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Chocolate Consumption is Inversely Associated with Prevalent Coronary Heart Disease: The National Heart, Lung, and Blood Institute Family Heart Study

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Abstract

Background and Aims—Epidemiologic studies have suggested beneficial effects of flavonoids on cardiovascular disease. Cocoa and particularly dark chocolate are rich in flavonoids and recent studies have demonstrated blood pressure lowering effects of dark chocolate. However, limited data are available on the association of chocolate consumption and the risk of coronary heart disease (CHD). We sought to examine the association between chocolate consumption and prevalent CHD.

Methods—We studied in a cross-sectional design 4,970 participants aged 25 to 93 years who participated in the National Heart, Lung, and Blood Institute (NHLBI) Family Heart Study. Chocolate intake was assessed through a semi-quantitative food frequency questionnaire. We used generalized estimating equations to estimate adjusted odds ratios.

Results—Compared to subjects who did not report any chocolate intake, odds ratios (95% CI) for CHD were 1.01 (0.76-1.37), 0.74 (0.56-0.98), and 0.43 (0.28-0.67) for subjects consuming 1-3

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times/month, 1-4 times/week, and 5+ times/week, respectively (p for trend <0.0001) adjusting for age, sex, family CHD risk group, energy intake, education, non-chocolate candy intake, linolenic acid intake, smoking, alcohol intake, exercise, and fruit and vegetables. Consumption of non-chocolate candy was associated with a 49% higher prevalence of CHD comparing 5+/week vs. 0/week [OR=1.49 (0.96-2.32)].

Conclusions—These data suggest that consumption of chocolate is inversely related with prevalent CHD in a general population.

Keywords

epidemiology; carbohydrate; nutrition; cardiovascular disease

Introduction

Epidemiologic data have shown that regular consumption of whole grains, fruit, vegetables, nuts, and perhaps tea is associated with lower incidences of coronary heart disease (CHD) and stroke^{1,2}. It has been postulated that a higher content of polyphenols in these foods is partially responsible for the beneficial effects on CHD. Flavonoids are among the most well studied polyphenols. In the Iowa Women's Health Study, there was an inverse association between dietary catechins (one of the 6 major subclasses of flavonoids³) and CHD mortality among postmenopausal women after 13 years of follow up⁴. The French paradox has been partially attributed to a higher consumption of wine in France. Wine, especially red wine, contains polyphenolic compounds with possible health benefits. In a meta-analysis, Di Castelnuovo et al.⁵ reported that consumption of 150 ml/d of wine was associated with 32% reduction of CVD risk. Dark chocolate is another flavonoid-rich food that may have health benefits. Besides nutrients such as saturated fat (60%), monounsaturated fat (35%), and linoleic acid (3%), chocolate contains important minerals such as potassium and magnesium and flavonoids (particularly epicatechin) that might lower the risk of CHD^{6,7}. In a randomized crossover trial of 13 healthy subjects, daily consumption of 100 g of dark chocolate for 14 days was associated with 5.1 mm Hg decline in systolic blood pressure (p <0.001) and 1.8 mm Hg decline in diastolic blood pressure compared with baseline⁸. These findings on blood pressure have been reproduced by others⁹. Other studies have shown that cocoa consumption improved flow-mediated dilation of the brachial artery^{10-11,12}, inhibited platelet activation and function¹³, regulated nitric oxide production⁹, and may exert favorable effects on cardiovascular mortality¹⁴. We have recently reported an inverse relation between chocolate consumption and subclinical atherosclerosis in the coronary arteries¹⁵.

While the above data support beneficial effects of chocolate on CVD risk factors, limited data are available on the association between chocolate intake and CHD. In particular, little is known about the effects of smaller amounts of chocolate consumed by the general population on CHD. Thus, in the present paper, we sought to examine the association between dietary chocolate intake and prevalent CHD among participants of the NHLBI Family Heart Study.

