Soft Drink Consumption and Risk of Developing Cardiometabolic Risk Factors and the Metabolic Syndrome in Middle-Aged Adults in the Community

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Background—Consumption of soft drinks has been linked to obesity in children and adolescents, but it is unclear whether it increases metabolic risk in middle-aged individuals.

Methods and Results—We related the incidence of metabolic syndrome and its components to soft drink consumption in participants in the Framingham Heart Study (6039 person-observations, 3470 in women; mean age 52.9 years) who were free of baseline metabolic syndrome. Metabolic syndrome was defined as the presence of ≥3 of the following: waist circumference ≥35 inches (women) or ≥40 inches (men); fasting blood glucose ≥100 mg/dL; serum triglycerides ≥150 mg/dL; blood pressure ≥135/85 mm Hg; and high-density lipoprotein cholesterol <40 mg/dL (men) or <50 mg/dL (women). Multivariable models included adjustments for age, sex, physical activity, smoking, dietary intake of saturated fat, trans fat, fiber, magnesium, total calories, and glycemic index. Cross-sectionally, individuals consuming ≥1 soft drink per day had a higher prevalence of metabolic syndrome (odds ratio [OR], 1.48; 95% CI, 1.30 to 1.69) than those consuming <1 drink per day. On follow-up (mean of 4 years), new-onset metabolic syndrome developed in 765 (18.7%) of 4095 participants consuming <1 drink per day and in 474 (22.6%) of 2059 persons consuming ≥1 soft drink per day. Consumption of ≥1 soft drink per day was associated with increased odds of developing metabolic syndrome (OR, 1.44; 95% CI, 1.20 to 1.74), obesity (OR, 1.31; 95% CI, 1.02 to 1.68), increased waist circumference (OR, 1.30; 95% CI, 1.09 to 1.56), impaired fasting glucose (OR, 1.25; 95% CI, 1.05 to 1.48), higher blood pressure (OR, 1.18; 95% CI, 0.96 to 1.44), hypertriglyceridemia (OR, 1.25; 95% CI, 1.04 to 1.51), and low high-density lipoprotein cholesterol (OR, 1.32; 95% CI 1.06 to 1.64).

Conclusions—In middle-aged adults, soft drink consumption is associated with a higher prevalence and incidence of multiple metabolic risk factors. **(*Circulation*. 2007;116:480-488.)**

Key Words: diabetes mellitus ■ metabolic syndrome ■ epidemiology ■ obesity ■ risk factors ■ carbonated beverages

Several reports from the United States and Europe indicate increasing consumption of soft drinks among children, adolescents, and adults over the past 3 decades.[1,2] Many clinical studies have linked the rising consumption of soft drinks to the present epidemic of obesity and diabetes mellitus among children and adolescents[3–6] and to the development of hypertension in adults.[7] Furthermore, added sweeteners in soft drinks have been linked to an increase in serum triglycerides levels in some reports[8,9] but not in others.[10,11] The association of soft drink consumption with obesity and higher insulin resistance has been attributed to multiple factors, including greater caloric intake, the high

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fructose corn syrup content,[12] less satiety and compensation, and a general effect of consuming refined carbohydrates (see review by Drewnowski and Bellisle[13]).

The aforementioned data raise the possibility that the consumption of soft drinks can fuel metabolic derangements, including insulin resistance, that can translate into a greater risk of developing abdominal obesity, high triglyceride levels, low levels of high-density lipoprotein cholesterol (HDL-C), elevated blood pressure, and impaired glucose tolerance; this constellation of metabolic traits has been collectively referred to as the metabolic syndrome.[14] Higher prevalence of the metabolic syndrome poses greater risk for cardiovascular disease in the community,[15] although the independent contribution of this entity to vascular risk beyond its components has been questioned.[16]

In the present prospective investigation, we tested the hypothesis that greater soft drink consumption increases the risk of developing metabolic risk factors (alone and in combination [metabolic syndrome]) in middle-aged adults in the community. Additionally, we evaluated whether metabolic risk varied on the basis of consumption of sugar-sweetened ("regular") versus artificially sweetened ("diet") soft drinks.

Methods

Study Sample

The Framingham Heart Study began in 1948 with the enrollment of 5209 participants into the original study cohort.[17] In 1971, children of the original cohort participants and the spouses of the children were enrolled into the Framingham Offspring Study (n=5124).[18] Offspring study participants are evaluated approximately every 4 years. Information on daily consumption of soft drinks was collected via a physician-administered questionnaire at each study visit from the fourth (1987–1991) through the sixth (1995–1998) examination cycles. That examination questionnaire did not elicit information regarding consumption of regular versus diet soft drinks; however, such information was available from the self-administered food frequency questionnaires (FFQ; Willett questionnaire)[19] completed by participants at the fifth (1992–1995) and sixth examination cycles (see below).

