

Original Research



Chocolate consumption and the prevalence of metabolic syndrome in the Korean adult population: an analysis based on the 2014-2016 Korea National Health and Nutrition Examination Survey

NaRae Kim 🕞 and Min-Sun Jeon 🕞 §

Department of Food and Nutrition, Chungnam National University, Daejeon 34134, Korea



Received: Feb 4, 2020 **Revised:** Mar 16, 2020 **Accepted:** May 29, 2020

§Corresponding Author:

Min-Sun Jeon

Department of Food and Nutrition, Chungnam National University, 99 Daehak-ro, Yuseong-gu, Daejeon 34134, Korea. Tel. +82-42-821-6836 Fax. +82-42-821-8887 E-mail. dearms@cnu.ac.kr

©2021 The Korean Nutrition Society and the Korean Society of Community Nutrition
This is an Open Access article distributed under the terms of the Creative Commons
Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

NaRae Kim 🝺

https://orcid.org/0000-0002-3673-1388 Min-Sun Jeon (D)

https://orcid.org/0000-0002-3396-5939

Conflict of Interest

The authors declare no potential conflicts of interests.

ABSTRACT

BACKGROUND/OBJECTIVES: Recent studies have reported chocolate consumption has beneficial effects on blood pressure, obesity, and dyslipidemia, which are components of metabolic syndrome (MetS). However, evidence regarding these relationships in Asia is limited. The aim of this study was to investigate relations between chocolate consumption and MetS in Korea.

SUBJECTS/METHODS: Study subjects were 6,982 adults aged 19-64 years free of major chronic diseases that participated in the 2014–2016 Korea National Health and Nutrition Examination Survey. Information on chocolate consumption was obtained using food frequency questionnaires. For primary analysis, subjects were divided into two groups: non-consumer (n = 3,741, 53.6%); consumer (n = 3,241, 46.4%). In order to investigate doseresponse effects on MetS, chocolate consumers were divided into quartiles based on amounts consumed: Q1 (n = 789, 24.3%); Q2 (n = 837, 25.8%); Q3 (n = 863, 26.6%); Q4 (n = 752, 23.2%) in second analysis.

RESULTS: Chocolate consumers; 1) were more physically active(P < 0.0001); 2) less likely to smoke(P < 0.0001); 3) paid more attention to food nutrition labels (P < 0.0001), and 4) had healthier dietary patterns, that is, they consumed vegetables, fruits, and dairy products more frequently(P < 0.0001) than non-consumers. Furthermore, chocolate consumers had a 30% lower risk of MetS (odds ratio, 0.70; 95% confidence interval, 0.58–0.86; P = 0.0005). However, dose-response effects between chocolate intake and MetS was not found by secondary analysis after excluding non-consumers.

CONCLUSIONS: In conclusion, chocolate consumers had healthier lifestyles and dietary patterns and a lower prevalence of MetS than non-consumers, as determined by our primary analysis. Although dose-response effects were not found to be significant among chocolate consumers during secondary analysis, the patterns were partially similar. This cross-sectional finding shows chocolate consumption does not increase the risk of MetS. The prospective studies and intervention trials in Korea are needed to confirm this cross-sectional finding.

Keywords: Chocolate; metabolic syndrome; epidemiologic studies; Republic of Korea



Author Contributions

Conceptualization: Kim NR; Data curation: Kim NR; Formal analysis: Kim NR; Investigation: Kim NR; Methodology: Kim NR; Project administration: Kim NR; Resources: Kim NR; Software: Kim NR; Supervision: Jeon MS, Kim NR; Validation: Kim NR; Visualization: Kim NR; Writing - original draft: Kim NR; Writing - review & editing: Kim NR.

INTRODUCTION

Chocolate is a highly popular food that is considered an "energy-dense nutrient-poor snack" because of high levels of added sugars and saturated fats [1]. However, recent evidence from intervention trials have reported that intake of chocolate resulted in decreased blood pressure [2], increased high-density lipoprotein (HDL) cholesterol concentration [3], and improved insulin sensitivity [4], which have been suggested to be due to the antioxidant effects of flavonoids in cocoa of chocolate [5,6]. Furthermore, recent epidemiologic observational studies have reported chocolate consumption is associated with lower risks of metabolic diseases, such as cardiovascular disease [7,8] and diabetes [9,10]. However, these observational trials are limited because commercially available chocolates contains not only cacao but also other ingredients (e.g., sugar, milk, nuts etc.). Although attempts have been made to address this issue [11-14], it has not been resolved.

Metabolic syndrome (MetS) is a cluster of risk factors of cardiovascular disease and diabetes and is characterized by abdominal obesity, high fasting glucose level, high triglyceride, low HDL cholesterol, and high blood pressure [15]. Although the etiology of MetS remains unclear, it is known to be associated with interactions between genetic and lifestyle-associated environmental risk factors, and of the modifiable environmental factors, diet is considered of prime importance for the prevention and treatment of MetS [16]. Therefore, it is important that dietary risk factors and beneficial foods that could help reduce the risk of MetS be identified.

In Korea, the prevalence of MetS and chocolate intake have steadily increased [17,18]. However, the majority of previous epidemiology studies on chocolate consumption have performed in the US and Europe where chocolate intake is relatively high, and results obtained may not be applicable in Asian populations [19,20]. Therefore, we investigated the relationship between chocolate consumption and the prevalence of MetS in Korean adults using the 2014–2016 Korea National Health and Nutrition Examination Survey (KNHANES) in the hope that the results obtained would aid the development of disease prevention strategies.

SUBJECTS AND METHODS

Study design and population

The KNHANES is an annual nationwide cross-sectional survey conducted with the aim of providing reliable information on nutrition and health-related data. The design of KNHANES and the methods used have been previously described in detail [21]. In brief, each survey includes a sample of about 10,000 individuals and involves; 1) a health interview, 2) a health examination and 3) a nutrition survey.

We analyzed KNHANES data obtained during the three year periods from January 2014 to December 2016, including 23,080 subjects (10,431 men and 12,649 women). Of these, 16,098 were excluded from the analysis because they; 1) did not provide information on chocolate intake (n = 12,990), 2) had a history of diabetes, hypertension, or dyslipidemia (n = 1,683), 3) were not assessed for components of metabolic syndrome (n = 859), 4) did not provide information on major residual confounding factors (n = 523) and 5) had an extreme energy intake (< 500 kcal/day or > 5,000 kcal/day) (n = 43). As a result, 6,982 individuals (2,659 men and 4,323 women) were included in this study (**Fig. 1**).