Methods

Study population

A detailed description of the NHLBI Family Heart Study has been previously published¹⁶. Briefly, between 1993 and 1995, groups of individuals participating in each of the parent studies were selected at random and invited to furnish an updated family health history that contained information on their parents, children, and siblings. Of 4,679 individuals

contacted, responses were obtained from 3,150 (67%); their family members were then contacted, and self-reported health data obtained from a total of 22,908 individuals (86% of those contacted). From the families responding to the health questionnaire, 588 families were chosen at random and 566 families were selected based on higher than expected risk of CHD. Families chosen at random are subsequently referred to as random group and those selected based on a higher than expected risk of CHD are referred to as high-risk group. The high-risk group was defined based on a family risk score, which compares the family's age and sex-specific incidence of CHD to that expected in the general population¹⁷. All members of these families were invited to come to one of the four study clinics for an approximate 4-hour clinical evaluation. Of the total 5,710 Caucasians and 265 African-Americans, 101 white subjects were excluded because of missing data on CHD and additional 904 subjects (874 whites and 30 blacks) were excluded because of missing data on chocolate consumption. Subjects with missing data on chocolate were slightly older than those with complete data on chocolate; however, other characteristics including body mass index, glucose, blood cholesterol, race, risk group, or prevalent diabetes were comparable. Thus, 4,970 participants were used for present analyses. We obtained informed consent from each participant and the study protocol was reviewed and approved by each of the participating institutions.

Assessment of chocolate consumption

Dietary information was collected through a staff-administered semi-quantitative food frequency questionnaire developed by W.C. Willett¹⁸. The reproducibility and validity of the food frequency questionnaire has been documented elsewhere^{19,20}. Each subject was asked the following question: "In the past year, how often on average did you consume chocolate bars or pieces, such as Hershey's Plain, M & M, Snickers, Reeses; 1 ounce?" (Item # 39 in the questionnaire). Possible answers were: "> 6 per day, 4-6 per day, 2-3 per day, 1 per day, 5-6 per week, 2-4 per week, 1 per week, 1-3 per month, and almost never".

Ascertainment of coronary heart disease

Prevalent CHD was assessed from the medical history and a 12-lead electrocardiogram. Individuals were defined as a case of CHD if there was a self-reported history of myocardial infarction, percutaneous transluminal coronary angioplasty, or coronary artery bypass graft that could be validated by review of medical records, or if abnormal Q waves (Minnesota codes 1.1-1.2) were detected on a resting 12-lead electrocardiogram²¹.

Other variables

Resting blood pressure was measured three times on seated participants after a 5-minute rest using a random zero sphygmomanometer by trained and certified technicians. The appropriate cuff size was determined by the arm circumference. For analyses, the average systolic and diastolic blood pressures from the second and third measurements were used. We used the JNC VII classification to define hypertension (stages 1 or 2 – systolic blood pressure of at least 140 mm Hg or diastolic blood pressure of at least 90 mm Hg) or if the subject reported that, he/she was currently taking medications for hypertension.

Information on other dietary factors was obtained through the food frequency questionnaire. Intake of specific nutrients was computed by multiplying the frequency of consumption of an item by the nutrient content of specified portions. Composition values for nutrients were obtained from the Harvard University Food Composition Database derived from the U.S. Department of Agriculture sources²² and manufacturer information. For non-chocolate candy assessment, each subject was asked "in the past year, how often on average did you consume candy without chocolate; 1oz? (Item # 40 of the questionnaire, subsequently

referred to as non-chocolate candy). Possible responses were similar to those of chocolate described above.

Information on cigarette smoking, alcohol intake, and education was obtained by interview during the clinic visit. Use of multivitamins, vitamin E or C, or hormone replacement therapy was assessed using a questionnaire and medication inventory. Frequency of vegetable consumption was obtained by a food frequency questionnaire. Physical activity during the previous year was self-reported. Anthropometric data were collected with participants wearing scrub suits. A balance scale was used to measure body weight, and height was measured using a wall-mounted vertical ruler. Diabetes mellitus was defined as any of the following: (a) a self-reported history of diabetes, (b) fasting glucose of at least 7.8 mmol/L, or (c) current usage of a hypoglycemic agent. Low-density lipoprotein cholesterol (LDL) was measured using the method of Friedewald²³ except for participants with triglycerides above 4.5 mmol/L, whose LDL was measured by ultracentrifugation. Triglycerides were measured using triglycerides GB reagent on the Roche COBAS FARA centrifugal analyzer (Boehringer Mannheim Diagnostics, Indianapolis). Total cholesterol was performed using a commercial cholesterol oxidase method on a Roche COBAS FARA centrifugal analyzer (Boehringer Mannheim Diagnostics, Indianapolis). HDL cholesterol was measured after precipitation of the other lipoprotein fractions by dextran sulfate.