For the present investigation, we selected offspring cohort participants who attended any 2 consecutive examinations from the fourth through the seventh (1998–2001) examination cycles. We excluded participants with missing data on covariates (n=207) and those with prevalent cardiovascular disease (n=926). After exclusions, a total of 8997 person-observations (4871 in women) were eligible for the cross-sectional analyses. For prospective analyses, we excluded individuals with baseline metabolic syndrome (n=2897 person-observations; metabolic syndrome as defined below) and those with any missing metabolic syndrome components on follow-up (n=61 person-observations). The schema for selection of individuals eligible for cross-sectional and longitudinal analyses is displayed in the Figure. All participants provided written informed consent, and the protocol for the study was approved by institutional review board of Boston Medical Center.

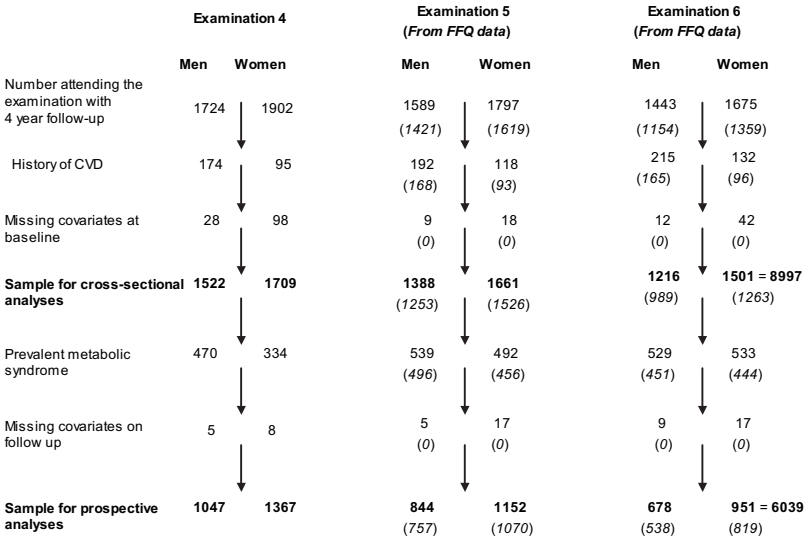
Measurement of Covariates

At each Framingham Heart Study examination, participants provided a medical history and underwent a complete standardized physical examination that included anthropometry, blood pressure measurements, and laboratory assessment of vascular risk factors. Fasting levels of blood glucose, triglycerides, and HDL-C were measured with standard assays. Blood pressure was measured by a physician using a mercury sphygmomanometer and with the participant resting in a seated position for 5 minutes; the average of 2 readings obtained on the participant's left arm constituted the examination blood pressure. Physical activity was assessed by calculating a "physical activity index"; participants were asked specific questions regarding how many hours in a typical day they spent sitting, sleeping, or performing light-moderate or heavy physical activities.[20] Alcohol intake was assessed by averaging the number of alcoholic beverages consumed per week. Participants who reported smoking 1 or more cigarettes per day in the year before the Framingham Heart Study examination were considered current smokers.

Assessment of Soft Drink Consumption and Dietary Intake of Other Foods

At the index examinations, participants reported the average number of 12-oz servings of soft drinks (Coke, Pepsi, Sprite, or other carbonated soft drinks, separately categorized into caffeinated or decaffeinated drinks) consumed per day in the year preceding the examination. The responses to the questions were entered as integers (0 or more) separately for caffeinated and decaffeinated soft drinks. This questionnaire (referred to as the "examination cola questionnaire") did not separate nondrinkers from infrequent drinkers (<1 drink per day). Accordingly, we compared individuals who reported consuming 1, ≥1, or ≥2 soft drinks per day with attendees who reported consuming <1 soft drink per day (infrequent drinkers and nondrinkers, who served as the referent).

Intake of regular and diet soft drinks was assessed from FFQs[19] that were administered at the fifth and sixth examinations. We also



Selection of study sample from baseline examinations using the examination cola questionnaire and from the sample with available FFQ data (within parentheses, for examinations 5 and 6). Eligible participants and exclusions are indicated in the Figure. CVD indicates cardiovascular disease.

assessed the dietary information on consumption of total calories, saturated fat, trans fat, fiber, magnesium, and glycemic index from the FFQ.[19] Because a FFQ was not administered at the fourth examination cycle, dietary covariate data from the fifth examination cycle were used for analyses using information from the examination cola questionnaire at all 3 examinations.