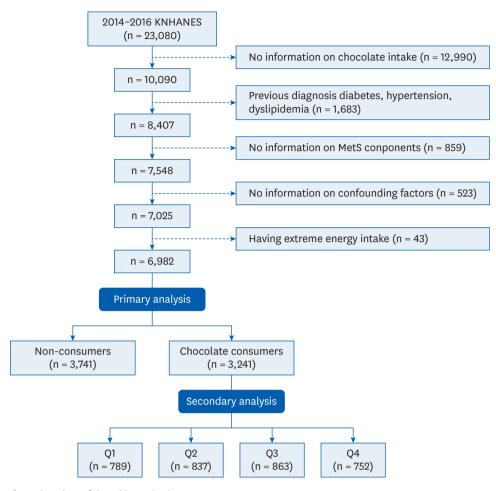


Fig. 1. Flow chart of the subject selection. Q1 (median intake=2.5 g/week); Q2 (median intake=3.8 g/week); Q3 (median intake=9.6 g/week); Q4 (median intake=33.0 g/week).

Ethical approval

The 2014 KNHANES protocol was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention (2013-12EXP-03-5C), whereas the 2015 and 2016 KNHANES protocols were exempted from research ethics review in accord with the Bioethics and Safety Act. Written informed consent was obtained from all participants.

Chocolate consumption

Chocolate consumption was the exposure variable in all analyses. The self-administered food-frequency questionnaire (FFQ) was used to obtain information on habitual chocolate consumption. Subjects were asked to report chocolate consumption frequencies (never, 1/month, 2–3/month, 1/week, 2–4/week, 5–6/week, 1/day, 2/day, 3+/day) and portion sizes (0 g, 5.5 g, 11 g, or 22 g) over the previous year. This item did not differentiate between different types of chocolate (dark, milk, and white). For the primary analysis, we divided subjects into two groups, that is, a non-consumer group (n = 3,741, 53.6%) and a consumer group (n = 3,241, 46.4%). In order to investigate dose-response effects on MetS, we conducted secondary analysis on chocolate consumers by categorizing them by median chocolate intake (g/week) quartiles: Q1 (n = 789, 24.3%, median intake = 2.5 g/week); Q2 (n = 837, 25.8%, median intake



= 3.8 g/week); Q3 (n = 863, 26.6%, median intake = 9.6 g/week); Q4 (n = 752, 23.2%, median intake = 33.0 g/week). We excluded non-consumers in the secondary analysis in order to provide adequate statistical power for subgroup analyses. The validity and reproducibility of FFQ have been previously reported [22].

MetS

The main outcome of the present study was the prevalence of MetS. We applied the definition of MetS suggested by the Adult Treatment Panel III of the National Cholesterol Education Program [15] and used the modified abdominal obesity cutoff for Korean adults [23]. MetS was defined as the presence of three or more of the following components; 1) waist circumference (WC) \geq 90 cm for men and \geq 85 cm for women; 2) triglyceride (TG) \geq 150 mg/dL or treatment for dyslipidemia; 3) HDL cholesterol < 40 mg/dL for men and < 50 mg/dL for women or treatment of dyslipidemia; 4) systolic blood pressure (SBP) \geq 130 mmHg or diastolic blood pressure (DBP) \geq 85 mmHg or antihypertensive treatment; and 5) fasting glucose level (FGL) \geq 100 mg/dL or treatment for diabetes. In order to collect information about MetS, we used health examination data, which included anthropometric measurements and biochemical test results. WCs were measured at midpoints between rib cages and iliac crests in the standing position. Blood pressure measurements were taken three times and averages of second and third measurements of SBP and DBP were used. Blood samples were collected during mornings after an overnight fast, and serum concentrations of glucose, HDL cholesterol, and TG were measured.

Covariates

In order to determine the independence of the relationship between chocolate consumption and MetS, potential confounders such as socio-demographics, anthropometric profiles, and health-related behaviors previously identified as risk factors of MetS were included in the analysis. Information on gender, age, income level, education, physical activity, smoking status, current alcohol use, and subjective health and stress statuses were obtained by questionnaire during health interviews. Heights were measured to within 0.1 cm, and weights to the nearest 0.1 kg with subjects wearing light clothing without shoes during health examination. Body mass index (BMI), which was viewed as a crucial confounder, was calculated by dividing body weight in kilograms by height in meters squared (kg/m²). Data about dietary behaviors (skipping breakfast, use of nutrition labels, a nutrition education), nutrient intake variables (g/day), and food group variables (times/week) were collected using the nutrition survey.

Statistical methods

All analyses were performed using SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA) using PROC SURVEY because KNHANES data were collected using a complex sampling design, involving a variety of weightings, stratification variables, and clusters.

The χ^2 test (for categorical variables) and the general linear model (for continuous variables) were used to analyze the characteristics of the study subjects with respect to chocolate consumption. A multivariable logistic regression model was used to determine whether chocolate consumption was independently associated with the presence of MetS using non-consumers as the reference in the primary analysis and using the lowest quartile of chocolate consumption as the reference in the secondary analysis. We calculated adjusted odds ratios (ORs) (95% confidence interval [CI]) using 5 following models: 1) adjusted for nothing (Model 1); 2) adjusted for socio-demographic variables such as gender, age (years),



income level (low, medium-low, medium-high, high), education level (elementary school or less, middle school, high school, college or more) (Model 2); 3) Model 2 with additional adjustment for health-related lifestyle factors such as current smoker (yes/ no), current drinker (yes/ no), and regular exercise (yes/ no) (Model 3); 4) Model 3 with additional adjustment for dietary factors such as total energy intake (kcal/day), skipping breakfast (yes/ no), use of nutrition labels (yes/ no), receipt of nutrition education (yes/ no), and total energy intake (kcal/day) (Model 4); and 5) Model 4 with additional adjustment for BMI (kg/ m²) (Model 5). For secondary analysis, median values were assigned to each categories of chocolate quartile group and linear trend testing was conducted.

Based on previous epidemiological studies which reported remarkable gender differences for the prevalence and incidence of chronic diseases [20,24], we conducted effect modifier analysis to determine the effect of gender on the relation. However, no gender interaction was observed (P = 0.1147, data not shown), thus, our analyses were performed on combined groups of men and women.

Statistical significance was defined as a 2-sided P < 0.05.

RESULTS

Socio-demographics and health-related characteristics

The characteristics of all subjects are summarized in **Table 1**. The number of all subjects was 6,982, 46.4% (n = 3,241) were chocolate consumers and 53.6% (n = 3,741) were nonconsumers. Chocolate consumers were younger, more likely to be highly-educated and physically active, but less likely to smoke. In addition, chocolate consumers were more likely to read nutrition labels, had higher energy, protein, and fat intakes, and more frequently consumed vegetables, fruits, and dairy products, but consumed less carbohydrate-sourced energy and grain-based products. Secondary analysis revealed a similar pattern (**Table 2**), but although chocolate intake was found to be significantly related to some characteristics, the magnitudes of these relations were weak or inconsistent across quartiles.