Statistical analyses

We initially examined the distribution of CHD cases according to all possible responses for chocolate consumption (Never, 1-3/month, 1/week, 2-4/week, 5-6/week, 1/d, 2-3/d, 4-6/d, and >6/d). However, because there were only 18 and 25 cases for chocolate consumption of 5-6 per week and 1/d or greater, respectively, we combined these groups to have sufficient number of cases for multivariable analyses. From the lowest to the highest frequency of chocolate intake, we observed similar inverse relations with CHD in men [1.0 (reference), 0.67 (0.50-0.90), 0.48 (0.37-0.63), and 0.24 (0.16-0.38), *p* for trend <0.0001] and women [1.0, 1.10 (0.72-1.68), 0.67 (0.43-1.05), and 0.54 (0.29-0.97), respectively, (*p* for trend 0.006)] in the crude analyses; in addition, there was no evidence for interaction between sex and chocolate consumption on CHD (*p* for interaction 0.28); thus, we analyzed the data with men and women combined. We used univariate analyses to evaluate potential confounders and used partial likelihood ratio tests to compare nested models. We built sequential models as follows: after a crude model, we adjusted for age, sex, and risk group in a simplest model and also controlled for education, smoking, alcohol intake, energy intake, fruit and vegetables, exercise, dietary linolenic acid, and non-chocolate candy consumption (4 groups using frequencies used for chocolate consumption) in a parsimonious model. Then, we examined potential mediating factors through additional adjustment for body mass index, diabetes, weight loss diet, lipids, and hypertension. Additional adjustment for field center, myristic acid or palmitic acid, saturated fat, a composite variable representing foods frequently avoided in cholesterol-lowering diets (butter, eggs, hot dogs, and hamburgers), and antioxidant vitamins (E, C, multivitamins) did not alter the results (data not shown). Because subjects were not independent, we used generalized estimating equations to control for familial clustering (exploring different correlation matrix structures). *P* values for linear trend were obtained by assigning ordinal numbers to chocolate frequency and using the new variable in the regression model. We conducted sensitivity analyses by a) restricting analyses to Caucasians, b) excluding subjects with diabetes mellitus or those on weight loss diet, c) using 5-year age categories, and d) stratified analyses by age (≤ 60 y and >60 y) and smoking status. We also examined whether chocolate consumption was related to prevalent hypertension. Alpha level was set at 0.05 for statistical significance. All analyses were performed using windows SAS version 9.1 (SAS Institute Inc, Cary, NC).

Results

Of the 4,970 participants used for analysis, 2,258 were men and 2,712 were women. The mean age (SD) was 52.0 (13.7) years and CHD prevalence was 10.9%. Table 1 presents baseline characteristics according to chocolate intake. Frequent chocolate consumption was associated with younger age, higher body mass and energy intake and lower HDL; lower frequency of fruit and vegetable consumption, wine consumption, multivitamin use; higher consumption of non-chocolate candy, saturated fat, and dietary cholesterol. Age-, sex-, and energy-adjusted means of dietary cholesterol, saturated fat, and polyunsaturated fat were 0.21 vs. 0.23 g/d, 0.24 vs. 0.25 g/d, and 9.2 vs. 9.0 g/d when comparing subjects with prevalent CHD vs. those without CHD, respectively.