Data from the FFQ were considered valid only if total energy intakes reported were ≥2.51 MJ/d (600 kcal/d) for men and women but <17.54 MJ/d (4200 kcal/d) for men or <16.74 MJ/d (4000 kcal/d) for women and if fewer than 13 food items were left blank. Each food item was categorized in 9 categories that ranged from never or <1 serving per month to >6 servings per day. For assessment of saturated fat, trans fat, or dietary fiber, the nutrient intakes from all specific food items were multiplied by the frequency of consumption. The validity of the FFQ has been demonstrated previously.[21]

Definition and Components of the Metabolic Syndrome

The metabolic syndrome was considered present if 3 or more of the following individual components were present[14,22]: waist circumference ≥35 inches (88 cm) for women or ≥40 inches (102 cm) for men; fasting blood sugar ≥100 mg/dL (5.5 mmol/L) or treatment with oral hypoglycemic agents or insulin; blood pressure ≥135/85 mm Hg or treatment for hypertension; serum triglycerides ≥150 mg/dL (1.7 mmol/L) or treatment for hypertriglyceridemia (with niacin or fibrates); and HDL-C <40 mg/dL (1.03 mmol/L) in men or <50 mg/dL (1.3 mmol/L) in women.

Statistical Analyses

Age- and sex-adjusted baseline characteristics of the participant groups defined according to the number of soft drinks consumed in 1 day (<1, 1, or ≥2 per day) were compared by multiple linear and multiple logistic regression analysis for continuous and categorical characteristics, respectively. Data on consumption of soft drinks at each of the 3 eligible baseline examinations (examination cola questionnaire) were used for this purpose. Tests for trend in baseline characteristics across soft drink consumption categories were performed with multiple regression. We also assessed the baseline characteristics after excluding participants with prevalent metabolic syndrome at baseline examinations (sample used for incidence analyses; see below).

Soft Drink Consumption and Prevalence of the Metabolic Syndrome

We used data from examinations 4, 5, and 6 (examination cola questionnaire) and generalized estimating equations to compare the prevalence of metabolic syndrome in participants who consumed ≥1 soft drink per day with those who consumed <1 soft drink per day (referent). Each participant could contribute up to 3 person-examinations of data for analysis. We also evaluated a dose response by comparing individuals who consumed 1 soft drink per day and those who consumed ≥2 soft drinks per day with the referent group. We constructed multivariable models in hierarchical fashion with adjustment for age and sex (model I) and for age, sex, physical activity index, smoking, dietary consumption of saturated fat, trans fat, fiber, magnesium, total calories, and glycemic index (model II).

We used soft drink consumption data from FFQs at examinations 5 and 6, which yielded a smaller sample (Figure), to relate the prevalence of metabolic syndrome across the following categories of intake of regular versus diet soft drinks using generalized estimating equations: (1) <1 diet or regular soft drink per week (referent), (2) 1 to 6 diet soft drinks per week, (3) ≥1 diet soft drink per day, (4) 1 to 6 regular soft drinks per week, (5) 1 to 6 regular or diet soft drinks per week, and (6) ≥1 regular soft drink per day. Individuals reporting consumption of both diet and regular soft drinks ≥1/d (n=16) were grouped into the last category empirically. We evaluated the 2 sets of models (I and II) noted above.

Soft Drink Consumption and Incidence of the Metabolic Syndrome

To assess the relations of soft drink consumption to the incidence of metabolic syndrome, we excluded participants with prevalent metabolic syndrome at each of examination cycles 4, 5, and 6 (n=2897 person-observations). Then, we used pooled logistic regression analyses by combining each 4-year follow-up period of observations to relate the number of soft drinks consumed per day (examination cola questionnaire) to the incidence of metabolic syndrome (from examination cycles 4 to 5, 5 to 6, and 6 to 7).[23] The eligible participants were free of metabolic syndrome at each baseline examination, and in this setting, pooled logistic regression has been shown to provide risk estimates similar to time-dependent Cox models.[24] We compared the consumption of soft drinks ≥1 per day with infrequent drinkers (<1 per day; referent) and also tested for a dose response by comparing groups consuming 1 and ≥2 soft drinks per day with the referent group. We evaluated 2 sets of models (covariates as in models I and II above), which paralleled the analyses of prevalence of metabolic syndrome.

