Supplemental Figure 1. Portion size and package amount of chocolate consumption. *

KUVA 117. Suklaata. Pakkauksessa on sama määrä kuin sen edessä olevalla lautasella.

* The package has the same amount as the plate in front of it. a) Da Capo chocolate; b) Geisha Fazer chocolate; c) Karl Fazer chocolate.

Supplemental Figure 2. Risk of CVD Mortality Associated with Daily Chocolate Consumption by Selected Factors in the ATBC Study [a][b]

Subgroup	Absolute risk difference, % (95% CI)	Hazard ratio (95% CI)		P for interaction
Age at baseline, years				
<57	-1.60 (-3.13, -0.20)	0.82 (0.73, 0.91)		0.29
>=57	-0.51 (-1.11, 0.083)	0.92 (0.84, 1.00)		
Cigarettes smoked/d				
<16	-0.87 (-2.17, 0.32)	0.85 (0.75, 0.95)		0.16
16 to <20	-2.17 (-3.39, -0.98)	0.84 (0.75, 0.95)		
>=20	-0.13 (-1.16, 0.92)	0.94 (0.84, 1.06)		
BMI (kg/m2)				
<30	-0.66 (-1.35, -0.04)	0.90 (0.84, 0.97)		0.17
>=30	-2.79 (-4.97, -0.59)	0.74 (0.62, 0.89)		
History of cardiovascular disease				
No	-0.84 (-1.74, 0.03)	0.88 (0.80, 0.97)		0.29
Yes	-1.04 (-2.04, -0.08)	0.87 (0.79, 0.96)		
Trial intervention arm				
Alpha-tocopherol	-0.67 (-1.57, 0.17)	0.90 (0.82, 0.99)		0.58
No alpha-tocopherol	-1.14 (-2.13, -0.17)	0.85 (0.77, 0.93)		
Beta-carotene	-1.28 (-2.10, -0.47)	0.84 (0.76, 0.92)		0.39
No beta-carotene	-0.47 (-1.56, 0.50)	0.92 (0.84, 1.01)		
Eating a high-quality diet				
No	-0.65 (-1.36, 0.07)	0.88 (0.82, 0.95)		0.54
Yes	-2.17 (-3.76, -0.72)	0.84 (0.73, 0.97)		
Saturated fatty acids intake				
Low or medium	-0.72 (-1.56, 0.06)	0.86 (0.79, 0.93)		0.50
High	-1.33 (-2.44, -0.25)	0.92 (0.81, 1.05)		
Serum total cholesterol, mg/dL				
<205	-0.67 (-1.46, 0.19)	0.92 (0.83, 1.01)		0.15
>=205	-1.11 (-2.20, -0.19)	0.84 (0.76, 0.92)		
Serum alpha-tocopherol, mg/L				
<11.5	-0.54 (-1.37, 0.24)	0.94 (0.85, 1.04)		0.65
>=11.5	-1.20 (-2.18, -0.28)	0.83 (0.75, 0.91)		
Serum beta-carotene, ug/L				
<172	-0.94 (-1.94, 0)	0.91 (0.82, 1.00)		0.70
>=172	-0.71 (-1.58, 0.10)	0.87 (0.79, 0.96)		
Serum retinol, ug/L				
<577	-1.18 (-2.11, -0.26)	0.86 (0.78, 0.95)		0.50
>=577	-0.63 (-1.63, 0.26)	0.89 (0.80, 0.98)		
Years of follow-up				
0-13	-0.18 (-0.68, 0.29)	0.86 (0.77, 0.95)		0.11
13 to <23	-0.71 (-1.29, -0.17)	0.96 (0.86, 1.06)		
>=23	-1.92 (-3.51, -0.41)	0.79 (0.67, 0.93)		