Metabolic profiles

Chocolate consumers had significantly lower mean waist circumstances (81.3 \pm 0.2 vs. 80.2 \pm 0.2 cm²; P < 0.0001), BMIs (23.8 \pm 0.1 vs. 23.4 \pm 0.1 kg/m²; P < 0.0001), FGL (95.9 \pm 0.4 vs. 94.3 \pm 0.3 mg/dL; P < 0.0001), TG (138.0 \pm 2.0 vs. 125.6 \pm 2.4 mg/dL; P < 0.0001), SBP (114.2 \pm 0.3 vs. 113.1 \pm 0.3 mmHg; P < 0.0001), and DBP (75.8 \pm 0.2 vs. 75.3 \pm 0.2 mmHg; P < 0.0001) and furthermore, they had significantly higher mean HDL cholesterol (51.6 \pm 0.2 vs. 52.8 \pm 0.2 mg/dL; P < 0.0001) than non-consumers after adjusting for age and gender (**Table 3**). However, secondary analysis showed chocolate intake was not significantly related to metabolic markers among chocolate consumers (**Table 4**).

Risk of MetS

Consumers had a 30% lower prevalence of MetS than non-consumers (OR, 0.70; 95% CI, 0.58–0.86; P = 0.0005) after adjusting for confounding factors in Model 5 (**Table 5**). Consumers in the highest quartile had a 32% lower prevalence of MetS than those in the lowest quartile (OR, 0.68; 95% CI, 0.50–1.00; P = 0.0342) but significance was lost after adjusting for confounding factors (**Table 6**).



Table 1. Characteristics of all subjects (n = 6,982)

Characteristics	Non consumers (n = 3,741)	Consumers (n = 3,241)	<i>P</i> -value
Socio-demographic characteristics			
Gender			0.0163
Men	1,465 (39.2)	1,194 (36.8)	
Women	2,276 (60.8)	2,047 (63.2)	
Age (yrs)	41.7 ± 0.2	35.9 ± 0.3	< 0.0001
Income			0.0008
Lowest	935 (24.9)	646 (19.9)	
Medium-low	950 (25.4)	810 (24.9)	
Medium-high	949 (25.4)	875 (27.0)	
Highest	907 (24.2)	910 (28.0)	
Education			< 0.0001
Elementary school or less	347 (9.3)	92 (2.8)	
Middle school	378 (10.1)	114 (3.5)	
High school	1,488 (39.8)	1,239 (28.2)	
College or more	1,528 (40.8)	1,796 (55.4)	
Health related characteristics			
Current drinker, yes	2,215 (59.2)	1,917 (59.1)	0.5557
Current smoker, yes	786 (21.0)	505 (15.6)	< 0.0001
Regular exerciser, yes	1,909 (51.0)	1,844 (56.9)	< 0.0001
Subjective health statue			0.0152
Good	1,254 (33.5)	1,225 (37.8)	
Normal	1,990 (53.2)	1,637 (50.5)	
Bad	497 (13.3)	379 (11.7)	
Stress statue	, ,	• •	0.5695
Felt a lot	1,066 (28.5)	971 (30.0)	
Dietary characteristics		,	
Skipping breakfast, yes	971 (25.9)	932 (28.7)	0.0499
Use of nutrition label, yes	1,113 (29.7)	1,203 (37.1)	< 0.0001
Receiving nutrition education, yes	136 (3.6)	119 (3.7)	0.3068
Total energy (kcal/day)	1,826 ± 13	2,048 ± 15	< 0.0001
Energy from carbohydrate (%)	67.7 ± 0.1	65.1 ± 0.1	< 0.0001
Energy from protein (%)	13.8 ± 0.0	14.2 ± 0.0	< 0.0001
Energy from fat (%)	18.5 ± 0.1	20.7 ± 0.1	< 0.0001
Rice (times/week)	16.5 ± 0.1	15.6 ± 0.1	< 0.0001
Vegetable (times/week)	8.9 ± 0.1	9.5 ± 0.2	0.0067
Fruit (times/week)	7.1 ± 0.1	7.7 ± 0.1	0.0003
Beans (times/week)	3.5 ± 0.1	3.6 ± 0.1	0.3787
Eggs (times/week)	2.6 ± 0.0	2.9 ± 0.1	< 0.0001
Meat (times/week)	4.4 ± 0.1	4.7 ± 0.1	0.0001
Dairy (times/week)	3.9 ± 0.1	4.4 ± 0.1	< 0.0001

Categorical variables are presented as frequencies (percentages). Continuous variables (except age) are presented as means ± SEs adjusted for gender and age. Food group variables are presented as means ± SEs with additional adjustment for total energy intake.



Table 2. Characteristics of chocolate consumers (n = 3,241)

