Published in final edited form as:

Am Heart J. 2017 January ; 183: 18–23. doi:10.1016/j.ahj.2016.10.002.

Chocolate Intake and Incidence of Heart Failure: Findings from the Cohort of Swedish Men

Daniel A. Steinhaus, MD[a], **Elizabeth Mostofsky, ScD**[b,c], **Emily B. Levitan, ScD**[d], **Kirsten S. Dorans, BSc**[b,c], **Niclas Håkansson, PhD**[e], **Alicja Wolk, DrMedSci**[e], and **Murray A. Mittleman, MD, DrPH**[b,c]

[a] Cardiovascular Division, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, 375 Longwood Avenue, Boston, MA 02215

[b] Cardiovascular Epidemiology Research Unit, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, 375 Longwood Avenue, Boston, MA 02215

[c] Department of Epidemiology, Harvard School of Public Health, 677 Huntington Ave, Boston, MA, 02215

[d] Department of Epidemiology, University of Alabama at Birmingham, 1665 University Blvd, Birmingham, AL 35294

[e] Institute of Environmental Medicine, Karolinska Institutet, SE-171 77 Stockholm, Sweden

Abstract

Aims—The objective of this study was to evaluate the association of chocolate consumption and heart failure in a large population of Swedish men.

Methods and Results—We conducted a prospective cohort study of 31,917 men 45-79 years old with no history of myocardial infarction, diabetes, or HF at baseline who were participants in the population-based Cohort of Swedish Men (COSM) study. Chocolate consumption was assessed through a self-administrated food frequency questionnaire. Participants were followed for HF hospitalization or mortality from January 1, 1998 to December 31, 2011 using record linkage to the Swedish inpatient and cause-of-death registries. During 14 years of follow up, 2,157 men were hospitalized (n = 1901) or died from incident HF (n = 256). Compared with subjects who reported no chocolate intake, the multivariable-adjusted rate ratio of HF was 0.88 (95%CI 0.78-0.99) for those consuming 1-3 servings per month, 0.83 (95%CI 0.72-0.94) for those consuming 1-2 servings per week, 0.82 (95%CI 0.68-0.99) for those consuming 3-6 servings per

Corresponding author: Murray A Mittleman, MD, DrPH, Cardiovascular Epidemiology Research Unit, Beth Israel Deaconess Medical Center, 375 Longwood Avenue, Room 423 Boston, MA 02215, mmittlem@bidmc.harvard.edu, Tel: (617) 632-7653, Fax: (617) 632-7698.

Conflicts of Interest: None

Conflicts of Interest

All authors have no conflicts to declare. The authors are solely responsible for the design and conduct of this study, all study analyses and drafting and editing of the paper.

week, and 1.10 (95%CI 0.84-1.45) for those consuming ≥1 servings per day (*P* for quadratic trend= 0.001).

Conclusions—In this large prospective cohort study, there was a J-shaped relationship between chocolate consumption and HF incidence. Moderate chocolate consumption was associated with a lower rate of HF hospitalization or death, but the protective association was not observed among individuals consuming ≥1 servings per day.

Keywords

Heart failure; chocolate; epidemiology; diet

Introduction

Heart failure (HF) is a common cause of morbidity and mortality worldwide. There are an estimated 5.1 million people with HF in the United States and 23 million worldwide.[1,2] Traditional contributors to the development of HF include coronary heart disease, hypertension, cigarette smoking, obesity, diabetes, and valvular heart disease. With the increasing epidemic of HF, prevention is an important public health concern.[3]

Recent studies indicate that chocolate products may have beneficial effects on cardiovascular health. [4-9] Importantly, multiple studies have demonstrated that consumption of chocolate reduces systolic and diastolic blood pressure after acute and chronic intake. [10-14] In addition, observational studies have shown that habitual chocolate intake is associated with lower incidence of stroke and myocardial infarction (MI),[15] lower incidence of mortality from coronary heart disease,[5,6] lower cardiac mortality and heart failure after incident MI,[16] and improved vascular function in patients with HF. [15,17,18]

There is limited research on the association of chocolate consumption and heart failure. Therefore, we studied whether chocolate intake is associated with the risk of incident HF hospitalization or mortality in a population of Swedish men.