There was evidence for an inverse association between frequency of chocolate consumption and prevalent CHD in crude and adjusted models (Table 2). In the fully adjusted model, consumption of 5+ /week was associated with 57% lower prevalent CHD compared with subjects who did not consume chocolate (Table 2). Exclusion of subjects with prevalent diabetes and those who were on weight loss diet made the association stronger: from the lowest to the highest category of chocolate, ORs were 1.0, 0.98, 0.68, and 0.38 (*p* for trend 0.0002, Table 3, Model 2). Similar association was observed in subjects who were 60 years of age or younger and those above the age of 60 (Table 4). Furthermore, similar associations were seen among smokers and non-smokers (e.g., for the highest category of chocolate intake, the ORs were 0.44 for smokers and 0.43 for non-smokers). Including a composite variable for consumption of butter, eggs, hot dogs, and hamburgers resulted in a slight attenuation of the findings (data not shown). Similar results were seen after additional adjustment for myristic acid (C14:0) – a saturated fatty acid found in low concentration in chocolate. In addition, 5-year age categories to control residual confounding by age did not alter the results (*p* for trend 0.0002). Finally, restriction to Caucasians did not alter the findings: from the lowest to the highest category of chocolate consumption, multivariable adjusted odds ratios (95% CI) were 1.0 (reference), 1.03 (0.76-1.40), 0.75 (0.56-1.01), and 0.44 (0.28-0.70), respectively (*p* for trend 0.0002). Adjustment for potential intermediate factors such as lipids, blood pressure, diabetes, measures of adiposity led to a minimal attenuation [OR: 1.0 (ref), 1.05 (0.77-1.43), 0.75 (0.56-1.01), and 0.43 (0.27-0.68) from the lowest to the highest category of chocolate, *p* for trend 0.0002]. There was no association between chocolate consumption and blood pressure: from the lowest to the highest category of chocolate consumption, adjusted odds ratios for hypertension were 1.0 (reference), 0.99 (0.77-1.26), 0.96 (0.75-1.23), and 1.11 (0.81-1.53), respectively (*p* for trend 0.72).

In contrast, non-chocolate candy consumption was suggestive of an increased prevalence of CHD. Multivariable adjusted odds ratios (95% CI) were 1.0 (ref), 0.96 (0.72-1.27), 1.05 (0.79-1.39), and 1.49 (0.96-2.32) for non-chocolate candy consumption of 0, 1-3/month, 1-4/week, and 5+ /week, respectively, adjusting for age, sex, exercise, energy, linolenic acid, education, risk group, chocolate consumption, alcohol, smoking, and fruit and vegetables.

Discussion

Chocolate consumption and CHD

In this cross-sectional study, we have demonstrated that frequent chocolate consumption was associated with a lower prevalence of CHD in men and women independent of traditional risk factors. Our findings were robust in that exclusion of subjects with prevalent diabetes and those on weight loss diet did not alter the conclusions. In addition, an inverse association was seen in subjects under and above 60 years of age as well as in smokers and non-smokers. In contrast, consumption of non-chocolate candies 5 times or more per week was suggestive for an 49% increased prevalent CHD compared with no consumption. One

possible explanation for the observed inverse association between chocolate consumption and CHD prevalence is confounding by indication. In such a scenario, subjects with prevalent CHD might have avoided chocolate and other foods rich in saturated fats (per friends' or clinicians' advice). However, this is unlikely as higher frequency of chocolate intake was associated with increased consumption of dietary cholesterol and saturated fat in this study. In addition, there was no clinically meaningful difference in mean dietary cholesterol, saturated fat, or polyunsaturated fat between subjects with prevalent CHD and those without CHD. While inclusion of a composite variable for foods frequently avoided in cholesterol-lowering diets or estimated intake of myristate did attenuate the inverse association between chocolate and CHD, the association remained statistically significant and of similar magnitude.

