLC and SGGT, and by controlling for possible confounding by diet.

Cardiovascular Risk Factors among Hypertensive Latinos: Comparison with Blacks and Whites.

Paul R. Marantz, Andrew Dunn, Dara Lee, Hillel Cohen, Wee L. Ooi, Michael H. Alderman. Albert Einstein College of Medicine, Bronx, NY

Information about cardiovascular disease (CVD) in US Latinos (L) is confounded by access to health care. To determine if CVD risk factors and rates differ between L, Black (B), and White (W) hypertensives, we evaluated 1258 L, 2313 B, and 3584 W patients (pts) in a worksite program which provides uniform care. L pts were significantly younger; 64% were young (<55 yrs), compared with 57% (B) and 42% (W). Entry characteristics were compared, stratifying by age and gender. Serum cholesterol was significantly higher for W than B or L; L had lower systolic BP than B or W; and B had higher diastolic BP than W or young L. Fasting blood sugar was similar among the groups. The prevalence of LVH by ECG was highest in L, followed by L and then by W, for each age-gender stratum. Renin profile was significantly lower for B than L or W; L tended to be lower than W (p=NS). Average BP reduction did not differ among the groups. The proportion of subjects who developed CVD (MI, stroke, or IHD) over a median of 3 yrs of follow-up tended to be lowest among L, although no statistically significant differences were noted when stratified by age and gender (low event rates, p=NS). Thus, for hypertensive pts under standard treatment, CVD risk and rates were generally lower for L than B or W.
Use of Life Style Factors to Identify Young Adults With Low HDL Cholesterol: The CARDIA Study
Samuel Gidding, Kiang Liu, Diane Bild, Lynne Wagenknecht, John Flack, Stephen Hulley, Northwestern University Medical School, Chicago, IL.

Though HDL cholesterol (HDL) is an important coronary risk factor, strategies to identify young adults who should be screened for low HDL have not been developed. We reviewed life style factors in adults aged 18-30 yrs at study entry to develop an effective strategy for identification of HDL < 35 mg/dl. Of 4450 with 2 lipid measurements performed two yrs apart, 178 (4.0%) had average HDL < 35 mg/dl. White males were 3 times more likely than white females or blacks to have low HDL. Life style factors associated with low HDL included body mass index (BMI) ≥ 25 kg/m² (p < 0.0001) and smoking (p < 0.0001). The prevalence of these factors in low HDL individuals differed by race and sex, with blacks being more obese than whites (64% vs 67%, p < 0.05), and white females more likely to smoke than white males or blacks (75% vs 37%, p < 0.001). Measuring TC and HDL in young adults who smoked or had BMI ≥ 25 (56% of CARDIA pts) would identify 156/178 (87.6%) with HDL < 35 mg/dl whereas measuring TC alone and relying on the average of TC ≥ 200 mg/dl would identify only 58/178 (32.6%). In conclusion, obesity and smoking are strongly related to low HDL, however, characteristics of this association differed by race and sex. Most young adults with HDL < 35 mg/dl can be identified by pre-screening for these two life style factors.

Prevalence of and Factors Related to Orthostatic Hypotension Among the Elderly: Results From the Cardiovascular Health Study (CHS)
Diane E. Bild, Gale H. Rutan, Bonnie Hermanson, Gretse S. Tell, Steven J. Kittner, Frances LaBaw, National Heart, Lung, and Blood Institute, Bethesda, MD.

Orthostatic hypotension (OH) is a common finding among elderly patients and has been associated with cardiovascular and neurologic dysfunction as well as with syncope and falls. The prevalence of OH (≥20 mmHg decrease in systolic pressure or ≥10 mmHg decrease in diastolic pressure upon standing from supine) in a population-based sample of 4,930 men and women aged 65 years and older participating in CHS was 16.2% (n=899) when the definition of OH also included those in whom the procedure was aborted due to dizziness. The prevalence of OH was similar in men and women and increased with age from 15.0% (259/1727) among those 65-69 years to 25.4% (46/181) among those 85 years and older (p<0.001). After adjusting for age, OH was significantly associated with stenosis of the carotid artery as measured by ultrasound, major ECG abnormalities and reported diabetes but not with use of antihypertensive medications or diuretics, history of stroke, myocardial infarction or angina, or reported hypertension. We conclude that OH is common in the elderly, increases with age and is associated with subclinical cardiovascular disease but not with prevalent disease, perhaps due to poorer survival of individuals with both OH and cardiovascular disease.