Characteristics	Q1 (n = 789)	Q2 (n = 837)	Q3 (n = 863)	Q4 (n = 752)	<i>P</i> -value
Socio-demographic characteristics					
Gender					0.0260
Men	262 (33.2)	329 (39.3)	333 (38.6)	270 (36.9)	
Women	527 (66.8)	508 (60.7)	530 (61.4)	482 (64.1)	
Age (yrs)	40.8 ± 0.46	37.1 ± 0.47	34.5 ± 0.47	32.0 ± 0.45	< 0.0001
Income					0.2347
Lowest	138 (17.5)	191 (22.8)	173 (20.0)	144 (19.2)	
Medium-low	204 (25.7)	206 (24.6)	213 (24.7)	187 (24.9)	
Medium-high	231 (29.3)	216 (25.8)	232 (26.7)	196 (26.1)	
Highest	216 (27.4)	224 (26.8)	245 (28.4)	225 (29.9)	
Education					0.0008
Elementary school or less	34 (4.8)	30 (3.6)	16 (1.9)	8 (1.1)	
Middle school	40 (5.1)	27 (3.2)	23 (2.7)	24 (3.2)	
High school	267 (33.8)	316 (37.8)	347 (40.2)	309 (41.1)	
College or more	444 (56.3)	464 (55.4)	477 (55.3)	411 (54.7)	
Health related characteristics	` ,	, ,	, ,	, ,	
Current drinker, yes	448 (56.8)	484 (57.8)	540 (62.6)	445 (59.2)	0.0474
Current smoker, yes	116 (14.7)	141 (16.9)	121 (14.0)	127 (16.9)	0.0979
Regular exerciser, yes	412 (52.2)	467 (55.8)	503 (58.3)	462 (61.4)	0.0033
Subjective health statue	` ,	, ,	, ,	` ,	0.4318
Good	300 (38.0)	301 (36.0)	334 (38.7)	290 (38.6)	
Normal	399 (50.6)	428 (51.1)	441 (51.1)	369 (49.1)	
Bad	90 (11.4)	108 (12.9)	88 (10.2)	93 (12.4)	
Stress statue	,	` ′	` ′	` ,	0.0397
Felt a lot	205 (26.0)	253 (30.2)	256 (29.7)	257 (34.2)	
ietary characteristics	()	,	,	()	
Skipping breakfast, yes	168 (21.3)	236 (28.2)	280 (32.4)	248 (33.0)	< 0.0001
Use of nutrition label, yes	287 (36.4)	295 (35.2)	325 (37.7)	296 (39.4)	0.7432
Receiving nutrition education, yes	35 (4.4)	19 (2.3)	42 (4.9)	23 (3.7)	0.0007
Total energy (kcal/day)	1,893.6 ± 26.5	1,966.0 ± 25.8	2,134.3 ± 27.3	2,316.2 ± 32.6	< 0.0001
Energy from carbohydrate (%)	65.4 ± 0.3	65.2 ± 0.3	63.5 ± 0.3	63.1 ± 0.3	< 0.0001
Energy from protein (%)	14.3 ± 0.1	14.2 ± 0.1	14.5 ± 0.1	14.3 ± 0.1	< 0.0001
Energy from fat (%)	20.4 ± 0.2	20.6 ± 0.2	21.9 ± 0.2	22.6 ± 0.2	< 0.0001
Rice (times/week)	16.2 ± 0.2	15.9 ± 0.2	15.4 ± 0.2	14.9 ± 0.2	< 0.0001
Vegetable (times/week)	9.6 ± 0.2	9.5 ± 0.2	10.1 ± 0.3	9.9 ± 0.3	0.2670
Fruit (times/week)	7.6 ± 0.3	7.5 ± 0.2	7.8 ± 0.2	8.4 ± 0.3	0.1270
Beans (times/week)	3.5 ± 0.1	3.6 ± 0.1	3.6 ± 0.1	3.7 ± 0.1	0.6186
Eggs (times/week)	2.8 ± 0.1	2.8 ± 0.1	3.0 ± 0.1	3.0 ± 0.1	0.1256
Meat (times/week)	5.4 ± 0.1	5.3 ± 0.1	5.3 ± 0.1	5.2 ± 0.2	0.7216
Dairy (times/week)	4.9 ± 0.2	4.6 ± 0.2	4.8 ± 0.2	4.7 ± 0.2	0.5552

Categorical variables are presented as frequencies (percentages). Continuous variables (except age) are presented as means ± SEs adjusted for gender and age. Food group variables are presented as means ± SEs with additional adjustment for total energy intake.

Table 3. Metabolic marker levels of all subjects (n = 6,982)

Metabolic markers	Non consumers (n = 3,741)	Consumers (n = 3,241)	P-value ¹⁾
WC (cm ²)	81.3 ± 0.2	80.2 ± 0.2	< 0.0001
Weight (kg)	65.7 ± 0.2	64.7 ± 0.2	< 0.0001
BMI (kg/m²)	23.8 ± 0.1	23.4 ± 0.1	< 0.0001
FGL (mg/dL)	95.9 ± 0.4	94.3 ± 0.3	< 0.0001
HDL-C (mg/dL)	51.6 ± 0.2	52.8 ± 0.2	< 0.0001
TG (mg/dL)	138.0 ± 2.0	125.6 ± 2.4	< 0.0001
SBP (mmHg)	114.2 ± 0.3	113.1 ± 0.3	< 0.0001
DBP (mmHg)	75.8 ± 0.2	75.3 ± 0.2	< 0.0001

All values are presented as means \pm SEs adjusted for gender and age.

WC, waist circumstance; BMI, body mass index; FGL, fasting glucose level; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Q1 (median intake=2.5 g/week); Q2 (median intake=3.8 g/week); Q3 (median intake=9.6 g/week); Q4 (median intake=33.0 g/week).

¹⁾P-values are derived using PROC SURVEYREG.



Table 4. Metabolic marker levels of chocolate consumers (n = 3,241)

Metabolic markers	Q1 (n = 789)	Q2 (n = 837)	Q3 (n = 863)	Q4 (n = 752)	P-value ¹⁾
WC (cm ²)	80.0 ± 0.4	79.7 ± 0.4	79.9 ± 0.4	79.5 ± 0.4	0.7916
Weight (kg)	65.4 ± 0.4	64.7 ± 0.4	65.1 ± 0.5	64.7 ± 0.4	0.5715
BMI (kg/m²)	23.5 ± 0.1	23.2 ± 0.1	23.3 ± 0.1	23.1 ± 0.1	0.3592
FGL (mg/dL)	93.3 ± 0.5	92.7 ± 0.4	94.0 ± 0.7	93.8 ± 0.5	0.2667
HDL-C (mg/dL)	52.9 ± 0.5	53.2 ± 0.5	53.3 ± 0.5	52.8 ± 0.4	0.7959
TG (mg/dL)	122.5 ± 5.1	122.5 ± 4.2	123.2 ± 4.0	115.9 ± 3.3	0.3841
SBP (mmHg)	111.8 ± 0.5	112.7 ± 0.5	112.5 ± 0.5	111.8 ± 0.5	0.3182
DBP (mmHg)	74.5 ± 0.4	73.9 ± 0.4	75.0 ± 0.4	74.4 ± 0.4	0.5647

All values are presented as means \pm SEs adjusted for gender and age.

WC, waist circumstance; BMI, body mass index; FGL, fasting glucose level; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 5. OR (95% CI) of metabolic syndrome among all subjects (n = 6,982)

Metabolic syndrome	Non consumers (n = 3,741)	Consumers (n = 3,241)	P-value ¹⁾
Model 1	1.00	0.53 (0.44-0.62)	< 0.0001
Model 2	1.00	0.67 (0.57-0.80)	< 0.0001
Model 3	1.00	0.69 (0.58-0.81)	< 0.0001
Model 4	1.00	0.64 (0.55-0.77)	< 0.0001
Model 5	1.00	0.70 (0.58-0.86)	0.0005

Data calculated using 5 following models: 1) Not adjusted (Model 1), 2) Adjusted for gender, age, income level and education level (Model 2), 3) Model 2 with additional adjustment for current smoke, current drinking and regular exercise (Model 3), 4) Model 3 with additional adjustment for skipping breakfast, use of nutrition label, and total energy intake (Model 4), and 5) Model 4 with additional adjustment for BMI (kg/m²).