Consumption of soft drinks varies with age and by sex.[25] It has also been suggested that the effects of soft drinks and carbohydrates on metabolic traits may vary according to age, sex,[26] and baseline body weight.[27] Therefore, we assessed for effect modification by age (modeled as a continuous variable), sex, and body mass index (<30 versus ≥30 kg/m^2) by incorporating appropriate interaction terms in the multivariable models. We repeated analyses with additionally adjustment for alcohol consumption and baseline levels of systolic and diastolic blood pressure, blood glucose, serum triglycerides, and HDL-C. These models were constructed to account for baseline levels of metabolic traits. Additionally, we repeated analyses to examine the association between consumption of caffeinated and decaffeinated soft drinks, considered separately, and incidence of the metabolic syndrome. Because individuals with diabetes mellitus are a particularly high-risk group for developing metabolic abnormalities, we also repeated our analyses after excluding those with prevalent diabetes mellitus at baseline.

To compare the risk of new-onset metabolic syndrome according to the type of soft drink consumed (regular versus diet), we used data from the FFQs at examinations 5 and 6 and evaluated the incidence of the metabolic syndrome across categories of soft drinks consumed. The 6 categories of regular and diet soft drinks were those noted above (for the analyses of the prevalence of metabolic syndrome), and 2 sets of models were evaluated (models I and II, as described above).

Incidence of Individual Components of Metabolic Syndrome

We used multivariable logistic regression to evaluate the relations of soft drink consumption to the incidence of each individual component of metabolic syndrome using data from the examination cola questionnaire. We excluded participants who had the specific metabolic trait prevalent at baseline; for example, we excluded individuals with blood glucose ≥100 mg/dL (5.5 mmol/L) from the "at-risk" group for analysis that examined the incidence of impaired fasting glucose. Thus, we examined the incidence of increased waist circumference, impaired fasting glucose, high blood pressure, hypertriglyceridemia, and low HDL-C (all defined as above) according to the number of soft drinks consumed per day.

We evaluated 2 sets of models (I and II, as noted above) and compared the risk of developing metabolic traits associated with consumption of ≥1 soft drinks per day with that in infrequent drinkers (<1 soft drinks per day). We also evaluated for a dose response as detailed above. We did not perform analyses of development of individual metabolic syndrome components in relation to regular versus diet soft drink intake using the FFQ data at examinations 5 and 6 because the grouping of incident events into 6 categories resulted in modest numbers of events in each category.

All analyses were performed with SAS software version 9.0 (SAS Institute, Cary, NC). A 2-sided probability value of <0.05 was considered statistically significant.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

The baseline characteristics of participants according to the categories of soft drinks consumed per day are presented in Table 1. Approximately 35% of the participants reported consuming ≥1 soft drink per day in response to the examination cola questionnaire (data based on all 3 examinations). In comparison, only 22% of participants reported intake of at least 1 soft drink (diet or regular) per day in response to the FFQ (data available for examinations 5 and 6 only). The lower proportion reporting daily intake on the FFQ may be related to the greater number of options available to indicate soft drink intake; participants drinking 1 to 6 soft drinks per week (also 22% on the FFQ) may have rounded their responses on the examination cola questionnaire to the nearest integer.

In age- and sex-adjusted models, the prevalence of obesity (assessed both by body mass index and by waist circumference), high blood pressure, glucose intolerance, low HDL-C, and hypertriglyceridemia was significantly higher in those who consumed a greater number of soft drinks per day. Serum total cholesterol, low-density lipoprotein cholesterol, physical activity index, and alcohol consumption did not vary across categories of soft drinks consumed. Similar trends were obtained when we excluded individuals with prevalent metabolic syndrome (Data Supplement, Table I).

Prevalence of the Metabolic Syndrome

There was a 48% higher adjusted prevalence of metabolic syndrome among those who consumed 1 or more soft drinks per day relative to individuals with infrequent soft drink consumption (Table 2). We observed a rising prevalence of metabolic syndrome across categories of 1 and ≥2 soft drinks per day. In parallel analyses with the data from the FFQ (Table 2), participants who consumed ≥1 diet or regular soft drink per day had nearly a 1.8-fold adjusted prevalence of metabolic syndrome compared with infrequent drinkers (<1 per week).

Incidence of the Metabolic Syndrome

Individuals who consumed at least 1 soft drink per day had a 44% higher adjusted risk (95% CI, 20% to 74%) of developing metabolic syndrome compared with infrequent drinkers in multivariable-adjusted analyses (Table 3). There was no effect modification by age, body mass index, or sex (interaction terms were not statistically significant). After additional adjustment for baseline levels of covariates (blood sugar, systolic and diastolic blood pressure, triglycerides, and HDL-C) and alcohol consumption in our models, the association of consumption of ≥1 soft drink per day with incidence of metabolic syndrome remained robust (odds ratio [OR], 1.44; 95% CI, 1.19 to 1.74). Further exclusion of individuals with diabetes mellitus at baseline (n=138) attenuated the association (OR for ≥1 soft drink per day, 1.16; 95% CI 1.00 to 1.34). After stratification of analyses by caffeinated versus decaffeinated drinks, results were consistent with the primary analyses; consumption of ≥1 soft drink per day was associated with incident metabolic syndrome for both types of beverages (Data Supplement, Table II).