Decreased Risk of Stroke Among Postmenopausal Hormone Users: Results From the NHANES I Epidemiologic Followup Study

Although evidence strongly suggests that hormone replacement therapy (HRT) reduces the risk of coronary heart disease, the association of HRT with stroke is not well defined. To assess the relationship between HRT and the incidence of stroke, we followed 2,233 women aged 55 years or older who had participated in the first National Health and Nutrition Examination Survey (NHANES I), conducted in 1971-75. They were followed for an average of 12 years as part of the NHANES I Epidemiologic Followup Study. Endpoints were determined from health care facility records and death certificates. Stroke was reported for 11% of hormone users (46 of 423) during the followup period, compared to 18% of non-users (333 of 1,801). A protective association of HRT with stroke incidence still was observed after adjustment for cardiovascular disease risk factors, including hypertension and diabetes, using a Cox multivariable model (relative risk (RR)=.66, 95% confidence interval (CI)=.48,.90). HRT showed a protective effect for fatal stroke (RR=.20, 95 CI=.06,.66) and nonfatal stroke (RR=.78, 95 CI=.56,1.08). A protective effect also was found across selected risk subgroups. These results suggest that HRT may reduce the risk of stroke in older women.

Neurogenic Salt Sensitivity in Childhood: The Muscatine Study
Larry T. Mahoney, Ray-Hahn Hsieh, William R. Clarke, Ronald M. Lauer. University of Iowa, Iowa City, IA.

Adults with essential and borderline high blood pressure (BP) are more likely to demonstrate sensitivity to a high salt diet (i.e. increase in BP and forearm vascular resistance [FVR]) than those with normal BP. We sought to determine whether adolescents, 16 yrs of age and whose systolic BP's were measured 3-6 times over 6-10 yrs, with persistently high (mean BP ≥ 80 mmHg) (N=20) or labile high BP (at least 1 BP > 80%tile but mean < 80%tile; N=17) versus those with normal BP (all BP's < 80%tile; N=17) demonstrated exaggerated hemodynamic responses after one week of high sodium diet (410 mEq/day) compared to responses after one week of low sodium diet (10 mEq/day). No group differences by diet were observed for BP (systolic, diastolic or mean), heart rate or FVR. Compared to low sodium diet, during high sodium diet, we observed similar BP (126.0 ± 11.2 vs 126.6 ± 10.8) and FVR (24.7 ± 8.3 vs 22.6 ± 9.2 U) but significantly (p < 0.05) lower heart rates (64.8 ± 9.6 vs 70.0 ± 10.3), and greater neurogenic forearm vasodilation during baroreceptor inhibition induced by lower body negative pressure (increase in FVR 18.5 ± 12.65 vs 15.05 ± 13.64 U) despite equivalent maximal vasodilation during peak reactive hyperemia, a measure of the structural contribution to vascular resistance.

Conclusion: In adolescents with high BP (persistent or labile) and lower BP, a high salt diet results in greater neurogenic vasodilation. This suggests that excessive salt intake may adversely affect vascular responses at all levels of BP at a young age.
Validation of Previous Acute Myocardial Infarction (AMI): Minnesota Heart Survey Registry

Wayne D. Rosamond, Russell V. Luepker. University of Minnesota, Minneapolis, MN

Distinguishing between incident and prevalent cases of AMI is important to the understanding of coronary heart disease trends. In population surveys, patient recall is often relied upon in making this distinction. This study investigated the validity of recall of a physician-diagnosed AMI, among patients consecutively registered in the Minnesota Heart Survey (MHS) Registry. In six representative hospitals with coronary care units (CCU), patients 25 years of age or older with suspicion of AMI were identified and interviewed. During the first two months of registration, 272 (61%) men and 175 (39%) women were eligible. Ninety-five percent (426) agreed to participate in the study. Among the participants, 33% (141) gave a positive history of a previous AMI diagnosed by a physician. Ninety-six percent (136) of the patients giving a positive history said they were hospitalized for their previous event. Previous hospital records were sought in those and 118 (87%) complete discharge summaries obtained. Seventy-one percent (84) of self reported AMI, where a discharge summary was evaluated, were confirmed by a discharge diagnosis of definite AMI while 27% (32) were discharged as no AMI. Angina pectoris was the most common (50%) discharge diagnosis for those cases determined not to have had a previous AMI. Discharge summaries were also evaluated using the MHS AMI Diagnostic Algorithm which is based on chest pain history, cardiac enzyme changes and electrocardiographic evidence. An AMI diagnosis derived from the algorithm was compared to the discharge diagnosis listed on the summaries. The listed discharge diagnosis agreed with the algorithm in 78% of the cases. This study suggests that patient recall of previous AMI may frequently be inaccurate in identifying prevalent cases.