Methods

Study Cohort

The Cohort of Swedish Men (COSM) is a population-based cohort study established in central Sweden (Västmanland and Örebro counties) and includes 48,850 men aged 45-79 years old in 1997, when baseline data were collected.[19,20] The cohort includes questionnaire-based information about such modifiable lifestyle factors as diet, physical activity, smoking, weight, use of dietary supplements, some prescribed drugs, and alcohol. Cardiovascular and other diseases as well as surgeries and causes of death are identified by linkage to the National Inpatient and other registries at the Swedish Board of Health and Welfare.

We excluded subjects with an incorrect or incomplete national registration number, subjects with implausible reported energy intakes (defined as more than 3 standard deviations from the mean value of the natural logarithm-transformed energy intake), missing data for more

than half of the food and beverage items, prior history of cancer, heart failure, prior myocardial infarction (MI) or diabetes, and those with missing information on chocolate consumption. We excluded men with a history of MI or diabetes at baseline because these men were more likely to have received dietary counseling that could affect their reporting of diet. After these exclusions, data on 31,917 participants were available for this analysis.

Chocolate Consumption

Diet was assessed at baseline using a self-administered 96-item, validated, food frequency questionnaire.[21] For foods such as milk, coffee, cheese, and bread, which are commonly eaten in Sweden, participants reported their consumption in servings per day or per week in the past year. For chocolate and other foods, there were 8 predefined responses, ranging from never to 3+ times per day (no regular intake, 1 to 3 servings per month, 1 to 2 servings per week, 3 to 4 servings per week, 5 to 6 servings per week, 1 serving per day, 2 servings per day, and 3 or more servings per day). Participants were not asked about what type of chocolate they ate, but in the 1990s, approximately 90% of chocolate consumption in Sweden was milk chocolate, and it contained approximately 30% cocoa solids.[16] A study comparing our questionnaire to 7-day diet records indicated that among Swedish men, the average portion of chocolate ranged from 26 to 42 grams.[22] In contrast, the standard portion size in the United States is 28.4 grams.[23]

Other Covariates

We calculated total calorie intake based on the food frequency questionnaire. The questionnaire included items on education, cigarette smoking, frequency of consumption of beer, wine, and spirits, family history of MI before age 60, history of hypertension, and history of high cholesterol. History of MI at baseline was assessed through the Swedish inpatient register. We considered participants to have diabetes if they self-reported diabetes on the questionnaire or had been given any diagnosis of diabetes as recorded in the inpatient register. Physical activity was estimated by calculating metabolic equivalent in hours per day for occupational physical activity, exercise, and sedentary behavior.[24] Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2; both self-reported).

A Dietary Approaches to Stop Hypertension (DASH) diet component score was calculated by ranking participants on intake of 1) fruits, 2) vegetables, 3) nuts and legumes, 4) low-fat dairy, 5) whole grains, 6) sodium, 7) sweetened beverages, and 8) red and processed meats.[25] Participants in the highest quintile of fruits, vegetables, nuts and legumes, low-fat dairy and whole grains received a score of 5 and those in the lowest quintile received a score of 1. Participants in the highest quintile of sodium, sweetened beverages, and red and processed meats received a score of 1 and those in the lowest quintile received a score of 5. The score for each component was summed to get the overall DASH score. Participants were then categorized into quartiles based on the DASH diet component score.[26]

Follow-Up and Ascertainment of HF

Individuals were observed from January 1, 1998, until the date of first hospital admission or death from heart failure (HF), death from other causes, or end of follow-up (December 31, 2011), whichever came first. The primary end point was defined as a composite of

hospitalization for HF as a primary or secondary diagnosis as determined through the Swedish Inpatient Registry records and the Swedish National Death Register records using the International Classification of Diseases (ICD-9) code 428 and the ICD-10 codes I50 or I11.0. The Swedish inpatient register was validated in a previous study, and 95% of the patients with these ICD codes as the primary diagnosis were confirmed to have a diagnosis of HF by medical record review, as defined by European Society of Cardiology criteria.[27] Heart failure was confirmed in 82% of patients with primary or secondary diagnosis of HF.[27]

Statistical Analysis

Chocolate intake was categorized as no regular chocolate intake, 1 to 3 servings of chocolate per month, 1 to 2 servings per week, 3 to 6 servings per week, and ≥1 servings per day. Because some of the participants were missing data on BMI (4%) and physical activity (19%), we used Markov chain Monte Carlo multiple imputation to simulate 5 complete data sets, as previously described.[19,28] All statistical analyses were performed in each data set separately. The results were averaged, and CIs and *P* values were calculated, accounting for the uncertainty in the imputed estimates.[28]