In analyses with FFQ data (Table 3), intake of at least 1 regular or diet soft drink per day was associated with a >50% higher incidence of metabolic syndrome than among those who drank <1 soft drink per week, although the association was borderline significant for intake of ≥1 regular soft drink per day ($P=0.07$). We also observed a graded increase in the risk of metabolic syndrome from those who were consuming 1 to 6 diet or regular soft drinks per week to those who drank ≥1 soft drinks per day (diet or regular).

Incidence of Individual Components of the Metabolic Syndrome

Compared with infrequent drinkers, individuals who consumed ≥1 soft drink per day had a 25% to 32% higher adjusted risk of incidence of each individual metabolic trait (Table 4), with the exception of development of high blood pressure, for which there was a borderline significant 18% higher adjusted odds ($P=0.10$).

Discussion

In the present study, we observed a significantly higher prevalence of metabolic syndrome among middle-aged adults who consumed ≥1 soft drink per day. This association was consistent for intake of both regular and diet soft drinks. Our prospective analyses corroborated the cross-sectional findings; we observed an increase in the incidence of metabolic syndrome among adults consuming at least 1 soft drink per day, regardless of whether it was of the regular or diet type. Additionally, consumption of soft drinks daily was associated with a higher incidence of each metabolic syndrome component. The present study extends results from prior studies that reported that a greater intake of soft drinks is associated with increased prevalence of metabolic syndrome,[28] higher risk of obesity,[4–6] high blood pressure,[7] and diabetes mellitus.[5] The similar metabolic hazard posed by both regular and diet soft drinks is noteworthy given the lack of calories in the latter; however, other studies have also reported associations of diet soft drinks with weight gain in boys[29] and with hypertension in adult women.[7]

Mechanisms

There are several mechanisms that can explain the higher risk of metabolic abnormalities associated with greater consumption of soft drinks. These can be broadly grouped under physiological effects, dietary behavior, and the economics of food choice.[13]

There are several physiological effects of soft drinks that may pose an adverse metabolic risk. Larger consumption of added nutritive sweeteners such as high fructose corn syrup (the primary sweetener in soft drinks) can lead to weight gain, increased insulin resistance,[30,31] a lowering of HDL-C,[32] and an increase in triglyceride levels.[27] Typically, in the United States, the high fructose corn syrup added to the beverages contains ≈55% fructose.[30,31] Al-

TABLE 1. Baseline Characteristics of Participants According to Soft Drink Consumption (n=8997)

	No. of Soft Drinks Consumed Per Day			
Characteristic	<1 (n=5840)	1 (n=1918)	≥2 (n=1239)	*P**
Age, y	56±10	53±10	51±9	···
Men, %	42.8	50.2	53.4	···
Systolic BP, mm Hg	127±19	125±17	126±18	<0.0001
Diastolic BP, mm Hg	76±10	77±10	78±11	<0.0001
BP ≥130/85 mm Hg or on treatment, %	48.9	46.7	48.4	<0.0001
Hypertension, %	22.5	18.7	21.6	0.0014
Treatment for hypertension, %	18.9	16.1	17.6	0.0011
BMI, kg/m^2	26.8±4.8	27.8±5.1	28.5±5.4	<0.0001
BMI ≥30 kg/m^2, %	20.9	27.1	32.1	<0.0001
Weight, kg	75.5±16.1	79.4±16.9	82.1±18.1	<0.0001
Waist circumference, in	36.0±5.6	36.9±5.7	37.8±6.1	<0.0001
Increased waist circumference, %†	33.9	37.2	41.1	<0.0001
Men	36.3	40.9	48.1	<0.0001¶
Women	32.0	33.4	33.2	<0.0001¶
Total cholesterol, mg/dL	206±37	204±37	202±38	0.72
Low-density liporotein cholesterol, mg/dL	129±34	128±33	127±34	0.30
Triglycerides, mg/dL	127±83	141±119	148±118	<0.0001
High triglycerides, %‡	28.3	32.7	35.9	<0.0001
HDL-C, mg/dL	52±16	50±15	47±14	<0.0001
Low HDL-C, %§	34.8	38.7	46.1	<0.0001
Men	37.5	42.0	45.1	<0.0001¶
Women	32.8	35.5	47.2	<0.0001¶
Blood sugar, mg/dL	97±21	99±26	105±39	<0.0001
Impaired fasting glucose, %‖	28.2	30.4	33.7	<0.0001
Diabetes mellitus, %	6.1	7.5	12.4	<0.0001
Metabolic syndrome, %	29.1	32.2	37.3	<0.0001
Physical activity index, %	36±6	36±7	36±7	0.74
Alcohol, drinks/wk	2.6±3.9	2.7±3.8	2.7±4.1	0.14
Smoking, %	17.5	17.5	25.7	0.0009
Dietary variables, g/d				
Saturated fat	20.9±9.8	22.3±9.6	24.6±11.5	<0.0001
Trans fat	2.9±1.9	3.1±1.9	3.5±2.3	<0.0001
Dietary fiber	18.4±7.9	17.9±7.1	17.0±7.6	<0.0001
Magnesium, mg/d	308±111	304±105	296±111	0.0002
Glycemic index	54±3	55±3	55±4	0.0001
Total energy, cal/d#	1855±611	1959±654	2009±745	0.0837