Table 6. OR (95% CI) of metabolic syndrome among chocolate consumers (n = 3,241)

Metabolic syndrome	Q1 (n = 789)	Q2 (n = 837)	Q3 (n = 863)	Q4 (n = 752)	P-trend ¹⁾
Model 1	1.00	0.99 (0.7-1.4)	0.89 (0.6-1.3)	0.68 (0.5-1.0)	0.0342
Model 2	1.00	1.03 (0.7-1.5)	1.04 (0.7-1.5)	0.90 (0.6-1.4)	0.5059
Model 3	1.00	1.04 (0.7-1.5)	1.07 (0.7-1.6)	0.92 (0.6-1.4)	0.5358
Model 4	1.00	0.98 (0.7-1.4)	0.93 (0.6-1.4)	0.75 (0.5-1.2)	0.1520
Model 5	1.00	1.07 (0.7-1.6)	1.04 (0.7-1.6)	0.91 (0.6-1.4)	0.5158

Data calculated using 5 following models: 1) Not adjusted (Model 1), 2) Adjusted for gender, age, income level and education level (Model 2), 3) Model 2 with additional adjustment for current smoke, current drinking and regular exercise (Model 3), 4) Model 3 with additional adjustment for skipping breakfast, use of nutrition label, and total energy intake, and 5) Model 4 with additional adjustment for BMI (kg/m²).

DISCUSSION

In this cross-sectional study, we found an inverse relationship between chocolate consumption and the prevalence of MetS among all subjects by primary analysis. Although statistical significance of dose-response effects was not found during the second analysis among chocolate consumers, a similar pattern was partially observed. Many issues have to be taken into account when interpreting the results of this cross-sectional study.

Commercially available chocolates contains many ingredients (e.g., cocoa, cocoa butter, sugar, milk, nuts, etc.) and can be classified simply as dark chocolate or milk chocolate. Here, we discuss the effects of chocolate ingredients on health, focusing on potential mechanisms involved in the response to cocoa, milk, and sugar.

¹⁾P-values are derived using PROC SURVEYREG.

Q1 (median intake=2.5 g/week); Q2 (median intake=3.8 g/week); Q3 (median intake=9.6 g/week); Q4 (median intake=33.0 g/week).

OR, odds ratio; CI, confidence interval; BMI, body mass index.

¹⁾P-values are derived using PROC SURVEYLOGISTIC.

OR, odds ratio; CI, confidence interval; BMI, body mass index.

¹⁾Linear trends across categories of chocolate consumption were tested using the median consumption value for each category as a continuous variable.

Q1 (median intake=2.5 g/week); Q2 (median intake=3.8 g/week); Q3 (median intake=9.6 g/week); Q4 (median intake=33.0 g/week).



Nutritional epidemiologists have already found that the polyphenols in cocoa have the following beneficial effects by their activation of nitric oxide and antioxidant effects: 1) the prevention of oxidative damage to low-density lipoprotein cholesterol; 2) the disruption of inflammatory atherosclerotic processes; 3) a reduced risk of thrombosis; and 4) the promotion of normal endothelial function and these effects ultimately lead to lower blood pressure and insulin resistance [5,6], that are related with MetS [25]. The results of the present study show that chocolate consumers enjoyed better health than non-consumers. However, could it be possible to explain that our cross-sectional results are due to the effects of polyphenols?

Unfortunately, we were not able to investigate the effects of polyphenol on MetS because the KNHANES FFQ data do not distinguish between different types of chocolate (e.g., dark, milk, and white). We analyzed 24 hour-recall data in order to determine what types of chocolate were most consumed in Korea. Among chocolate consumers, 7% consumed dark chocolate, 92% consumed milk chocolate or snacks covered with milk chocolate, and only 1% consumed white (data not shown). According to this additional data analysis, far more milk chocolate was consumed in Korea, which raises questions concerning the health benefits of milk versus dark chocolate. Furthermore, this might have led to our inaccuracies in our assessment of the relationship between chocolate consumption and MetS, because ingredients in chocolate, such as cocoa, sugar, and milk, have different health effects.

Though researchers have conducted several experimental trials to examine the effects of different chocolate types on health, the situation remains unclear. For example, one study published in *Nature* found that dark chocolate resulted in an increase in total antioxidant capacity, but that milk chocolate significantly reduced antioxidant capacity. Serafini *et al.* [11] suggested this was due to reduced absorption of cocoa polyphenols in the gastrointestinal tract due to binding by milk proteins. On the other hand, other studies on milk chocolate have reported positive effects on serum cholesterol levels [13,26], blood pressure [26], and antioxidant capacity [26,27]. Clearly, the has not been resolved, further study is needed to elucidate the mechanism responsible for the health benefits of milk chocolate due to its far greater consumption in Korea and other countries.

Sugar is another major ingredient of chocolate, and much epidemiological evidence indicates sugar consumption is associated with the risk of metabolic diseases such as obesity [28,29], diabetes [29,30], and cardiovascular disease [31]. Interestingly, in our study, chocolate consumers paid more attention to food nutrition labels (**Table 1**). We assumed that this health-related habit may naturally lead to their choice of dark chocolate with less sugar and also lead to their health MetS markers (**Table 3**). In order to confirm this presume, prospective studies used the modified FFQ to enable assessments of chocolate types are needed.

Primary analysis showed that chocolate consumers; 1) were more physically active; 2) less likely to smoke; 3) paid more attention to food nutrition labels, and 4) had healthier dietary patterns, that is, they consumed vegetables, fruits, and dairy products more frequently than non-consumers (**Table 1**). Secondary analysis of chocolate consumers revealed a similar though non-significant pattern (**Table 2**). These health-related characteristics could be the result of chocolate consumers having better metabolic bio-markers than non-consumers (**Table 3**) and the fact that Q4 had better (though non-significant) metabolic markers than Q1 (**Table 4**). Furthermore, before adjusting for socio-demographic variables, health-related lifestyle variables, and dietary characteristics, we found 47% relative reduction in MetS prevalence in consumers compared to non-consumers (OR, 0.53; 95% CI, 0.44–0.62; P < 0.0001) and 32% relative



reduction in Q4 than in Q1 (OR, 0.68; 95% CI, 0.50–1.00; P = 0.0342) in secondary analysis, which may be explained by results of following cross-sectional studies: 1) Kim *et al.* [32] reported that high activity was associated with a lower risk of MetS; 2) Oh *et al.* [33] demonstrated that smoking increases risks of MetS; 3) Kang *et al.* [34] reported that the practice of reading nutrition labels was associated with a lower risk of MetS; and 4) Hong *et al.* [35] found that a fruit and dairy consumption pattern was significantly associated reduced risk of MetS.