Dark chocolate belongs to the flavonoid-rich foods such as fruit and vegetables, tea, and red wine. Epidemiologic evidence indicates that beneficial effects of whole grains, fruit, vegetables, tea, and red wine on CHD are partly mediated through the effects of their polyphenolic compounds^{7,24,25}. Although, interventional studies have demonstrated beneficial effects of dark chocolate on blood pressure^{8,9,26,27} and endothelial function^{10,11,12}, limited data are available on the effects of total chocolate intake on CHD. In the Iowa Women's Health Study, dietary catechins were inversely associated with coronary heart disease death⁴. In that study⁴, chocolate contributed 6% of total catechins and when analyzed by catechin source, there was suggestive evidence for an inverse association between chocolate derived-catechin and CHD death [RR (95% CI): 0.88 (0.71-1.08)] in a multivariable adjusted model comparing the 3rd with the 1st tertile of catechin. Our data are also consistent with findings among 19,357 subjects in whom dark chocolate intake was associated with a 39% lower risk of myocardial infarction and stroke combined [RR: 0.61 (95% CI 0.44-0.87)]²⁸.

Is CHD effect mediated through the effects of chocolate intake on blood pressure?

In the crude data, we observed an inverse association between frequency of chocolate intake and prevalent hypertension. From the lowest to the highest category of chocolate consumption, prevalence of hypertension was 18.5%, 14.9%, 13.5%, and 14.0%, respectively (p for trend 0.001). However, this association did not persist after adjustment for age, sex, risk group, exercise, fruit and vegetables, non-chocolate candy, energy, alcohol intake, smoking, education, and linolenic acid (p for trend 0.72). Contrary to our findings, a meta-analysis of randomized trials reported a mean systolic blood pressure change of -4.5 mm Hg (95% CI: -5.9 to -3.2) in the active treatment arms across all trials; corresponding change for diastolic blood pressure was -2.5 mm Hg (95% CI: -3.9 to -1.2)²⁹. The inconsistency between these studies and our findings merits comments. While subjects in the ten trials meta-analyzed²⁹ were either normotensive healthy subjects, prehypertensive, or stage 1 hypertensive subjects, our study included subjects with prevalent clinical disease with a wider range for age. Chocolate consumption in our study was self reported – a possible source of misclassification, whereas the trials used specific amounts of dark chocolate per day. Another shortcoming of our study is that we were not able to differentiate between dark and lighter or milk chocolate. However, since milk chocolate has much lower content of polyphenols (and is substantially more frequently consumed in the US), inclusion of subjects consuming exclusively milk or lighter chocolate would have biased our results towards the null in the absence of an effect of milk of lighter chocolate. Another possible explanation for the lack of association with hypertension could be the relatively lower amount of chocolate consumed in our study (only few times per week) compared with 10 to 100 g of chocolate used in intervention studies.

Possible mediation by lipids, diabetes, and adiposity

Inclusion of potential mediating factors such as adiposity, diabetes, hypertension, triglycerides, LDL-, and HDL- cholesterol led to a minimal attenuation of the relation between chocolate consumption and CHD. This suggests that these factors only explain part of the observed relation. Grassi et al.⁹ did not find any change in HDL, LDL, or triglycerides after 15 days of ingesting 100 g of dark chocolate daily. While cocoa butter contains relatively higher amounts of saturated fat [stearic acid (35%) and palmitic acid (25%)], it has been suggested that stearic acid does not elevate blood cholesterol concentration like other saturated fats^{30,31}. A possible explanation for the disparity is hepatic desaturation of stearic acid into oleic acid, inefficient absorption, or chain length³². Other researchers have presented evidence supporting neutral effects of cocoa butter on cholesterol^{33,34}. Lastly, there is evidence from randomized trials suggesting favorable effects of dark chocolate on total and LDL-cholesterol³⁵. It is important to mention that our findings could be partly attributable to the lack of adequate intake of dark chocolate in our population to observe a large effect. We were unable to quantify the proportion of total chocolate contributed by milk vs. dark chocolate in our sample, as we did not query about such details in the food questionnaire. Furthermore, our food questionnaire did not query about cocoa or flavonoid contents, source of chocolate, or chocolate preparation.