All values are mean±SD unless otherwise noted. BP indicates blood pressure; BMI, body mass index; and LDL-C, LDL cholesterol.

*P comparing all 3 categories of soft drink consumption, adjusted for age and sex.

†Increased waist circumference ≥40 in (102 cm) for men and ≥35 in (88 cm) for women.

‡≥150 mg/dL (1.7 mmol/L) or undergoing treatment with fibrates or nicotinic acid.

§Low HDL-C (men <40 mg/dL [1.03 mmol/L], women <50 mg/dL [1.3 mmol/L]).

‖≥100 mg/dL or undergoing treatment.

¶Age-adjusted.

#Sample sizes are n=2742, 820, and 466, respectively.

though the association of high fructose corn syrup intake and insulin resistance may be a contributory mechanism,[31] in the present study, both regular and diet soft drinks appeared to pose similar metabolic hazards, which suggests that other factors may be operational. Consumption of liquids is associated with a lesser degree of dietary compensation (the adjustment in energy intake made in subsequent meals in response to food intake). Some

TABLE 2. Cross-Sectional Relationships of Soft Drink Consumption With Prevalence of Metabolic Syndrome

Soft Drink Consumption, Servings/d	Metabolic Syndrome, n	No. at Risk*	Age- and Sex-Adjusted OR (95% CI)	Multivariable Adjusted OR (95% CI)†
Model I: any soft drink (regular or diet); data from all 3 examinations (4, 5, and 6; n=8997)				
None	1697	5840	Referent	Referent
1	618	1918	1.18 (1.06 to 1.33)	1.38 (1.19 to 1.61)
≥2	462	1239	1.43 (1.24 to 1.66)	1.67 (1.38 to 2.01)
≥1	1080	3157	1.26 (1.14 to 1.40)	1.48 (1.30 to 1.69)
Model II: regular vs diet soft drink; data from FFQ at examinations 5 and 6 (n=5031)‡				
Diet or regular, <1/wk	650	2129	Referent	Referent
Diet, 1 to 6/wk	359	882	1.72 (1.45 to 2.03)	1.81 (1.48 to 2.22)
Diet, ≥1/d	328	819	1.87 (1.57 to 2.23)	1.80 (1.45 to 2.25)
Regular, 1 to 6/wk	235	671	1.33 (1.09 to 1.61)	1.20 (0.94 to 1.53)
Diet and regular 1 to 6/wk	106	239	1.79 (1.35 to 2.38)	1.99 (1.40 to 2.83)
Regular, ≥1/d	130	291	2.31 (1.77 to 3.01)	1.81 (1.28 to 2.56)

*No. of people represents person-observations. FFQ indicates food frequency questionnaire; OR, odds ratio; and CI, confidence interval.

†Multivariable model adjusts for age, sex, physical activity index, smoking, dietary consumption of saturated fat, trans fat, fiber, magnesium, total calories, and glycemic index (No. eligible for multivariable models: model I, any soft drink, n=5350; model II, for regular vs diet soft drink, n=3493).