We reported baseline characteristics stratified by category of chocolate intake as mean and standard deviation or as counts with proportions, as appropriate. We used Cox proportional hazard models to compute multivariable-adjusted rate ratios with corresponding 95% confidence intervals (CIs), with participants in the lowest category of chocolate intake (none) as the reference group. For the Cox proportional hazard models, we chose covariates a priori that we considered potential confounders on the basis of their association with both chocolate intake and development of HF. In the first-stage model, we accounted for age by allowing the baseline rate to vary with age and adjusted for total energy intake (continuous). A second model was additionally adjusted for the DASH diet component score (quartile), education (less than high school, high school, university), cigarette smoking (current, past, never), alcohol consumption (never drinker, former drinker, current drinker <1 drink/week, current drinker 1-7 drinks/week, current drinker 7-14 drinks/week, current drinker >14 drinks/week), self-reported family history of MI before age 60 (yes, no), self-reported history of hypertension (yes, no), self-reported history of high cholesterol (yes, no), BMI (continuous) and physical activity (continuous). We conducted a test for the quadratic component of trend by using the median-centered value for each level of chocolate intake and determined the statistical significance of its squared value in the multivariable model.

We performed multiple sensitivity analyses. We used both primary and secondary diagnosis of heart failure in our primary analysis which has shown validity in this population;[27] however, we also performed an analysis restricted to only primary heart failure diagnosis. In order to assess whether the inverse association between chocolate intake and HF was mediated through history of hypertension, the rate ratios for chocolate intake in the multivariable-adjusted model were contrasted with the estimates for chocolate intake when the indicator variable for hypertension was removed from the model. In order to further exclude patients at high risk, we performed an analysis excluding patients with hypertension and hyperlipidemia. To examine the possibility that participants reporting lower intake of

chocolate had undiagnosed risk factors placing them at immediate HF risk, we conducted an analysis that excluded individuals with a follow-up time of <2 years. We evaluated the effect of healthy diet on the outcome with stratification by quartile of DASH score. We further performed an analysis stratified by smoking status for current, former, and never smokers and an analysis stratified by marital status (single, married/living with someone, divorced, widower).

Because milk consumption may inhibit the intestinal absorption of flavonoids, which may be responsible for the cardio-protective effects of chocolate,[29] we calculated the product of indicator variables for chocolate intake and for milk consumption above or below the median and tested the significance of this term in the multivariable model using a likelihood ratio test. We also examined whether the association varied by regular physical activity or BMI by performing a similar test of interaction using the product of indicator variables for chocolate intake and the potential modifier.

We tested the proportional hazard assumption by including product terms of the predictors and the log of survival time, and found no significant violations. Statistical analyses were performed using SAS version 9.3. Two-sided $P<0.05$ was considered statistically significant.

Results

During 14 years of follow up, 2,157 men were hospitalized for first HF (n=1,901) or died of HF (n=256), corresponding to a crude rate of 5.2 cases per 1,000 person-years. Median chocolate intake was 1-3 servings per month. Compared to men reporting no chocolate intake, men who ate more chocolate had higher total daily energy intake, were more likely to be never smokers and have university-level education, and were less likely to be previously diagnosed with hypertension (Table 1).

Compared with subjects who reported no chocolate intake, the multivariable-adjusted rate ratio of HF was 0.88 (95%CI 0.78-0.99) for those consuming 1-3 servings per month, 0.83 (95%CI 0.72-0.94) for those consuming 1-2 servings per week, 0.82 (95%CI 0.68-0.99) for those consuming 3-6 servings per week, and 1.10 (95%CI 0.84-1.45) for those consuming ≥1 servings per day (*P* for quadratic trend= 0.001; ‘ 2).

In sensitivity analyses, the results were not materially different when we restricted the analysis to primary heart failure diagnosis or to participants with follow-up times ≥2 years. The results remained similar when we did not adjust for self-reported hypertension, and when we excluded patients with hypertension and hyperlipidemia. When stratified by quartile of DASH score, the association was similar across categories of DASH score even among those with DASH scores consistent with healthy eating patterns. Stratification by smoking status or marital status did not materially change our results. The association between chocolate intake and HF was not modified by dairy intake, BMI or physical activity. Although consumption of biscuits, pastries, candy, ice cream, and chips and popcorn was strongly related to chocolate intake, it was not associated with HF incidence.