MetS is an obesity-related disorder and evidence concerning the association between chocolate consumption and obesity is inconsistent. Two cross-sectional studies [36,37] reported that habitual chocolate consumption was associated with a lower body weight, which supports our result in **Table 3** (65.7 \pm 0.2 vs. 64.7 \pm 0.2 kg; P < 0.0001), but two prospective cohort studies [38,39] showed that chocolate intake was dose-dependently associated with long-term weight gain. These differences between studies may have been due to different study designs, differences between the consumption level cutoffs used, or differences between the biochemical profiles of individuals.

A high FGL and a high BP are features of MetS. In the present study, chocolate consumers had a lower FGL (95.9 \pm 0.4 vs. 94.3 \pm 0.3 mg/dL; P < 0.0001) and a lower BP (SBP: 114.2 \pm 0.3 vs. 113.1 \pm 0.3 mmHg, P < 0.0001; DBP: 75.8 \pm 0.2 vs. 75.3 \pm 0.2 mmHg, P < 0.0001) than non-consumers. These results is in-line with the findings of previous observational [9,10,40] and experimental studies [2,4,41] And this beneficial effects on FGL and BP may be partially explained by the fact that the polyphenols in cocoa may decrease insulin resistance and reduce blood pressure by the activation of nitro oxide [5,6].

Cocoa butter is a fat derived from the cacao plant and contains around 33% stearic acid, a saturated fat [5]. Thus, our results on lipid profiles in **Table 3** (HDL cholesterol: $51.6 \pm 0.2 \text{ vs.} 52.8 \pm 0.2 \text{ mg/dL}$; P < 0.0001, TG: $138.0 \pm 2.0 \text{ vs.} 125.6 \pm 2.4 \text{ mg/dL}$; P < 0.0001) are somewhat surprising, because we believed that saturated fat in diet increases the risk of dyslipidemia. However, a number of chocolate feeding studies have shown stearic acids in cocoa butter have a neutral effect on blood lipid levels [12,42,43]. Furthermore, it was reported in a small-scale clinical trial that chocolate intake might increase HDL cholesterol concentration [3], which is in-line with our findings.

The results of our study are similar to those of a study performed in the US [44]. Both studies used data from NHANES (a nationwide cross-sectional survey conducted with the aim of providing reliable information on nutrition and health) and compared the odds of the risk of MetS by simply dividing into chocolate consumers and non-consumers. As a result, they found chocolate consumers had a 15% reduced risk of MetS (OR, 0.85; 95% CI, 0.73–1.00; P = 0.0453), which supports our result that chocolate consumers had a 30% lower risk of MetS (**Table 5**). However, the following differences should be considered when comparing the results of these 2 studies: 1) the US population was older (mean age = 45.7) than our population (mean age = 39.0); 2) dietary assessment instruments used were different (FFQ vs. 24-hour recall); 3) mean BMI was lower in our Korean subjects (23.4 vs. 27.9 kg/m²); and 4) the covariates adjusted in the final logistic regression model differed with the exception of age and gender.

Chocolate epidemiological studies have been conducted mostly in Europe and the United States where chocolate consumptions are relatively high [19,20]. Could their results be applied to people in Asia where chocolate consumption is relatively low? To our knowledge, only two chocolate observational studies [20,45] have been conducted in Asia, as they



adopted diabetes and stroke as outcome variables, which are closely related to MetS [25,46], so, it is meaningful to compare the two.

A study by Oba *et al.* [45] published in 2010 used Japanese cohort data and divided subjects into three groups based on frequency of chocolate consumption (never or almost never, once/month to less than once/week, once/week or more), and they found inverse association between chocolate consumption and diabetes. In the second study conducted in Asia by Dong *et al.* [20] in 2017 using data from a large Japanese cohort, subjects were divided into quartiles based on chocolate intake per week (g/week), and the consumption cut-offs used were similar to those used in the present study (Q1: 0 vs. 2.5 g/week; Q2: 5.8 vs. 3.8 g/week; Q3: 11.6 vs. 9.6 g/week; Q4: 37.5 vs. 33.0 g/week). Interestingly, Dong *et al.* [20] included non-consumers when allocating subjects to group even though almost 49.9% of men and 34.9% of women were non-consumers (55.1% of men and 52.6% of women in present study; data not shown). On the other hand, we excluded non-consumers in order to achieve adequate statistical power for subgroup analyses as discussed in Methods. And in this secondary observational study in Asia, an inverse association was observed between chocolate intake and stroke. These 2 results are in-line with our main result because MetS is known to increase the risk of chronic disease like diabetes and stroke [25,46]. Further intervention studies in Asia are needed to robust these results.

Because of the cross-sectional design of present study, we could not explore causal relationships. For example, we found that chocolate consumers had healthier life styles and dietary patterns and better metabolic profile than non-consumers. However, could there be a reverse causality that non-consumers did not eat chocolate for their better health condition?

There was an interesting study about this issue. Greenburg *et al.* [39] posed a hypothesis that a positive association exists between chocolate consumption and obesity, and that differences between cross-sectional and prospective study results are due to the presence of obesity-related disease. In a large US cohort, they found that cross-sectional analysis produced an inverse relationship, but that prospective analysis resulted in a positive association.

In view of this evidence, we excluded subjects with a history of diabetes, hypertension, or dyslipidemia during study subject selection, because the presence of individuals with these chronic disease might change dietary patterns, however, the inverse relationship between chocolate consumption and MetS did not change. We suggest prospective studies be conducted on chocolate consumption and the risk of MetS in a Korean population to confirm this cross-sectional finding.

The present study has several limitations that warrant consideration. First, due to its cross-sectional design, causal relationships were not examined as discussed above. Second, chocolate consumption was defined based on FFQ data, which provided no information on chocolate types as discussed above. Despite our efforts to identify chocolate types, we did not combine results obtained using the 24 recall method with FFQ derived results because these two assessment methods are quite different and complex to combine, although attempts have been made to combine the 2 methods [47-49]. Therefore, we suggest the FFQ be modified to enable assessments of chocolate types or the 24-hour recall method be modified to enable assessments of habitual chocolate intake. Third, our exposure variable, chocolate consumption, was self-reported and this may have resulted in measurement errors. Fourth, although we adjusted for crucial lifestyle and dietary factors, we cannot rule out the possibility that some unmeasured or residual confounders influenced our results. Finally,



our secondary analysis conducted on chocolate consumers failed to reveal a relation between quartiles of chocolate intake and MetS, which may have been due to the lower validity of FFQ for estimating intake amounts than the 24-hour recall method [50].