‡Individuals who reported drinking both diet and regular soft drinks ≥1/d (n=16) were included in the regular ≥1/d category.

investigators believe that intake of sugar-sweetened beverages induces less compensation than intake of artificially sweetened soft drinks,[33] but others disagree.[34] The high sweetness of diet or regular soft drinks may lead to conditioning for a greater preference for intake of sweetened items,[35] although this explanation also has been questioned by some experts.[13] The caramel content of both regular and diet drinks may be a potential source of advanced glycation end products,[5] which may promote insulin resistance[36] and can be proinflammatory.[37]

Dietary behavior among individuals consuming soft drinks may account in part for the clustering of metabolic risk factors in these people.[13] Individuals with greater intake of soft drinks also have a dietary pattern characterized by greater intake of calories and saturated and trans fats, lower consumption of fiber[38] and dairy products,[39] and a sedentary life.[40] These observations were corroborated by the our findings of increased consumption of saturated and trans fat, lower consumption of dietary fiber, and higher rates of smoking in those with greater intake of soft drinks. Nonetheless, in the present investigation, we adjusted for saturated fat and trans fat intake, dietary fiber consumption, smoking, and physical activity in multivariable analyses and still observed a significant association of

TABLE 3. Multiple Logistic Regression Examining Soft Drink Consumption and Incidence of Metabolic Syndrome (n=6154)

Soft Drink Consumption, Servings/d	Metabolic Syndrome, n	No. at Risk*	Age- and Sex-Adjusted OR (95% CI)	Multivariable-Adjusted OR (95% CI)†
Model I: any soft drink (regular or diet): data from all 3 examinations (4, 5, and 6; n=6154)				
None	717	4033	Referent	Referent
1	267	1259	1.34 (1.14 to 1.58)	1.53 (1.24 to 1.89)
≥2	166	747	1.46 (1.20 to 1.78)	1.29 (0.98 to 1.70)
≥1	433	2006	1.39 (1.21 to 1.59)	1.44 (1.20 to 1.74)
Model II: regular vs diet soft drink: data from FFQ at examinations 5 and 6 (n=3184)‡				
Diet or regular, <1/wk	253	1456	Referent	Referent
Diet, 1 to 6/wk	98	518	1.17 (0.90 to 1.52)	1.32 (0.96 to 1.81)
Diet, ≥1/d	106	486	1.42 (1.10 to 1.84)	1.53 (1.10 to 2.15)
Regular, 1 to 6/wk	79	434	1.01 (0.76 to 1.35)	1.13 (0.79 to 1.62)
Diet and regular 1 to 6/wk	29	130	1.21 (0.78 to 1.89)	1.41 (0.80 to 2.50)
Regular, ≥1/d	34	160	1.33 (0.88 to 2.02)	1.62 (0.96 to 2.75)

*No. of people represents person-observations. FFQ indicates food frequency questionnaire; OR, odds ratio; and CI, confidence interval.

†Multivariable models adjust for age, sex, physical activity index, smoking, dietary consumption of saturated fat, trans fat, fiber, magnesium, total calories, and glycemic index (No. eligible for multivariable models: any soft drink, n=3655; for regular vs diet soft drink, n=1864).

‡Individuals who reported drinking both diet and regular soft drinks ≥1/d (n=7) were included in the regular ≥1/d category.

TABLE 4. Multiple Logistic Regression Analysis Examining the Relations of Incidence of Individual Components of Metabolic Syndrome According to Soft Drink Consumption (Data From All 3 Examinations [4, 5, and 6])

Soft Drink Consumption, Servings/d	Incident, n	No. at Risk*	Age- and Sex-Adjusted OR (95% CI)	Multivariable-Adjusted OR (95% CI)
Incidence of obesity (BMI ≥30 kg/m^2)				
None	327	4665	Referent	Referent
1	130	1420	1.29 (1.04 to 1.60)	1.21 (0.90 to 1.62)
≥2	91	853	1.51 (1.18 to 1.94)	1.50 (1.06 to 2.11)
≥1	221	2273	1.37 (1.14 to 1.65)	1.31 (1.02 to 1.68)
Incidence of increased waist circumference (≥102 cm for men and ≥88 cm for women)				
None	840	3665	Referent	Referent
1	281	1113	1.29 (1.10 to 1.51)	1.25 (1.02 to 1.54)
≥2	181	645	1.55 (1.28 to 1.88)	1.40 (1.08 to 1.83)
≥1	462	1758	1.38 (1.20 to 1.58)	1.30 (1.09 to 1.56)
Incidence of impaired fasting glucose (≥5.5 mmol/L or diabetes)				
None	898	4264	Referent	Referent
1	322	1359	1.20 (1.03 to 1.39)	1.21 (0.99 to 1.47)
≥2	206	836	1.28 (1.07 to 1.53)	1.32 (1.03 to 1.69)
≥1	528	2195	1.23 (1.08 to 1.39)	1.25 (1.05 to 1.48)
Incidence of high blood pressure (≥135/85 mm Hg or on treatment)				
None	631	3055	Referent	Referent
1	232	1043	1.23 (1.03 to 1.46)	1.16 (0.92 to 1.47)
≥2	141	654	1.20 (0.97 to 1.49)	1.20 (0.90 to 1.60)
≥1	373	1697	1.22 (1.05 to 1.41)	1.18 (0.96 to 1.44)
Incidence of hypertriglyceridemia (≥1.7 mmol/L or on treatment)				
None	695	4258	Referent	Referent
1	250	1317	1.24 (1.05 to 1.46)	1.35 (1.09 to 1.67)
≥2	148	807	1.20 (0.98 to 1.46)	1.09 (0.82 to 1.44)
≥1	398	2124	1.22 (1.07 to 1.41)	1.25 (1.04 to 1.51)
Incidence of low HDL-C (<1.03 mmol/L for men or <1.3 mmol/L for women or on treatment)				
None	460	3878	Referent	Referent
1	183	1201	1.28 (1.06 to 1.54)	1.38 (1.08 to 1.77)
≥2	96	684	1.13 (0.89 to 1.43)	1.21 (0.87 to 1.68)
≥1	279	1885	1.22 (1.04 to 1.44)	1.32 (1.06 to 1.64)