Discussion

In this prospective study, we found that moderate habitual chocolate intake in men was associated with a lower rate of HF hospitalization or death, but the protective association was not observed with intake of ≥1 servings per day.

Chocolate has been shown to have multiple benefits to cardiovascular health, possibly mediated in part through their high concentration of plant-derived antioxidants called flavonoids. [7,30] Chocolate provides a significant dietary source of flavonoids, which are also present in tea and wine. Chocolate and cocoa flavonoids are associated with beneficial effects on endothelial function,[31-35] blood pressure,[7,10-14] platelets,[36-39] inflammation, [40,41] high-density lipoprotein cholesterol,[42] insulin sensitivity,[43] and cardiometabolic makers.[44] Chocolate may also have beneficial effects irrespective of flavonoid content including improved vascular function and lower leukocyte adherence capacity.[9]

Multiple observational studies have demonstrated that chocolate intake is associated with clinical outcomes. Chocolate intake is associated with lower incidence of stroke [22,45] and MI,[15] lower incidence of mortality from coronary heart disease,[5,6] and lower cardiac mortality in patients after their first MI.[16]

Recent prospective studies have shown that moderate chocolate consumption is associated with a lower incidence of HF in a cohort of Swedish women[46] and a cohort of American male physicians.[47] In the Physicians' Health Study of 20,278 US male physicians in multivariable-adjusted hazard ratios for HF were 0.86 (0.72–1.03), 0.80 (0.66–0.98), 0.92 (0.74–1.13), and 0.82 (0.63–1.07) for chocolate consumption of <1 serving per month, 1 – 3 servings per month, 1 serving per week, 2 – 4 servings per week, and ≥5 servings per week, respectively. After stratifying by BMI, there was evidence of an inverse relationship between chocolate consumption and HF only among men with a BMI <25 kg/m^2. While the distribution of BMI and the results of this study are similar to our current study, we found no modification by BMI in our population. The reason for this discrepancy is not clear but may be related to differences in the type and flavonoid content of chocolate consumed in the US compared to this Swedish cohort.

The observed J-shaped relationship between chocolate consumption and heart failure may be due to the fact that we adjusted for total daily caloric intake. Therefore, it is possible that men who consume higher levels of chocolate on a daily basis are consuming fewer calories from foods that may be salutary. Furthermore, as we were not not able to assess the exact consumption of cocoa flavonoids, it is unclear if a more linear relationship exists between flavonoids and heart failure.

There are a few limitations of our study. Because of the observational nature of the study, we cannot exclude residual or unmeasured confounding. However, we have extensive information on lifestyle, diet, and comorbid conditions and our results were robust after multivariable analyses. We also cannot exclude reverse causation, but we have attempted to limit this concern by performing a sensitivity analysis excluding the first two years of follow up."The flavonoid content of chocolate consumed in our sample was likely relatively low; therefore our findings may underestimate the protective effects of higher-flavonoid

chocolate. Alternatively, given the high percentage of milk chocolate consumption in Sweden at the time of the study, it is possible that other non-flavanoid compounds may account for our findings. However, Swedish milk chocolate has a much higher cocoa content (30%) compared to American milk chocolate which has a cocoa content of around 10%. Chocolate consumption and risk factors were measured at baseline, and there was no information on changes in chocolate consumption over time. Additionally, although the accuracy of the diagnosis of HF in the Swedish registers is high,[27] they only include cases of HF that resulted in hospitalization or death, and the registers do not have information on HF etiology or type (systolic or diastolic). Despite the limitations, this study has many strengths, including a large sample size, a long duration of follow-up, and a prospective design.

In conclusion, in this population of middle-aged and elderly Swedish men, moderate habitual chocolate intake was associated with a lower rate of HF hospitalization or death, but the protective association was not observed with intake of ≥1 servings per day. Future studies are needed to determine the optimal dose of chocolate and/or cocoa flavonoids and determine the underlying mechanisms.