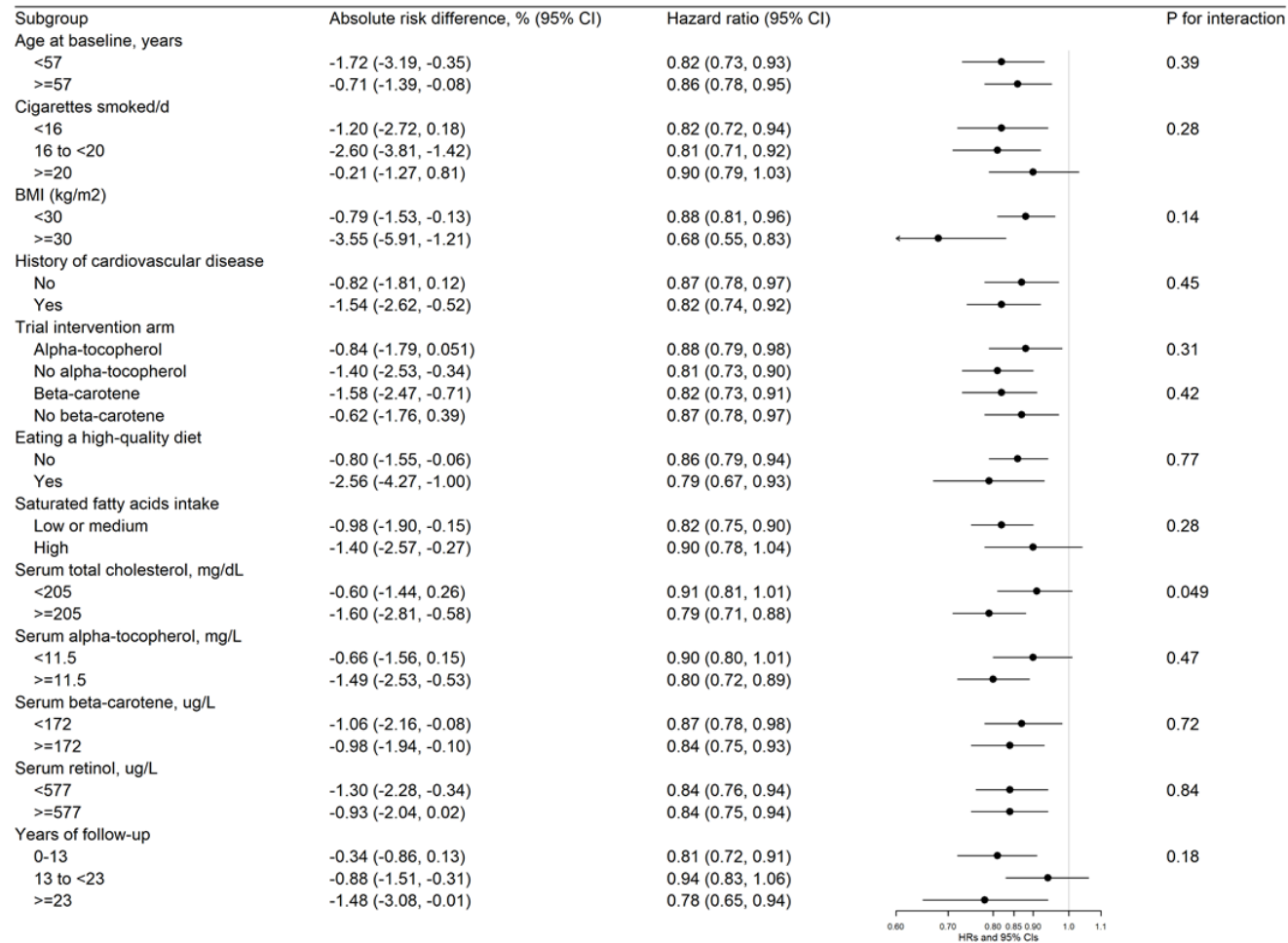0.70 0.75 0.80 0.85 0.90   1.0   1.1
HRs and 95% CIs

Abbreviations: ATBC = Alpha-Tocopherol, Beta-Carotene Cancer Prevention; CVD= cardiovascular disease; HDL = high-density lipoprotein, HR = hazard ratio

[a] Multivariable models were adjusted for age at entry, body mass index, cigarettes smoked per day, years of smoking, serum HDL cholesterol, intervention assignment, systolic and diastolic blood pressure, history of cardiovascular disease, diabetes, education, physical activity, and daily dietary total energy, alcohol, and Alternate Mediterranean Diet Score.

[b] Absolute risk differences and hazard ratios of CVD mortality are for the 5th category versus 1st category of chocolate consumption per day.