Sample sizes for multivariable models in each category differed from age-adjusted models for obesity (n=4277), waist circumference (n=3321), impaired fasting glucose (n=3858), high blood pressure (n=2803), high triglycerides (n=3792), and low HDL-C (n=3501). OR indicates odds ratio; CI, confidence interval.

*Participants without the individual component at baseline were eligible. No. of people represents person-observations.

†Multivariable models adjust for baseline level of the metabolic syndrome component and age, sex, physical activity index, smoking, dietary consumption of saturated fat, trans fat, fiber, magnesium, total calories, and glycemic index.

soft drink consumption with the risk of developing metabolic syndrome and its component traits. It is conceivable, though, that there may be residual confounding caused by lifestyle factors not adjusted for in the present analyses.

Last, it has been suggested that the obesity-promoting effects of soft drinks may be related in part to their costs, with less expensive drinks being associated with greater hazard by virtue of their preferential selection for economic reasons.[13] The present investigation could not explore this explanation.

Strengths and Limitations

The strengths of the present study include the large community-based sample of men and women and the adjustments for potential confounders; however, several limitations merit comment. We chose to use the modified definition of metabolic syndrome recommended by the National Cholesterol Education Program[14] and did not use other criteria for the syndrome (such as those suggested by the World Health Organization[41] or the European panel). Researchers have found high correlation between these guidelines.[42] Given the

observational nature of the present study, we cannot infer that the observed associations are causal. As noted above, it is conceivable that residual confounding by lifestyle/dietary factors not adjusted for may have contributed to the metabolic risks associated with soft drink intake. Finally, participants in the present study were all white Americans, which may limit the generalizability of our results to nonwhites.

Conclusions

In our large community-based sample of middle-aged adults, soft drink consumption was associated with higher risk of developing adverse metabolic traits and the metabolic syndrome. The present observational data raise the possibility that public health policy measures to limit the rising consumption of soft drinks in the community may be associated with a lowering of the burden of metabolic risk factors in adults.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Consumption of soft drinks among children, adolescents, and middle-aged adults has risen in the United States and Europe during the past 3 decades. Prior studies have shown a higher prevalence of obesity and diabetes mellitus in children who consume more soft drinks, although these associations are less clear for adults. We evaluated the relations of metabolic syndrome and its components to soft drink consumption in Framingham participants. Cross-sectionally, individuals consuming at least 1 soft drink per day had ≈50% higher prevalence of the metabolic syndrome than those consuming <1 drink per day. During a follow-up period of ≈4 years, consumption of ≥1 soft drink per day was associated with a higher incidence of metabolic syndrome and a higher incidence of each of its components, ie, obesity, increased waist circumference, impaired fasting glucose, higher blood pressure, hypertriglyceridemia, and low high-density lipoprotein cholesterol. Analyses that used food frequency questionnaire data suggested that intake of ≥1 drink per day of either regular or diet soft drinks was associated with a >50% higher incidence of metabolic syndrome compared with intake of <1 soft drink per week. We conclude that consumption of more than 1 soft drink per day is associated with a higher prevalence and incidence of multiple metabolic risk factors in middle-aged adults. Our observational data raise the possibility that public health measures to limit consumption of soft drinks may be associated with a lowering of the burden of cardiometabolic risk factors in adults.

Soft Drink Consumption and Risk of Developing Cardiometabolic Risk Factors and the Metabolic Syndrome in Middle-Aged Adults in the Community

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