Acknowledgments

Sources of Funding

This work was supported by grants from the National Heart, Lung, and Blood Institute [grant numbers HL-120505; HL-115623; HL-007575), the European Research Council (ERC), EU 7th Research Framework Program [grant number 281760], a KL2/Catalyst Medical Research Investigator Training award (an appointed KL2 award) from Harvard Catalyst | The Harvard Clinical and Translational Science Center, National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award [KL2 TR001100] and the Danish Cancer Society and the Danish Council for Strategic Research (Aalborg AF-Study Group). The content is solely the responsibility of the authors and does not necessarily represent the official views of the European Research Council, Harvard Catalyst, Harvard University and its affiliated academic healthcare centers, or the National Institutes of Health. No funding organization had any role in the design and conduct of the study; collection; management, analysis and interpretation of the data; and preparation of the manuscript.

References

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Magid D, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER, Moy CS, Mussolino ME, Nichol G, Paynter NP, Schreiner PJ, Sorlie PD, Stein J, Turan TN, Virani SS, Wong ND, Woo D, Turner MB, American Heart Association Statistics C, Stroke Statistics S. Heart disease and stroke statistics--2013 update: a report from the American Heart Association. Circulation. 2013; 127:e6–e245. [PubMed: 23239837]
2. McMurray JJ, Petrie MC, Murdoch DR, Davie AP. Clinical epidemiology of heart failure: public and private health burden. Eur Heart J. 1998; 19(Suppl P):P9–16. [PubMed: 9886707]
3. Schocken DD, Benjamin EJ, Fonarow GC, Krumholz HM, Levy D, Mensah GA, Narula J, Shor ES, Young JB, Hong Y, American Heart Association Council on E, Prevention, American Heart Association Council on Clinical C, American Heart Association Council on Cardiovascular N, American Heart Association Council on High Blood Pressure R, Quality of C, Outcomes Research Interdisciplinary Working G, Functional G, Translational Biology Interdisciplinary Working G. Prevention of heart failure: a scientific statement from the American Heart Association Councils on Epidemiology and Prevention, Clinical Cardiology, Cardiovascular Nursing, and High Blood Pressure Research; Quality of Care and Outcomes Research Interdisciplinary Working Group; and Functional Genomics and Translational Biology Interdisciplinary Working Group. Circulation. 2008; 117:2544–2565. [PubMed: 18391114]