Study limitations

The cross-sectional design limits our ability to draw causal inference. In addition, misclassification and reporting bias are inherent to self-reported data on chocolate consumption and we were not able to differentiate dark from milk or lighter chocolate. However, such inability to distinguish the different types of chocolate might have led to an underestimation of the true association between cocoa/chocolate polyphenol consumption and CHD in this study. We were unable to determine the polyphenol content of reported chocolate to contrast our findings with large doses administered in randomized trials where nutrient content is well documented. In particular, beneficial effects of dark chocolate on coronary vasodilation and platelet activity have been previously documented³⁶. Of note is that subjects in our study consumed chocolate only few times per week, indicating that even smaller amounts of chocolate (with few extra calories) may have beneficial effects on cardiovascular health. At this point, we are unable to determine the minimum amount of dark chocolate required for cardiac benefits (although we found beneficial effects only among subjects reporting intake at least once a week). In addition, we cannot completely exclude residual confounding or confounding by indication as alternative explanation for observed findings. Nevertheless, the large sample size (most of whom were from population-based studies), the availability on multiple CHD risk factors, and the multi-center nature of the study are strengths of our report.

In conclusion, our findings suggest that chocolate consumption is inversely associated with a lower prevalence of CHD. Our findings are supported by clinical trials assessing the effects dark chocolate on blood pressure, platelet function, and endothelial function and suggest that consumption of small amounts of chocolate might provide additional benefits in reducing CHD risk.

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Table 1
 Characteristics among 4,970 participants of the NHLBI Family Heart Study by chocolate intake

	Frequency of chocolate consumption					P*
	0 (n=1,093)	1-3 per month (n=1,167)	1-4 per week (n=1,931)	5+ per week (n=779)		
Age (y)	56.2±12.8	52.4±13.8	50.7±13.7	48.9±13.5	<0.0001	
Body Mass Index (kg/m ²)	27.3±5.5	27.6±5.4	27.7±5.6	28.1±5.9	0.0013	
Waist-to-Hip Ratio	0.92±0.09	0.92±0.09	0.92±0.09	0.91±0.08	0.07	
Linolenic acid (g/d)	0.65±0.32	0.71±0.36	0.78±0.36	0.97±0.53	<0.0001	
Energy intake (KJ/d)	1562±659	1661±716	1809±685	2274±984	<0.0001	
Dietary cholesterol (g/d)	0.22±0.14	0.23±0.14	0.25±0.14	0.30±0.17	<0.0001	
Saturated fat (g/d)	16.8±9.6	19.9±11.3	23.4±10.8	33.5±16.7	<0.0001	
Myristic acid (g/d)	1.49±0.98	1.77±1.23	2.01±1.14	2.71±1.56	<0.0001	
Palmitic acid (g/d)	9.33±5.27	11.0±6.2	12.8±5.9	17.8±9.0	<0.0001	
Ratio of total-to-HDL cholesterol	4.29±1.58	4.39±1.53	4.46±1.48	4.40±1.44	0.02	
Triglycerides (mmol/L)	1.71±1.39	1.73±1.34	1.62±0.99	1.69±1.18	0.18	
LDL-cholesterol (mmol/L)	3.21±0.97	3.20±0.87	3.27±0.90	3.21±0.91	0.31	
HDL cholesterol (mmol/L)	1.36±0.43	1.30±0.39	1.28±0.37	1.29±0.38	<0.0001	
Fruits & vegetables (servings/d)	3.73±1.95	3.37±1.79	3.24±1.75	3.22±1.86	<0.0001	
Exercise (min/d)	32.1±37.2	30.0±38.3	27.7±36.2	29.0±39.5	0.010	
Gender (%male)	44.1	44.3	47.9	43.0	0.47	
Random sample (%)	43.7	45.5	46.8	43.5	0.21	
African-Americans (%)	7.0	4.5	3.8	4.1	0.007	
College education (%)	61.0	62.5	66.5	64.9	0.02	
Hypertension (%)	18.5	14.9	13.5	14.0	0.001	
Current drinkers (%)	52.7	56.6	52.8	54.1	0.87	
Current wine consumption (%)	17.5	15.0	12.7	11.4	<0.0001	
Current beer consumption (%)	17.2	20.4	20.9	17.9	0.34	
Current spirits consumption (%)	16.9	18.0	16.9	14.9	0.26	
Current smoker (%)	15.4	14.7	13.8	17.7	0.51	
Currently on weight loss diet (%)	6.0	4.5	3.0	2.4	<0.0001	