Differences Between Men and Women with Left Ventricular Dysfunction


Baseline characteristics of the 6783 patients enrolled in Studies of Left Ventricular Dysfunction (SOLVD) were analyzed for gender differences. SOLVD entry criteria were LV ejection fraction <35 and age between 21 and 80. Characteristic Women (n = 979) Men (n = 6804)

Hypertension 252 25.7% 1054 18.1%

Diabetes 453 49.3% 2161 37.2%

Orthopnea 289 29.5% 1075 18.5%

Edema 357 36.4% 1242 21.3%

Exertional Dyspnea 574 58.6% 2808 48.3%

Etiology: CAD 659 67.3% 4675 80.5%

Etiology: Idiopathic 207 21.1% 663 11.4%

Previous CABG 148 15.1% 1666 29.0%

All differences are significant at p < .002 by Chi square with Bonferonni adjustment. More women had hypertension, diabetes and symptoms of orthopnea, edema and dyspnea on exertion than men. While the major cause of LV dysfunction in all was ischemic heart disease, women were less likely to have undergone bypass surgery. Idiopathic cardiomyopathy was more common in women. Thus, for similar degrees of LV dysfunction, women have different clinical presentations than men. SOLVD results may help determine if these differences alter clinical outcome.

Racial Differences in Coronary Heart Disease Risk Factors

Richard G. Hutchinson, Robert L. Watson, Clarence E. Davis, Fredric Romm, Jessie M. Spencer, H. Al Tyroler, Kenneth Wu, Spencer Brown, Ralph Barnes, and The ARIC Study Group. University of MS Medical Center, Jackson MS

The Atherosclerosis Risk in Communities Project is a multicenter study sponsored by the National Heart, Lung, and Blood Institute. In the period January 1987 to June 1989, 9336 white (W) and 3113 black (B) males (M) and females (F) ages 45-64 were screened. Comparative risk factor levels by race (and gender) are:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>BP</th>
<th>WP</th>
<th>WM</th>
<th>WM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>220.3</td>
<td>220.8</td>
<td>212.4</td>
<td>213.7</td>
</tr>
<tr>
<td>Low Density Lipo-protein (LDL)</td>
<td>137.4</td>
<td>134.6</td>
<td>133.9</td>
<td>138.6</td>
</tr>
<tr>
<td>High Density Lipo-protein (HDL)</td>
<td>59.9</td>
<td>59.9</td>
<td>52.6</td>
<td>44.7</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>111.1</td>
<td>129.1</td>
<td>117.2</td>
<td>149.5</td>
</tr>
<tr>
<td>Systolic Blood Pressure (SBP)</td>
<td>125.5</td>
<td>114.6</td>
<td>127.9</td>
<td>118.4</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (DBP)</td>
<td>77.2</td>
<td>68.8</td>
<td>81.8</td>
<td>72.7</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>58</td>
<td>26</td>
<td>54</td>
<td>28</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>25</td>
<td>25</td>
<td>37</td>
<td>24</td>
</tr>
</tbody>
</table>

Racial differences in BP and in TG and HDL noted in the 1960s and 70s, respectively, have persisted into the late 1980s. The differences between BM and WM HDL levels and B vs. W TG (for both genders) are especially interesting. Possible explanations for these differences will be offered.

Importance of Hypertriglyceridemia With Hypoalphalipoproteinemia in Families

Dennis L. Spracher, Leah R. Urbanosky, Heather S. Feigelson, Peter M. Laskarzewski. University of Cincinnati Lipid Research Clinic, Cincinnati, Ohio

To discern whether hypertriglyceridemia (hyperTG, TG \(\geq 90\text{th}\%ile\)) and hypoalphalipoproteinemia (hypoalpha, HDL-c \(<10\text{th}\%ile\)) are jointly transmitted in families, we studied 385 probands with marked reproducible elevations in TG levels (TG \(\geq 99\text{th}\%ile\) on visit 1, TG \(\geq 95\text{th}\%ile\) on visit 2) and their 2072 first degree (1°) relatives in the LRC Family Study. When the proband demonstrated an extreme conjoint trait (ECT, i.e. TG \(\geq 95\text{th}\%ile\), HDL-c \(\leq 10\text{th}\%ile\)), an average of 14.5% of 1° relatives had the conjoint trait (CT;TG \(\geq 90\text{th}\%ile\) and HDL-c \(\leq 10\text{th}\%ile\)) in contrast to only 4.3% of 1° relatives with CT whose proband expresses high TG levels with normal HDL-c levels (TG \(\geq 95\text{th}\%ile\), HDL-c \(\geq 25\text{th}\%ile\)). HyperTG is expressed in 35.4% of 1° relatives of probands with ECT. Of these hyperTG relatives; 41% had CT, and 59% hyperTG only. However, hyperTG is expressed in 25.5% of 1° relatives of probands with high TG alone. Of these hyperTG relatives, 17% had CT and 83% hyperTG only. These differences indicate that bottom decile HDL-c is not simply secondary to hyperTG, and that the HDL-c--TG interaction is familial. The incidence of hypoalpha in 1° relatives is enriched when the proband has ECT, but not enriched when the proband has high TG alone.
Reproductive factors and myocardial infarction.