4. Cooper KA, Donovan JL, Waterhouse AL, Williamson G. Cocoa and health: a decade of research. Br J Nutr. 2008; 99:1–11. [PubMed: 17666148]
5. Ding EL, Hutfless SM, Ding X, Girotra S. Chocolate and prevention of cardiovascular disease: a systematic review. Nutr Metab (Lond). 2006; 3:2. [PubMed: 16390538]
6. Mink PJ, Scrafford CG, Barraj LM, Harnack L, Hong CP, Nettleton JA, Jacobs DR Jr. Flavonoid intake and cardiovascular disease mortality: a prospective study in postmenopausal women. Am J Clin Nutr. 2007; 85:895–909. [PubMed: 17344514]
7. Hooper L, Kay C, Abdelhamid A, Kroon PA, Cohn JS, Rimm EB, Cassidy A. Effects of chocolate, cocoa, and flavan-3-ols on cardiovascular health: a systematic review and meta-analysis of randomized trials. Am J Clin Nutr. 2012; 95:740–751. [PubMed: 22301923]
8. Engler MB, Engler MM. The emerging role of flavonoid-rich cocoa and chocolate in cardiovascular health and disease. Nutr Rev. 2006; 64:109–118. [PubMed: 16572598]
9. Esser D, Mars M, Oosterink E, Stalmach A, Muller M, Afman LA. Dark chocolate consumption improves leukocyte adhesion factors and vascular function in overweight men. FASEB J. 2014; 28:1464–1473. [PubMed: 24302679]
10. Ried K, Sullivan TR, Fakler P, Frank OR, Stocks NP. Effect of cocoa on blood pressure. Cochrane Database Syst Rev. 2012; 8:CD008893.
11. Desch S, Kobler D, Schmidt J, Sonnabend M, Adams V, Sareban M, Eitel I, Bluher M, Schuler G, Thiele H. Low vs. higher-dose dark chocolate and blood pressure in cardiovascular high-risk patients. Am J Hypertens. 2010; 23:694–700. [PubMed: 20203627]
12. Desch S, Schmidt J, Kobler D, Sonnabend M, Eitel I, Sareban M, Rahimi K, Schuler G, Thiele H. Effect of cocoa products on blood pressure: systematic review and meta-analysis. Am J Hypertens. 2010; 23:97–103. [PubMed: 19910929]
13. Grassi D, Necozione S, Lippi C, Croce G, Valeri L, Pasqualetti P, Desideri G, Blumberg JB, Ferri C. Cocoa reduces blood pressure and insulin resistance and improves endothelium-dependent vasodilation in hypertensives. Hypertension. 2005; 46:398–405. [PubMed: 16027246]
14. Taubert D, Roesen R, Schomig E. Effect of cocoa and tea intake on blood pressure: a meta-analysis. Arch Intern Med. 2007; 167:626–634. [PubMed: 17420419]
15. Buijsse B, Weikert C, Drogan D, Bergmann M, Boeing H. Chocolate consumption in relation to blood pressure and risk of cardiovascular disease in German adults. Eur Heart J. 2010; 31:1616–1623. [PubMed: 20354055]
16. Janszky I, Mukamal KJ, Ljung R, Ahnve S, Ahlbom A, Hallqvist J. Chocolate consumption and mortality following a first acute myocardial infarction: the Stockholm Heart Epidemiology Program. J Intern Med. 2009; 266:248–257. [PubMed: 19711504]
17. Flammer AJ, Sudano I, Wolfrum M, Thomas R, Enseleit F, Periat D, Kaiser P, Hirt A, Hermann M, Serafini M, Leveques A, Luscher TF, Ruschitzka F, Noll G, Corti R. Cardiovascular effects of flavanol-rich chocolate in patients with heart failure. Eur Heart J. 2012; 33:2172–2180. [PubMed: 22173910]
18. Buijsse B, Feskens EJ, Kok FJ, Kromhout D. Cocoa intake, blood pressure, and cardiovascular mortality: the Zutphen Elderly Study. Arch Intern Med. 2006; 166:411–417. [PubMed: 16505260]
19. Levitan EB, Yang AZ, Wolk A, Mittleman MA. Adiposity and incidence of heart failure hospitalization and mortality: a population-based prospective study. Circ Heart Fail. 2009; 2:202–208. [PubMed: 19808341]
20. Wolk A, Larsson SC, Johansson JE, Ekman P. Long-term fatty fish consumption and renal cell carcinoma incidence in women. JAMA. 2006; 296:1371–1376. [PubMed: 16985229]
21. Messerer M, Johansson SE, Wolk A. The validity of questionnaire-based micronutrient intake estimates is increased by including dietary supplement use in Swedish men. J Nutr. 2004; 134:1800–1805. [PubMed: 15226472]
22. Larsson SC, Virtamo J, Wolk A. Chocolate consumption and risk of stroke: a prospective cohort of men and meta-analysis. Neurology. 2012; 79:1223–1229. [PubMed: 22933736]
23. United States Department of Agriculture. USDA National Nutrient Database for Standard Reference, Release 27 (revised). Version Current: May 2015. Internet: http://www.ars.usda.gov/ba/bhnrc/ndl