Despite these limitations, our study has several strengths. First, our findings are representative of healthy Korean adults because KNHANES provides a reliable, nationally representative database. Second, the large dataset used provided adequate statistical power for subgroup analyses. Third, to the best our knowledge, the present study is the first population-based, epidemiologic study to be undertaken on the relation between chocolate consumption and MetS in the Korean population.

In conclusion, chocolate consumers had healthier lifestyles and dietary patterns and a lower prevalence of MetS than non-consumers, as determined by our primary analysis. Although dose-response effects were not found to be significant among chocolate consumers during secondary analysis, the patterns were partially similar. This cross-sectional finding shows chocolate consumption does not increase the risk of MetS. Prospective studies and intervention trials in the Korea population are needed to confirm this cross-sectional finding.

REFERENCES

1. Mirmiran P, Bahadoran Z, Delshad H, Azizi F. Effects of energy-dense nutrient-poor snacks on the incidence of metabolic syndrome: a prospective approach in Tehran Lipid and Glucose Study. Nutrition 2014;30:538-43.

PUBMED | CROSSREF

 Almoosawi S, Fyfe L, Ho C, Al-Dujaili E. The effect of polyphenol-rich dark chocolate on fasting capillary whole blood glucose, total cholesterol, blood pressure and glucocorticoids in healthy overweight and obese subjects. Br J Nutr 2010;103:842-50.

PUBMED | CROSSREF

 Mursu J, Voutilainen S, Nurmi T, Rissanen TH, Virtanen JK, Kaikkonen J, Nyyssönen 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;37:1351-9.

PUBMED I CROSSREF

4. 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;81:611-4.

PUBMED | CROSSREF

 Corti R, Flammer AJ, Hollenberg NK, Lüscher TF. Cocoa and cardiovascular health. Circulation 2009;119:1433-41.

PUBMED | CROSSREF

6. Cooper KA, Donovan JL, Waterhouse AL, Williamson G. Cocoa and health: a decade of research. Br J Nutr 2008;99:1-11.

PUBMED I CROSSREF

7. 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;31:1616-23.

PUBMED | CROSSREF

8. 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 | CROSSREF

- Greenberg JA. Chocolate intake and diabetes risk. Clin Nutr 2015;34:129-33.
 PUBMED I CROSSREF
- Greenberg JA, Manson JE, Tinker L, Neuhouser ML, Garcia L, Vitolins MZ, Phillips LS. Chocolate intake and diabetes risk in postmenopausal American women. Eur J Clin Nutr 2017;71:1088-93.
 PUBMED | CROSSREF



11. Serafini M, Bugianesi R, Maiani G, Valtuena S, De Santis S, Crozier A. Plasma antioxidants from chocolate. Nature 2003;424:1013.

PUBMED | CROSSREF

12. Kris-Etherton PM, Mustad VA. Chocolate feeding studies: a novel approach for evaluating the plasma lipid effects of stearic acid. Am J Clin Nutr 1994;60:1029S-1036S.

PUBMED | CROSSREF

13. Kris-Etherton PM, Derr JA, Mustad VA, Seligson FH, Pearson TA. Effects of a milk chocolate bar per day substituted for a high-carbohydrate snack in young men on an NCEP/AHA Step 1 Diet. Am J Clin Nutr 1994;60:10378-428.

PUBMED | CROSSREF

14. Sørensen LB, Astrup A. Eating dark and milk chocolate: a randomized crossover study of effects on appetite and energy intake. Nutr Diabetes 2011;1:e21.

PUBMED | CROSSREF

- Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F; American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/ National Heart, Lung, and Blood Institute scientific statement. Circulation 2005;112:2735-52.
 PUBMED | CROSSREF
- Feldeisen SE, Tucker KL. Nutritional strategies in the prevention and treatment of metabolic syndrome. Appl Physiol Nutr Metab 2007;32:46-60.

PUBMED | CROSSREF

17. Lim S, Shin H, Song JH, Kwak SH, Kang SM, Won Yoon J, Choi SH, Cho SI, Park KS, Lee HK, Jang HC, Koh KK. Increasing prevalence of metabolic syndrome in Korea: the Korean National Health and Nutrition Examination Survey for 1998-2007. Diabetes Care 2011;34:1323-8.

PUBMED | CROSSREF

- 18. Korea Agro-Fisheries & Food Trade Corporation. Processed Food Segment Market Analysis in 2016: Chocolate. Naju: Korea Agro-Fisheries & Food Trade Corporation; 2016.
- Seligson FH, Krummel DA, Apgar JL. Patterns of chocolate consumption. Am J Clin Nutr 1994;60:1060S-4S.
 PUBMED | CROSSREF
- Dong JY, Iso H, Yamagishi K, Sawada N, Tsugane S; Japan Public Health Center–based Prospective Study Group. Chocolate consumption and risk of stroke among men and women: a large population-based, prospective cohort study. Atherosclerosis 2017;260:8-12.

PUBMED | CROSSREF

- 21. Kweon S, Kim Y, Jang MJ, Kim Y, Kim K, Choi S, Chun C, Khang YH, Oh K. Data resource profile: the Korea national health and nutrition examination survey (KNHANES). Int J Epidemiol 2014;43:69-77.

 PUBMED I CROSSREF
- Kim DW, Song S, Lee JE, Oh K, Shim J, Kweon S, Paik HY, Joung H. Reproducibility and validity of an FFQ developed for the Korea National Health and Nutrition Examination Survey (KNHANES). Public Health Nutr 2015;18:1369-77.

PUBMED | CROSSREF

23. Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, Kim DY, Kwon HS, Kim SR, Lee CB, Oh SJ, Park CY, Yoo HJ. Appropriate waist circumference cutoff points for central obesity in Korean adults. Diabetes Res Clin Pract 2007;75:72-80.

PUBMED | CROSSREF

 Regitz-Zagrosek V, Lehmkuhl E, Weickert MO. Gender differences in the metabolic syndrome and their role for cardiovascular disease. Clin Res Cardiol 2006;95:136-47.

PUBMED | CROSSREF

- 25. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005;365:1415-28. PUBMED | CROSSREF
- 26. Fraga CG, Actis-Goretta L, Ottaviani JI, Carrasquedo F, Lotito SB, Lazarus S, Schmitz HH, Keen CL. Regular consumption of a flavanol-rich chocolate can improve oxidant stress in young soccer players. Clin Dev Immunol 2005;12:11-7.