Julie R. Palmer, Lynn Rosenberg, Samuel Shapiro. Slone Epidemiology Unit, Brookline, MA.

We evaluated the relation of reproductive factors to the risk of nonfatal myocardial infarction (MI) in the largest study to date: 875 cases of first MI in Massachusetts women aged 45-69 were compared with 875 age-matched community controls. Age at menarche was not associated with MI risk. Postmenopausal women had an increased risk, and there was a trend of decreasing risk with increasing age at meno-pause. Both parity and age at first birth were independently associated with an increased risk after control for each other and for education, smoking, hypertension, high cholesterol, diabetes, family history, and exercise; compared to nulliparous women, the relative risk estimate was 1.6 (95% confidence interval (CI) 1.1-2.2) for women who had five or more births and 1.7 (95% CI 1.0-2.8) for women whose first birth was before age 20. The increased risk for early first birth was concentrated in women whose first birth was before age 18, for whom the relative risk was 3.8 (95% CI 1.2-12). Parity and age at first birth were somewhat correlated; further analyses indicated that early age at first birth was the more important factor. These results concerning age at first birth confirm the findings of three earlier small studies.

The Relation of Low Diastolic Blood Pressure to Coronary Heart Disease in the Presence of Myocardial Infarction: The Framingham Study

Ralph B. D’Agostino, Albert J. Belanger, William B. Kannel. Boston University, Boston MA

We examined the hypothesis that a J-curve relationship between blood pressure and death from coronary heart disease (CHD) is confined to high-risk subjects with myocardial infarction (MI). Analysis of the Framingham data using 34 years of follow-up shows that there is no significant relationship between diastolic blood pressure (DBP) or systolic blood pressure (SBP) and non-cardiovascular disease death. For CHD death there was a positive, monotonically increasing continuous relationship with both DBP and SBP in low-risk subjects i.e. without MI. By contrast, in a high-risk group, those with MI but free of congestive heart failure, there was a J-curve relationship between DBP and CHD deaths with the J point occurring in the high 70s (phase 5). The relation was not significant for SBP. The J-curve relationship between diastolic blood pressure and CHD death in the high-risk group with MI appears to be independent of treatment, age, sex, other coronary risk factors, ill-health and left-ventricular function.

Cardiovascular Disease Risk Factors and Atherosclerotic Lesions in Children and Young Adults: The Bogalusa Heart Study

William P. Newman III, Wendy A. Wattigney, Larry S. Webber, Gerald S. Berenson, Louisiana State University Medical Center, New Orleans, LA.

As a continuing study of the relation of early aortic and coronary-artery atherosclerotic lesions with cardiovascular disease risk factors in children and young adults, analyses were conducted on 54 deceased individuals. Individuals autopsied from 1984-89 were compared with previously reported cases who were autopsied during 1978-83. The percent of aortic fatty streak involvement (adjusted for age) correlated positively with serum total cholesterol and LDL cholesterol (p<0.01 for each association) in both time periods. In the second time period significant positive correlations were detected between coronary-artery fatty streaks and total cholesterol (r = 0.50, p=0.02), LDL cholesterol (r=0.65, p=0.002) and systolic blood pressure (r=0.44, p=0.03). Of the 26 cases autopsied from 1984-89, mean levels of LDL cholesterol, systolic blood pressure and diastolic blood pressure were significantly higher in the twelve subjects with coronary-artery fibrous plaques than in those without (p<0.05). These associations stress the importance of the evaluation of risk factors in children and young adults, during the evolution of the atherosclerotic process.

Continued Low Rates of Hypertension in Urban West Africa

Afolabi Ogunlesi, Babatunde Osotimehin, Richard S. Cooper, Youlian Liao, Fern R. Hauck and Fenwei Chen, University of Ibadan, Ibadan, Nigeria

U.S. blacks have the highest rates of hypertension (Htn) in the world. Despite conflicting reports, published data suggest that Htn is uncommon among blacks in West Africa, the ancestral genetic origin of U.S. blacks. We examined 408 men and 119 women at a work site in Ibadan, Nigeria, in the fall of 1989. Htn was relatively low in both sexes (SBP/DBP > 160/95 = 8%), and little rise in mean BP was seen with age. Obesity was likewise uncommon, although BMI was related to BP (p<.01). Contrary to findings in industrialized countries, education was a significant positive predictor of BP in men, independent of age, BMI, pulse rate, and alcohol use. Modernization is associated with rising BP in West Africa, but the absolute risk remains low. Class standing must effect BP through specific psychological processes, and cross-cultural studies on the opposite direction of this effect in rich and poor countries could shed light on these processes.
Influence of Parental Obesity and Hypertension on Blood Pressure and Weight of Offspring in Tecumseh, Michigan