Supplemental Figure 3. Risk of Heart Disease Mortality Associated With Daily Chocolate Consumption by Selected Factors in the ATBC Study [a, b]
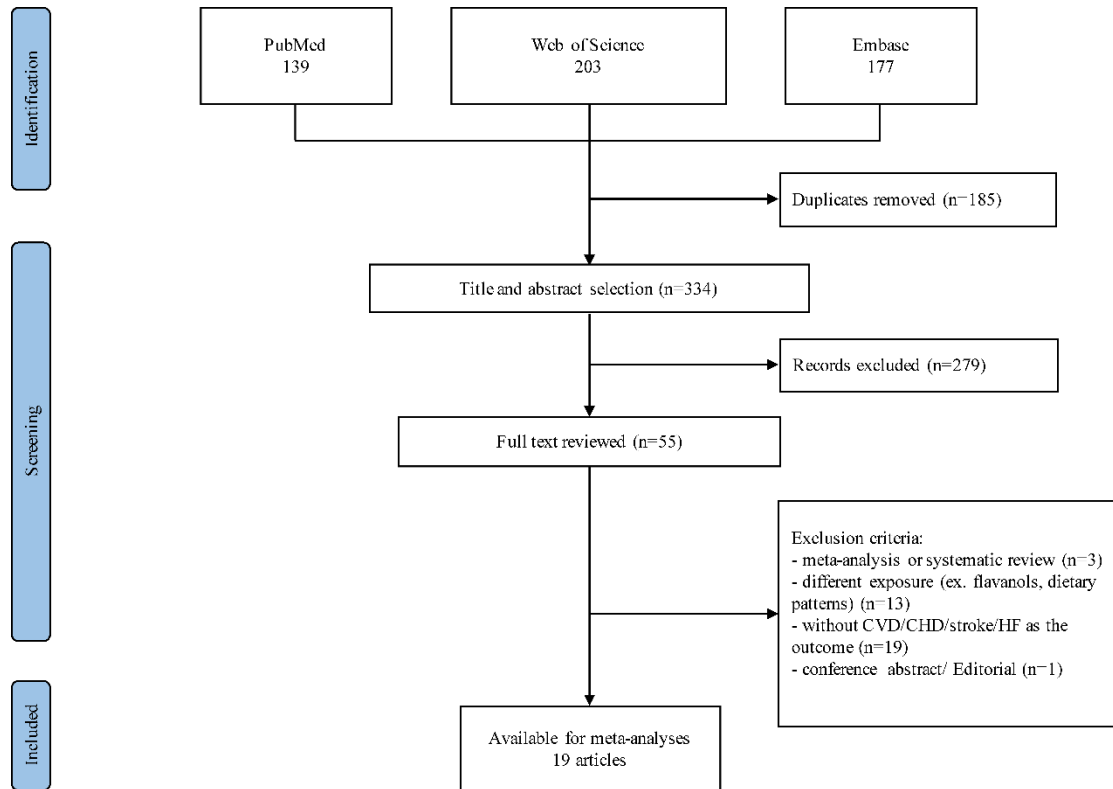
Subgroup	Absolute risk difference, % (95% CI)	Hazard ratio (95% CI)	P for interaction
Age at baseline, years			
<57	-1.72 (-3.19, -0.35)	0.82 (0.73, 0.93)	0.39
>=57	-0.71 (-1.39, -0.08)	0.86 (0.78, 0.95)	
Cigarettes smoked/d			
<16	-1.20 (-2.72, 0.18)	0.82 (0.72, 0.94)	0.28
16 to <20	-2.60 (-3.81, -1.42)	0.81 (0.71, 0.92)	
>=20	-0.21 (-1.27, 0.81)	0.90 (0.79, 1.03)	
BMI (kg/m2)			
<30	-0.79 (-1.53, -0.13)	0.88 (0.81, 0.96)	0.14
>=30	-3.55 (-5.91, -1.21)	0.68 (0.55, 0.83)	
History of cardiovascular disease			
No	-0.82 (-1.81, 0.12)	0.87 (0.78, 0.97)	0.45
Yes	-1.54 (-2.62, -0.52)	0.82 (0.74, 0.92)	
Trial intervention arm			
Alpha-tocopherol	-0.84 (-1.79, 0.051)	0.88 (0.79, 0.98)	0.31
No alpha-tocopherol	-1.40 (-2.53, -0.34)	0.81 (0.73, 0.90)	
Beta-carotene	-1.58 (-2.47, -0.71)	0.82 (0.73, 0.91)	0.42
No beta-carotene	-0.62 (-1.76, 0.39)	0.87 (0.78, 0.97)	
Eating a high-quality diet			
No	-0.80 (-1.55, -0.06)	0.86 (0.79, 0.94)	0.77
Yes	-2.56 (-4.27, -1.00)	0.79 (0.67, 0.93)	
Saturated fatty acids intake			
Low or medium	-0.98 (-1.90, -0.15)	0.82 (0.75, 0.90)	0.28
High	-1.40 (-2.57, -0.27)	0.90 (0.78, 1.04)	
Serum total cholesterol, mg/dL			
<205	-0.60 (-1.44, 0.26)	0.91 (0.81, 1.01)	0.049
>=205	-1.60 (-2.81, -0.58)	0.79 (0.71, 0.88)	
Serum alpha-tocopherol, mg/L			
<11.5	-0.66 (-1.56, 0.15)	0.90 (0.80, 1.01)	0.47
>=11.5	-1.49 (-2.53, -0.53)	0.80 (0.72, 0.89)	
Serum beta-carotene, ug/L			
<172	-1.06 (-2.16, -0.08)	0.87 (0.78, 0.98)	0.72
>=172	-0.98 (-1.94, -0.10)	0.84 (0.75, 0.93)	
Serum retinol, ug/L			
<577	-1.30 (-2.28, -0.34)	0.84 (0.76, 0.94)	0.84
>=577	-0.93 (-2.04, 0.02)	0.84 (0.75, 0.94)	
Years of follow-up			
0-13	-0.34 (-0.86, 0.13)	0.81 (0.72, 0.91)	0.18
13 to <23	-0.88 (-1.51, -0.31)	0.94 (0.83, 1.06)	
>=23	-1.48 (-3.08, -0.01)	0.78 (0.65, 0.94)	