24. Orsini N, Bellocco R, Bottai M, Pagano M, Wolk A. Reproducibility of the past year and historical self-administered total physical activity questionnaire among older women. Eur J Epidemiol. 2007; 22:363–368. [PubMed: 17333471]
25. Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. Arch Intern Med. 2008; 168:713–720. [PubMed: 18413553]
26. Levitan EB, Wolk A, Mittleman MA. Relation of consistency with the dietary approaches to stop hypertension diet and incidence of heart failure in men aged 45 to 79 years. Am J Cardiol. 2009; 104:1416–1420. [PubMed: 19892061]
27. Ingelsson E, Arnlov J, Sundstrom J, Lind L. The validity of a diagnosis of heart failure in a hospital discharge register. Eur J Heart Fail. 2005; 7:787–791. [PubMed: 15916919]
28. Schafer, JL. Analysis of incomplete multivariate data. Chapman & Hall; Boca Raton: 1997. p. xivp. 430
29. Serafini M, Bugianesi R, Maiani G, Valtuena S, De Santis S, Crozier A. Plasma antioxidants from chocolate. Nature. 2003; 424:1013. [PubMed: 12944955]
30. Natsume M, Osakabe N, Yamagishi M, Takizawa T, Nakamura T, Miyatake H, Hatano T, Yoshida T. Analyses of polyphenols in cacao liquor, cocoa, and chocolate by normal-phase and reversed-phase HPLC. Biosci Biotechnol Biochem. 2000; 64:2581–2587. [PubMed: 11210120]
31. Engler MB, Engler MM, Chen CY, Malloy MJ, Browne A, Chiu EY, Kwak HK, Milbury P, Paul SM, Blumberg J, Mietus-Snyder ML. Flavonoid-rich dark chocolate improves endothelial function and increases plasma epicatechin concentrations in healthy adults. J Am Coll Nutr. 2004; 23:197–204. [PubMed: 15190043]
32. Farouque HM, Leung M, Hope SA, Baldi M, Schechter C, Cameron JD, Meredith IT. Acute and chronic effects of flavanol-rich cocoa on vascular function in subjects with coronary artery disease: a randomized double-blind placebo-controlled study. Clin Sci (Lond). 2006; 111:71–80. [PubMed: 16551272]
33. Ferri C, Grassi D, Grassi G. Cocoa beans, endothelial function and aging: an unexpected friendship? J Hypertens. 2006; 24:1471–1474. [PubMed: 16877946]
34. Hermann F, Spieker LE, Ruschitzka F, Sudano I, Hermann M, Binggeli C, Luscher TF, Riesen W, Noll G, Corti R. Dark chocolate improves endothelial and platelet function. Heart. 2006; 92:119–120. [PubMed: 16365364]
35. Muniyappa R, Hall G, Kolodziej TL, Karne RJ, Crandon SK, Quon MJ. Cocoa consumption for 2 wk enhances insulin-mediated vasodilatation without improving blood pressure or insulin resistance in essential hypertension. Am J Clin Nutr. 2008; 88:1685–1696. [PubMed: 19064532]
36. Rein D, Paglieroni TG, Wun T, Pearson DA, Schmitz HH, Gosselin R, Keen CL. Cocoa inhibits platelet activation and function. Am J Clin Nutr. 2000; 72:30–35. [PubMed: 10871557]
37. Bordeaux B, Yanek LR, Moy TF, White LW, Becker LC, Faraday N, Becker DM. Casual chocolate consumption and inhibition of platelet function. Prev Cardiol. 2007; 10:175–180. [PubMed: 17917513]
38. Holt RR, Schramm DD, Keen CL, Lazarus SA, Schmitz HH. Chocolate consumption and platelet function. JAMA. 2002; 287:2212–2213. [PubMed: 11980520]
39. Innes AJ, Kennedy G, McLaren M, Bancroft AJ, Belch JJ. Dark chocolate inhibits platelet aggregation in healthy volunteers. Platelets. 2003; 14:325–327. [PubMed: 12944249]
40. di Giuseppe R, Di Castelnuovo A, Centritto F, Zito F, De Curtis A, Costanzo S, Vohnout B, Sieri S, Krogh V, Donati MB, de Gaetano G, Iacoviello L. Regular consumption of dark chocolate is associated with low serum concentrations of C-reactive protein in a healthy Italian population. J Nutr. 2008; 138:1939–1945. [PubMed: 18806104]
41. Selmi C, Mao TK, Keen CL, Schmitz HH, Eric Gershwin M. The anti-inflammatory properties of cocoa flavanols. J Cardiovasc Pharmacol. 2006; 47(Suppl 2):S163–171. discussion S172-166. [PubMed: 16794453]
42. Mursu J, Voutilainen S, Nurmi T, Rissanen TH, Virtanen JK, Kaikkonen J, Nyyssonen K, Salonen JT. Dark chocolate consumption increases HDL cholesterol concentration and chocolate fatty acids may inhibit lipid peroxidation in healthy humans. Free Radic Biol Med. 2004; 37:1351–1359. [PubMed: 15454274]

43. Grassi D, Lippi C, Necozione S, Desideri G, Ferri C. Short-term administration of dark chocolate is followed by a significant increase in insulin sensitivity and a decrease in blood pressure in healthy persons. Am J Clin Nutr. 2005; 81:611–614. [PubMed: 15755830]

44. Sarria B, Martinez-Lopez S, Sierra-Cinos JL, Garcia-Diz L, Mateos R, Bravo L. Regular consumption of a cocoa product improves the cardiometabolic profile in healthy and moderately hypercholesterolaemic adults. Br J Nutr. 2014; 111:122–134. [PubMed: 23823716]