Alan B. Weder, Nicholas J. Schork, Steve Julius
University of Michigan Medical Center, Ann Arbor, MI

Both hypertension and obesity are heritable, but the relative influence of each in promoting hypertension in offspring is unknown. We examined the influence of parental hypertension (HYP: systolic BP > 140 mmHg or diastolic BP > 90 mmHg) and/or obesity (OB: >120% ideal body weight) on the expression of diastolic BP (DBP), body weight (Wt), overweight (Overw as % over ideal body weight) and a factor hypothesized as a link between HYP and OB, plasma insulin, in 643 of their offspring. Four offspring groups were defined by the presence (+) or absence (-) of OB and HYP in at least one of the parents (means):

<table>
<thead>
<tr>
<th>Group</th>
<th>PARENTS</th>
<th>OFFSPRING</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n)</td>
<td>HYP</td>
<td>OB</td>
</tr>
<tr>
<td>1 (398)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2 (58)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>3 (110)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4 (77)</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

A logistic analysis showed significant (p < .0001) differences in the time to onset of borderline hypertension in offspring of the 4 groups of parents (group 4 offspring had the greatest risk of developing borderline hypertension in youth and group 1 offspring the least). It appears that parental HYP and OB are additive risk factors for the development of hypertension and obesity in offspring. Hyperinsulinemia may contribute to this additive risk.

Serum Copper and the Risk of Acute Myocardial Infarction: A Prospective Population Study in Eastern Finnish Men

Jukka T. Salonen, Riitta Salonen, Heikki Korpela, Jaakko Tuomilehto. University of Kuopio, Kuopio, Finland

We investigated the association of serum copper concentration with the risk of acute myocardial infarction (AMI) in 1423 randomly selected men aged 42, 48, 54 or 60 years, free of previous ischaemic heart disease (IHD), examined in the Kuopio IHD Risk Factor Study (KIHD) in 1984-7. 47 of these had an AMI in 1984-8. In Cox multivariate survival models adjusting for age, examination year, maximal oxygen uptake, antihypertensive medication, mean systolic blood pressure, serum LDL and HDL2 cholesterol concentration, cigarette pack-years and body-mass index, serum copper concentration in the two upper tertiles (1.02-1.16 mg/l and 1.17 mg/l or more) associated with 3.8-fold (95% CI 1.4, 10.2, p<0.01) and 4.6-fold (95% CI 1.7, 12.3, p<0.01) risk of AMI. Our data indicate that high copper status, reflected by elevated serum copper concentration, is an independent risk factor for IHD.

Poster Presentations: Society of Preventive Cardiology

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Smoking Behavior Changes More After Aeroto coronary Bypass Than After Angioplasty
John R. Crouse, Amy P. Hagaman, Bowman Gray School of Medicine, Winston-Salem, NC

We evaluated smoking cessation in 136 patients who smoked cigarettes at the time of one of three cardiac procedures: coronary artery bypass graft surgery (CABG n = 60), angioplasty (PTCA n = 27), and catheterization with discovery of non-obstructive coronary disease (NOB n = 51). All patients were interviewed 1 year after the procedure for change in smoking behavior. Quit smoking rates in CABG patients after one year were twice those in PTCA patients and in NOB: BEHAVIOR AFTER 1 YR | CABG | PTCA | NOB
---|---|---|---
STILL SMK (n) | 25 | 20 | 36
STOP SMK (n) | 35 | 7 | 15
% QUIT | 58% | 26% | 29%

Mean age did not differ between the CABG and angioplasty patients nor did intensity of smoking at baseline or duration of smoking.

We conclude that PTCA is associated with smoking behavior change that differs in magnitude from that associated with CABG, and that is comparable to change associated with catheterization alone. These differences should be controlled for in any comparison of outcome between CABG and PTCA.
Effect of Lipid-lowering Medications on Plasma Levels of Vitamin A-Related Compounds
Sally F. Mackey, Jane E. Borchers, Joan M. Fair, Daphne A. Roe, William L. Haskell, the Stanford Coronary Risk Intervention Project, Stanford University, Stanford, CA.

Concern has been raised over the potential for malabsorption of vitamin A-related compounds consequent to the use of bile acid resins. We studied the effect of lipid lowering drug therapy and diet on plasma carotenoids in men with known CAD. A control group (C) not on drug or diet therapy was compared with dieters (D) and dieters + drug group (D+Dr). Calorific from fat were 20% for D and 24% for D+Dr. Multiple drug therapy included at least 20 gr/day of colesterol. Diet and drug therapy had been maintained for at least 1 year.