0.60   0.70   0.80 0.85 0.90   1.0   1.1
HRs and 95% CIs

Abbreviations: ATBC = Alpha-Tocopherol, Beta-Carotene Cancer Prevention; HDL = high-density lipoprotein, HR = hazard ratio

[a] Multivariable models were adjusted for age at entry, body mass index, cigarettes smoked per day, years of smoking, serum HDL cholesterol, intervention assignment, systolic and diastolic blood pressure, history of cardiovascular disease, diabetes, education, physical activity, and daily dietary total energy, alcohol, and Alternate Mediterranean Diet Score.

[b] Absolute risk differences and hazard ratios of heart disease mortality are for the 5th category versus 1st category of chocolate consumption per day.

Supplemental Figure 4. Flow Chart of Systematic Review Meta-Analysis

Identification

PubMed
139

Web of Science
203

Embase
177

Duplicates removed (n=185)

Title and abstract selection (n=334)

Records excluded (n=279)

Screening

Full text reviewed (n=55)

Exclusion criteria:
- meta-analysis or systematic review (n=3)
- different exposure (ex. flavanols, dietary patterns) (n=13)
- without CVD/CHD/stroke/HF as the outcome (n=19)
- conference abstract/ Editorial (n=1)

Included

Available for meta-analyses
19 articles

Supplemental Figure 5. Forest plot of influence analysis for the association between chocolate consumption and risk of cardiovascular disease incidence and mortality. Each dot represents the pooled RR (95% CIs) following omission of the study listed on the left using random-effects meta-analysis
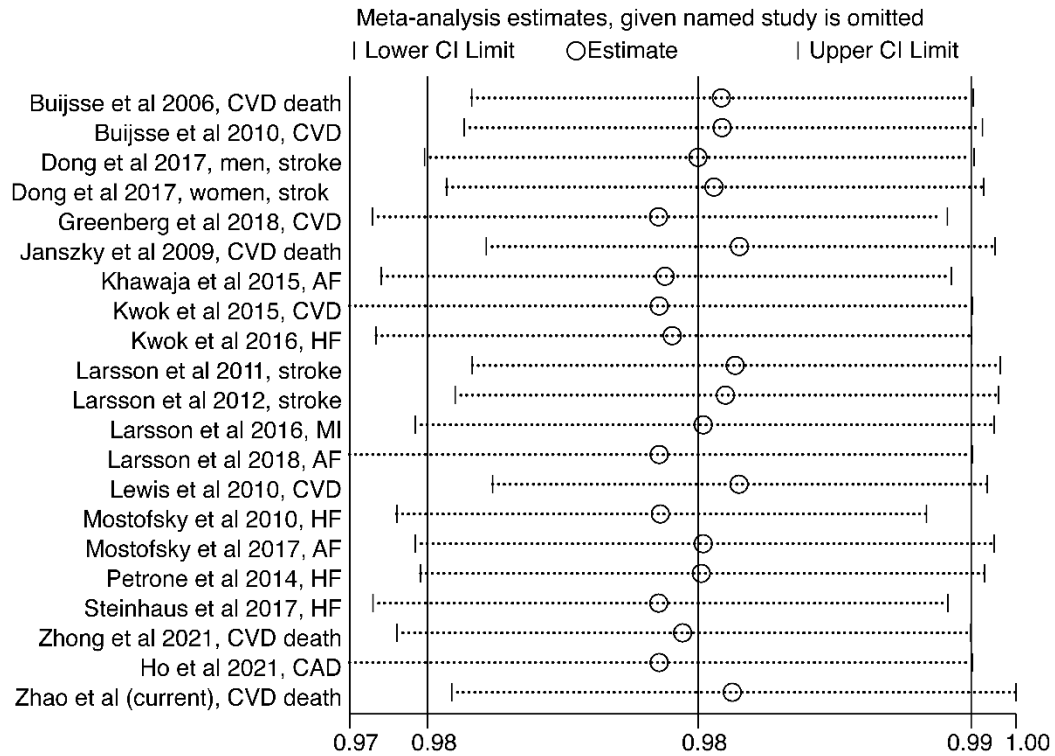
Abbreviations: AF = atrial fibrillation; CAD = coronary artery disease; CHD = coronary heart disease; CVD = cardiovascular disease; HF = heart failure; MI = myocardial infarction