45. Larsson SC, Virtamo J, Wolk A. Chocolate consumption and risk of stroke in women. J Am Coll Cardiol. 2011; 58:1828–1829. [PubMed: 21996399]

46. Mostofsky E, Levitan EB, Wolk A, Mittleman MA. Chocolate intake and incidence of heart failure: a population-based prospective study of middle-aged and elderly women. Circ Heart Fail. 2010; 3:612–616. [PubMed: 20713904]

47. Petrone AB, Gaziano JM, Djousse L. Chocolate consumption and risk of heart failure in the Physicians' Health Study. Eur J Heart Fail. 2014; 16:1372–1376. [PubMed: 25311633]

Table 1

Baseline Characteristics by Chocolate Intake

Characteristic	No Intake (n=4209)		1-3 Servings/mo (n=15759)		1-2 Servings/wk (n=9005)		3-6 Servings/wk (n=2416)		≥1 Servings/d (n=528)	
Age, y	59.4 ± 9.2		57.8 ± 8.9		57.4 ± 8.9		59.0 ± 9.5		62.1 ± 9.9	
Physical Activity, MET h/d	41.7 ± 5.1		41.7 ± 4.9		41.4 ± 4.8		41.2 ± 4.9		41.4 ± 5.1	
BMI, kg/m^2	25.9 ± 3.5		25.7 ± 3.2		25.5 ± 3.1		25.2 ± 3.1		25.2 ± 3.1	
Energy intake, kcal/d	2529 ± 814		2664 ± 773		2874 ± 792		3034 ±811		3480 ± 1118	
Alcohol consumption, g/d	17.2 ± 27.5		15.6 ± 22.9		16.0 ± 18.0		16.1 ± 16.8		19.3 ± 34.6	
DASH score	24.0 ± 4.4		24.0 ± 4.1		23.7 ± 4.0		23.6 ± 4.1		23.5 ± 4.3	
Cigarette smoking										
Current	1087	26.1	3688	23.7%	1974	22.2%	557	23.3%	113	21.8%
Past	1739	41.7%	6087	39.0%	3289	37.0%	848	35.5%	181	34.9%
Never	1344	32.2%	5818	37.3%	3637	40.9%	983	41.2%	225	43.4%
Education										
Less than high school	2913	69.8%	10432	66.5%	5432	60.6%	1443	60.2%	350	66.9%
High school	582	13.9%	2453	15.6%	1512	16.9%	416	17.3%	64	12.2%
University	681	16.3%	2792	17.8%	2019	22.5%	540	22.5%	109	20.8%
Family History of MI	504	12.0%	1847	11.7%	1082	12.0%	267	11.1%	54	10.2%
History of hypertension	938	22.3%	2915	18.5%	1497	16.6%	429	17.8%	91	17.2%
History of high cholesterol	534	12.7%	1895	12.0%	1021	11.3%	267	11.1%	54	10.2%

*MET indicates metabolic equivalent of task

Missing data on physical activity (n=6150), BMI (n=1222), smoking history (n=347), education (n=179), family history of MI (n=7381)

Table 2

Rate Ratios and 95% CIs Comparing Different Levels of Chocolate Intake to Those Reporting No Chocolate Intake

					Model 1*			Model 2†		
Chocolate Intake	**N**	**Cases**	**Person Years**	**Crude Rate per 1,000 person years**	**HR**	**95% CI**		**HR**	**95% CI**	
None	4,209	371	52,633	7.05	1.00	(Ref)		1.00	(Ref)	
1-3/month	15,759	1,026	204,488	5.02	0.82	0.73	0.93	0.88	0.78	0.99
1-2/week	9,005	532	117,570	4.52	0.76	0.67	0.87	0.83	0.72	0.94
3-6/week	2,416	163	30,847	5.28	0.74	0.61	0.89	0.82	0.68	0.99
≥1/day	528	65	6,417	10.13	1.01	0.77	1.32	1.10	0.84	1.45
P for quadratic trend						<0.0001			0.001	

*Cox proportional hazards model adjusted for total energy intake and accounting for age.

†Additionally adjusted for DASH diet component score, education, BMI, physical activity, cigarette smoking, alcohol consumption, family history of myocardial infarction, self-reported history of hypertension, and self-reported history of high cholesterol