Mean values reported are adjusted for smoking, alcohol and vitamin A intake. Adjustments for lipids, age and vitamin supplements were not significant. N Lycopene β-Carotene α-Carotene Retinol
µg/dl µg/dl µg/dl ng/100µl
C 18 44.80 17.02 6.09 27.14
D 11 46.49 24.16 7.88 32.89
D+Dr 18 29.10* 13.53* 5.47 27.57

* (D+Dr)-(C+D) p<.03 (ANCOVA)

We conclude that use of lipid lowering drugs is associated with significantly lower plasma lycopene and β-carotene levels. Dieters had similar or higher carotenoid values than Controls. Given the evidence of an inverse relationship between plasma vitamin A-related compounds and diseases such as cancer and CAD, the reduction of these compounds in plasma may be detrimental.

Changing Practice Patterns for Cardiovascular Disease Prevention by Primary Care Physicians
Roberd M. Bostick, Russell V. Luepker, Phillip M. Kofron, Phyllis L. Pirie. University of Minnesota, Minneapolis, MN

To determine recent changes in practice patterns for cardiovascular disease risk reduction, a randomly selected sample of practicing primary care physicians in the upper Midwest was interviewed by telephone in 1987 and again in 1989 (response rates >90%, N=241). The reported mean cutoff levels for labeling a total serum cholesterol abnormal dropped from 5.84 to 5.43 mmol/L (226 to 210 mg/dl), for initiating dietary therapy from 6.39 to 5.59 mmol/L (247 to 216 mg/dl), and for initiating medication from 7.34 to 6.54 mmol/L (284 to 253 mg/dl). There were significant increases in the proportion of physicians reporting advising non-pharmacologic treatments for both high normal serum cholesterol and blood pressures so that nearly all now do so. The proportion of physicians utilizing diuretics as preferred step one antihypertensive agents dropped from 60% to 32% (146 of 241 to 77 of 241, p<.001, McNemar’s test). Drug preferences became evenly divided among diuretics, ACE-inhibitors, and β-blockers. Reported care for hypertension was otherwise relatively stable and consistent with national guidelines. Advice about physical exercise changed little but consensus among practicing physicians was high. Substantial improvements were found in smoking cessation activities. Of the ten activities investigated, there were significant increases in four, including having office no smoking policies, routinely offering smokers smoking cessation literature, and asking for a quit date. Progress remains to be made in all areas, but practicing physicians report responsiveness to new scientific evidence and education in the prevention of cardiovascular disease.

Reproducibility of the Pawtucket Heart Health Step Test in the Health and Religion Project
Charles B Eaton, Annlouse Assaf, Martin Gardiner, Thomas Lasater, Richard Carleton. Brown University and Memorial Hospital of Rhode Island, Pawtucket, R. I.

To establish the reproducibility of a previously validated fitness test, the Pawtucket Heart Health Step test (PHHST), this study evaluated the test-retest reliability and the relationship of cardiovascular risk factors to calculated VO2 max measured by the PHHST.

Methods: A cohort of 569 men and 796 women from church groups in Rhode Island had self-reported vigorous exercise and physiologic variables measured. After exclusion for health risks, 380 men and 555 women performed the PHHST. Results: Of those with no reported change in vigorous exercise (VE), the test-retest reliability coefficient for cardiovascular fitness (CVF) measured 12 months apart was r = .88 (p<.001), and r = .90 (p<.001), 36 months apart. The correlation between VE and CVF in the entire cohort was r = 0.20 for men and r = 0.18 for women, (p<.001). The age adjusted partial correlation coefficients of VO2 max and cardiovascular risk factors are given below:

Gender SBP DBP Chol BMI HDL Cig #
Men -0.24** -0.29** -0.09 -0.65** 0.25** -0.08
Women -0.36** -0.39** -0.13 -0.63** 0.25** -0.08
*p<.01, **p<.001

Conclusions: The PHHST provides reliable and valid measurements of CVF in this population based study, allowing repeated measurements of CVF to test the hypothesis that regular exercise will improve CVF in free living populations.

The Association Between Chlamydia Pneumoniae Strain TWAR Antibody and Angiographically Demonstrated Coronary Artery Disease

We conducted a case-control study to investigate the relationship between C. pneumoniae IgG antibody titers and angiographically diagnosed coronary artery disease. Cases (n=461) were angiography patients with at least 1 coronary artery lesion occupying at least 50% luminal diameter. Controls (n=95) were angiography patients with no demonstrable coronary artery disease. Serum from blood obtained at the time of catheterization was tested for antibody to C. pneumoniae using the microimmunofluorescence test. The age and sex standardized geometric mean titer was significantly higher in the case group than the control group (30.0 vs. 24.0; p=0.04 by Mann-Whitney-U test). The estimated risk of coronary artery disease was greater among subjects with high (≥ 1:64) antibody titers than among subjects with low or absent (≤ 1:8) antibody titers (age and sex adjusted relative risk=2.0, 95% confidence interval=1.0-4.0). These preliminary results, in combination with the results of a recent case-control study from Finland, suggest a possible association between infection with C. pneumoniae and coronary artery disease.
Determinants of Diet and Cholesterol Counseling by Physicians