PUBMED | CROSSREF

- 27. Wiswedel I, Hirsch D, Kropf S, Gruening M, Pfister E, Schewe T, Sies H. Flavanol-rich cocoa drink lowers plasma F₂-isoprostane concentrations in humans. Free Radic Biol Med 2004;37:411-21.

 PUBMED | CROSSREF
- Berkey CS, Rockett HR, Field AE, Gillman MW, Colditz GA. Sugar-added beverages and adolescent weight change. Obes Res 2004;12:778-88.

PUBMED | CROSSREF



 Schulze MB, Manson JE, Ludwig DS, Colditz GA, Stampfer MJ, Willett WC, Hu FB. Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women. JAMA 2004;292:927-34.

PUBMED | CROSSREF

- Montonen J, Järvinen R, Knekt P, Heliövaara M, Reunanen A. Consumption of sweetened beverages and intakes of fructose and glucose predict type 2 diabetes occurrence. J Nutr 2007;137:1447-54.
- Fung TT, Malik V, Rexrode KM, Manson JE, Willett WC, Hu FB. Sweetened beverage consumption and risk of coronary heart disease in women. Am J Clin Nutr 2009;89:1037-42.

 PURMED LCROSSREF
- 32. Kim DI. The relationship between walking activity, vigorous physical activity, metabolic syndrome risk factors, and hypertension among Korean adult population: data from The Fifth Korea National Health and Nutrition Examination Survey V-3(2012). Korea J Sports Sci 2015;24:1111-22.
- 33. Oh SW, Yoon YS, Lee ES, Kim WK, Park C, Lee S, Jeong EK, Yoo T; Korea National Health and Nutrition Examination Survey. Association between cigarette smoking and metabolic syndrome: the Korea National Health and Nutrition Examination Survey. Diabetes Care 2005;28:2064-6.

 PUBMED | CROSSREF
- Kang HT, Shim JY, Lee YJ, Linton JA, Park BJ, Lee HR. Reading nutrition labels is associated with a lower risk of metabolic syndrome in Korean adults: the 2007–2008 Korean NHANES. Nutr Metab Cardiovasc Dis 2013;23:876-82.
 - PUBMED | CROSSREF
- 35. Hong S, Song Y, Lee KH, Lee HS, Lee M, Jee SH, Joung H. A fruit and dairy dietary pattern is associated with a reduced risk of metabolic syndrome. Metabolism 2012;61:883-90.
- 36. Cuenca-García M, Ruiz JR, Ortega FB, Castillo MJ; HELENA study group. Association between chocolate consumption and fatness in European adolescents. Nutrition 2014;30:236-9.
- 37. Golomb BA, Koperski S, White HL. Association between more frequent chocolate consumption and lower body mass index. Arch Intern Med 2012;172:519-21.
- Greenberg JA, Manson JE, Buijsse B, Wang L, Allison MA, Neuhouser ML, Tinker L, Waring ME, Isasi CR, Martin LW, Thomson CA. Chocolate-candy consumption and 3-year weight gain among postmenopausal U.S. women. Obesity (Silver Spring) 2015;23:677-83.
 PUBMED | CROSSREF
- 39. Greenberg JA, Buijsse B. Habitual chocolate consumption may increase body weight in a dose-response manner. PLoS One 2013;8:e70271.
 - PUBMED | CROSSREF
- 40. Matsumoto C, Petrone AB, Sesso HD, Gaziano JM, Djoussé L. Chocolate consumption and risk of diabetes mellitus in the Physicians' Health Study. Am J Clin Nutr 2015;101:362-7.
- 41. 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;95:740-51.
 - PUBMED | CROSSREF
- 42. Hunter JE, Zhang J, Kris-Etherton PM. Cardiovascular disease risk of dietary stearic acid compared with trans, other saturated, and unsaturated fatty acids: a systematic review. Am J Clin Nutr 2010;91:46-63.
- 43. Wan Y, Vinson JA, Etherton TD, Proch J, Lazarus SA, Kris-Etherton PM. Effects of cocoa powder and dark chocolate on LDL oxidative susceptibility and prostaglandin concentrations in humans. Am J Clin Nutr 2001;74:596-602.
 - PUBMED | CROSSREF
- 44. O'Neil CE, Fulgoni VL 3rd, Nicklas TA. Candy consumption was not associated with body weight measures, risk factors for cardiovascular disease, or metabolic syndrome in US adults: NHANES 1999–2004. Nutr Res 2011;31:122-30.
 - PUBMED | CROSSREF
- 45. Oba S, Nagata C, Nakamura K, Fujii K, Kawachi T, Takatsuka N, Shimizu H. Consumption of coffee, green tea, oolong tea, black tea, chocolate snacks and the caffeine content in relation to risk of diabetes in Japanese men and women. Br J Nutr 2010;103:453-9.

 PUBMED | CROSSREF



- Ninomiya JK, L'Italien G, Criqui MH, Whyte JL, Gamst A, Chen RS. Association of the metabolic syndrome with history of myocardial infarction and stroke in the Third National Health and Nutrition Examination Survey. Circulation 2004;109:42-6.
 PUBMED | CROSSREF
- 47. Subar AF, Dodd KW, Guenther PM, Kipnis V, Midthune D, McDowell M, Tooze JA, Freedman LS, Krebs-Smith SM. The food propensity questionnaire: concept, development, and validation for use as a covariate in a model to estimate usual food intake. J Am Diet Assoc 2006;106:1556-63.

 PUBMED | CROSSREF
- 48. Haubrock J, Nöthlings U, Volatier JL, Dekkers A, Ocké M, Harttig U, Illner AK, Knüppel S, Andersen LF, Boeing H; European Food Consumption Validation Consortium. Estimating usual food intake distributions by using the multiple source method in the EPIC-Potsdam Calibration Study. J Nutr 2011;141:914-20.

 PUBMED | CROSSREF
- Carroll RJ, Midthune D, Subar AF, Shumakovich M, Freedman LS, Thompson FE, Kipnis V. Taking advantage of the strengths of 2 different dietary assessment instruments to improve intake estimates for nutritional epidemiology. Am J Epidemiol 2012;175:340-7.
 PUBMED | CROSSREF
- Schatzkin A, Kipnis V, Carroll RJ, Midthune D, Subar AF, Bingham S, Schoeller DA, Troiano RP, Freedman LS. A comparison of a food frequency questionnaire with a 24-hour recall for use in an epidemiological cohort study: results from the biomarker-based Observing Protein and Energy Nutrition (OPEN) study. Int J Epidemiol 2003;32:1054-62.
 PUBMED | CROSSREF

https://e-nrp.org