	Frequency of chocolate consumption				P*
	0 (n=1,093)	1-3 per month (n=1,167)	1-4 per week (n=1,931)	5+ per week (n=779)	
Current use of vitamin C (%)	8.5	8.7	7.6	5.1	0.008
Current use of vitamin E (%)	13.2	13.5	10.9	8.1	0.0002
Current use of multivitamins (%)	26.4	23.5	22.8	21.1	0.005
Candy consumption (%) [†]	29.5	65.1	80.0	80.9	<0.0001

* P value for trend

[†] Non-chocolate candy

Table 2

Prevalence odds ratios (95% confidence intervals) of coronary heart disease according to chocolate consumption in 4,970 participants in the NHLBI Family Heart Study*

Frequency of chocolate intake	Cases/N	Crude	Model 1 [†]	Model 2 [‡]
0	168/1093	1.0	1.0	1.0
1-3 per month	147/1167	0.79 (0.62-1.01)	1.01 (0.76-1.37)	1.05 (0.77-1.43)
1-4 per week	182/1931	0.57 (0.46-0.72)	0.74 (0.56-0.98)	0.75 (0.56-1.01)
5+ per week	43/779	0.32 (0.23-0.45)	0.43 (0.28-0.67)	0.43 (0.27-0.68)
P for linear trend		<0.0001	<0.0001	0.0002

* Coronary heart disease was defined as history of myocardial infarction, PTCA, or CABG.

[†] Adjusted for age, sex, and risk group (random vs. high risk) using generalized estimating equations (GEE)

[‡] Variables in model 1 plus additional adjustment for dietary linolenic acid, education, exercise (min/d), smoking (yes/no), alcohol intake (yes/no), fruit and vegetables, energy intake, and non-chocolate candy (4 groups) consumption.

Table 3

Prevalence odds ratios (95% confidence intervals) of coronary heart disease according to chocolate consumption in 4,366 subjects free of diabetes mellitus and subjects who were on weight loss diet*

Frequency of chocolate intake	Cases/N	Crude	Model 1 [†]	Model 2 [‡]
0	121/870	1.0	1.0	1.0
1-3 per month	112/1023	0.76 (0.58-1.00)	0.90 (0.65-1.23)	0.98 (0.70-1.36)
1-4 per week	140/17481	0.54 (0.42-0.70)	0.65 (0.49-0.87)	0.68 (0.49-0.94)
5+ per week	32/725	0.29 (0.19-0.43)	0.36 (0.23-0.57)	0.38 (0.23-0.63)
P for linear trend		<0.0001	<0.0001	0.0002

* Coronary heart disease was defined as history of myocardial infarction, PTCA, or CABG.

[†] Adjusted for age, sex, and risk group (random vs. high risk) using generalized estimating equations (GEE)

[‡] Variables in model 1 plus additional adjustment for dietary linolenic acid, education, exercise (min/d), smoking (yes/no), alcohol intake (yes/no), fruit and vegetables, energy intake, and non-chocolate candy (4 groups) consumption.

Table 4

Prevalence odds ratios (95% confidence intervals) of coronary heart disease according to chocolate consumption and age in 4,970 subjects in the NHLBI Family Heart Study*

Age:	≤ 60 years		> 60 years	
	Cases/N	OR (95% CI) [†]	Cases/N	OR (95% CI) [†]
0	51/595	1.0	117/498	1.0
1-3 per month	46/763	0.80 (0.49-1.31)	101/404	1.12 (0.78-1.60)
1-4 per week	49/1347	0.48 (0.29-0.79)	133/584	0.90 (0.64-1.27)
5+ per week	13/584	0.36 (0.17-0.75)	30/195	0.48 (0.28-0.83)
P for linear trend		0.0004		0.016

* Coronary heart disease was defined as history of myocardial infarction, PTCA, or CABG.

[†] Adjusted for age, sex, risk group (random vs. high risk), dietary linolenic acid, education, exercise, smoking (yes/no), alcohol intake (yes/no), fruit and vegetables, energy intake, and non-chocolate candy (4 groups) consumption, using GEE.