Alice S. Ammerman, Thomas C. Keyserling, Timothy S. Carey, Robert F. DeVellis, Pamela S. Haines, Ross J. Simpson Jr., University of North Carolina, Chapel Hill, NC

National guidelines urge physicians to play a larger role in diet counseling for cholesterol reduction. Patients are demanding these services from their physicians as well. We examined the relationship of dietary knowledge, attitudes, beliefs, organizational barriers, and treatment practices for cholesterol management among sixty resident physicians practicing in a general medicine clinic serving predominantly low-income patients. Ninety-two percent (55 of 60) of physicians surveyed believe that dietary treatment effectively lowers cholesterol and 68% (41 of 60) feel responsible for providing such therapy. However, 72% (43 of 60) feel ill prepared to give diet counseling, 95% (57 of 60) lack confidence in their ability to help patients make meaningful dietary changes, and cite organizational barriers, such as limited time (72%, 43 of 60) and inadequate educational materials (47%, 28 of 60). Knowledge about the biological basis of diet and heart disease was better than practical understanding of dietary recommendations. Physicians were more likely to report behaviorally focused diet counseling practices if they felt prepared to counsel (r=.2, p<.001) and confident in their counseling skills (r=.39, p<.01). Our results suggest that diet counseling for cholesterol reduction by physicians could be improved with programs designed to: a) require minimal time, b) provide appropriate educational resources, c) prompt physicians with practical dietary information, and d) boost confidence by incorporating sound behavior change principles that will increase the likelihood of patient behavior change.

Cholesterol Management - Dietitian Knowledge and Attitudes

Gail L. Underbakke, Mary E. Plane, Patrick E. McBride. University of Wisconsin, Madison, WI

We surveyed the 1500 members of the Wisconsin Dietetics Association to assess their attitudes, knowledge, and educational interests in cholesterol management. Of the 689 (46%) dietitians returning surveys, 93% (639) reported being familiar with NCEP guidelines for cholesterol levels to treat, 70% (479) were familiar with the Step 1 and 2 diets, and 63% (303) were familiar with guidelines for drug treatment. Ninety-five percent (660) said they believe reducing blood cholesterol levels will reduce the risk of heart disease. Respondents consider a patient to be at high risk at a mean cholesterol level of 237 mg/dl (SD 27), consistent with NCEP guidelines. Dietitians report that physicians are referring patients for diet counseling at an average cholesterol level of 221 mg/dl (SD 23). They estimate that patients make recommended diet changes 58% of the time. Of the 484 dietitians who provide direct patient care, only 51% (246) feel it is appropriate for physicians to do Step 1 diet counseling as recommended by the NCEP, citing reasons of incomplete nutrition knowledge and ineffective education methods. More than half said physicians do not refer patients for diet treatment often enough, and many said they could be more available as nutrition consultants. Interest in education centered on recent diet research, patient education materials, and recommendations for treating the elderly, children, and women. These results have important implications for dietitian education and the physician/dietitian interaction in cholesterol management.

Frequency of Hyperapolipoproteinemia B Among Individuals with Desirable Levels of Low Density Lipoprotein Cholesterol (LDL-c).

Anne N. Nafziger, Steven J. Bowlin, Thomas A. Pearson. The Mary Imogene Bassett Hospital Research Institute, Cooperstown, NY.

We evaluated the frequency of hyperapolipoproteinemia B (HApoB) among individuals with "desirable" LDL-c in a free-living population. A sample of 611 adults was selected by Wakasberg random digit dialing. Fasting serum was obtained for apolipoprotein B-100 (ApoB) and lipid determination. ApoB was assayed by rate nephelometry. LDL-c was calculated using Friedewald's formula. HApoB was defined as ≥ 90th percentile (≥120 mg/dl) for ApoB. LDL-c was grouped as ≤130, 130-159, & ≥160 mg/dl according to NCEP guidelines. Individuals with LDL-c that could not be calculated were excluded.

<table>
<thead>
<tr>
<th>LDL-c (mg/dl)</th>
<th>Apo B (mg/dl)</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>&lt;120</td>
<td>&lt;120</td>
<td></td>
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<tr>
<td>&gt;120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;130</td>
<td>268 (98.9%)</td>
<td>3 (1.1%)</td>
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<tr>
<td>&gt;130</td>
<td>175 (95.1%)</td>
<td>9 (4.9%)</td>
</tr>
<tr>
<td>≥160</td>
<td>105 (67.3%)</td>
<td>51 (32.7%)</td>
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In our sample, only 5% (3 of 611) had HApoB with desirable LDL-c levels. This suggests that the prevalence of HApoB is rare in the absence of high LDL-c. In selected individuals (such as those with borderline LDL-c or a positive family history of cardiovascular disease) screening for HApoB may be helpful, but general HApoB screening offers little over LDL-c screening.

The NCEP Adult Treatment Panel Guidelines: How Well Are Primary Care Providers Doing?

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The Adult Treatment Panel Guidelines of the National Cholesterol Education Program (NCEP) have been available for over two years, but the extent to which primary care physicians incorporated them into practice is unknown. To study this, we used an ambulatory lipid management chart audit tool in 40 medical records for each of 35 PCPs. Of the 1400 outpatients, 56.9% had cholesterol measured, but the % of patients measured varied by PCP from 30% to 81%. Factors associated with cholesterol being measured included a family history of coronary heart disease (CHD), the presence of CHD, hypertension, diabetes and obesity (P<.01) but smoking was not. The presence of health insurance markedly increased screening rates over those who were self paid (60.3% vs. 39.32%). Of those 796 measured, 455 (57.2%) had blood cholesterol levels ≥200mg/dl. Of these, 330 (50.5%) were given a Step 1 diet and 201 (44.4%) received lipid profiles. Secondary causes were infrequently ruled out and no family screening was recorded. A very low use of cholesterol-lowering drugs was seen (7%). These data record substantial provider activity (rather than self-reports), largely in parallel to the NCEP guidelines, but still less than recommended. Further strategies to assist physicians, including the reimbursement for these services, are needed to fully implement this national health policy.
Low Educational Attainment: The Greatest Challenge in the Prevention of Heart Disease?

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An inverse association between coronary heart disease (CHD) and educational attainment has been documented, yet the reasons for this are less well understood. To study this in a rural population with high prevalences of low educational attainment (LEA), we analyzed data from Health Census '89, a private health census of Otsego County, NY, in which 17444 of 19800 (86.6%) of eligible households participated. Questionnaires were collected door-to-door on all adults (N=33428). Striking increases were seen in self-reported prevalences of CHD in all age–gender strata in those with LEA (e.g., in 30–49 year old white males, 7.8% in those with 8th grade vs. 2.7% in those with college degrees). After stratification by age and gender, marked increases in the prevalences of smoking, diabetes, and obesity were seen in those with LEA. A history of having had blood pressure or cholesterol measurements in the past two years, or participation in a regular exercise program were also much less common with LEA. These results suggest that in this rural population, the presence of LEA identifies a subgroup with high prevalences of CHD and its risk factors, implying that LEA subjects may not have heeded or benefitted from recent health education efforts and, as such, may pose the greatest challenge to further reduction of CHD in our society.

Impact of serum total cholesterol on death from IHD and stroke during 20.5 years of follow-up. The Värmiland Study.

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In 1964–1965, a general health survey including the measurement of serum cholesterol was conducted in Värmland county, Sweden. Overall participation rate was 80%. The cause specific mortality surveillance (ischemic heart disease (IHD) and stroke) presented here includes a geographically determined subset of 26,693 male and 27,692 female participants, followed for an average 20.5 years. Using poisson regression, there was a continuously and graded increasing relative risk (RR) of death by IHD in men, from the lowest to the highest decile of total serum cholesterol (table). In women, only the 10th decile was associated with significantly higher relative risk compared to the 1rst decile. However, after separation by longevity of follow-up, a strong relationship with duration was observed, with the impact of high cholesterol level increasing from the first seven-year period to the second and in turn to the third. During years 14–20 of follow-up, the risk in women was similar to that of men. In both genders, there was negative association between cholesterol and risk of stroke, strong in women and only marginal in men.

<table>
<thead>
<tr>
<th>RR of IHD death by decile of serum cholesterol (<em>p&lt;0.05</em>)</th>
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<tbody>
<tr>
<td>Men: 1.00 1.18 1.49 1.62 1.70 1.72 2.39</td>
</tr>
<tr>
<td>Women: 1.00 1.41 1.16 0.99 1.25 1.18 1.10 1.13 1.32 1.72</td>
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<tr>
<th>RR of stroke death by decile of serum cholesterol (<em>p&lt;0.05</em>)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men: 1.00 0.88 1.03 0.78 0.62 0.73 0.78 0.73 0.67 0.83</td>
</tr>
<tr>
<td>Women: 1.00 0.81 0.64 0.52 0.54 0.58 0.53 0.59 0.55 0.45</td>
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</table>

The study confirms earlier observations regarding the risk of IHD with higher serum cholesterol levels in men. One reason for the weak lacking association between female cholesterol levels and risk of IHD demonstrated earlier, might well be that earlier studies have failed to follow female cohorts of sufficient size long enough.
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