Supplemental Figure 6. Funnel plot for assessment of publication bias for meta-analysis of the association between chocolate consumption and risk of cardiovascular disease incidence and mortality
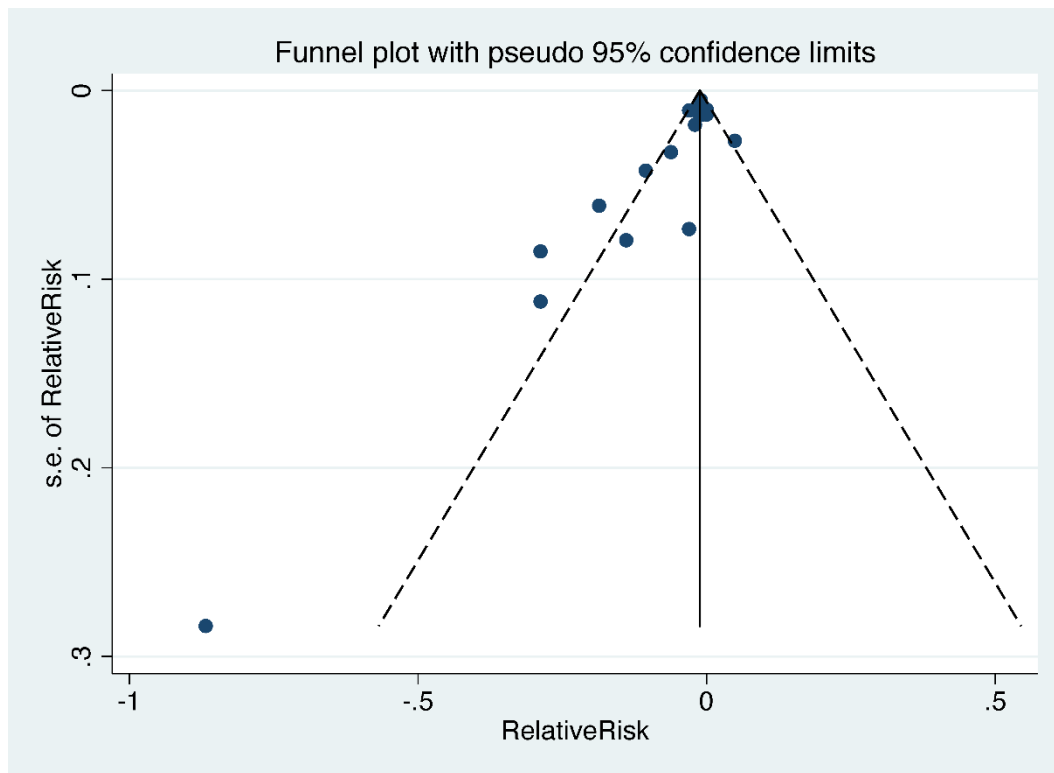
P value for Egger's test = 0.001

Supplemental Figure 7. Trim and Fill analysis of adjustment for publication bias in meta-analysis of the association between chocolate consumption and risk of cardiovascular disease incidence and mortality.
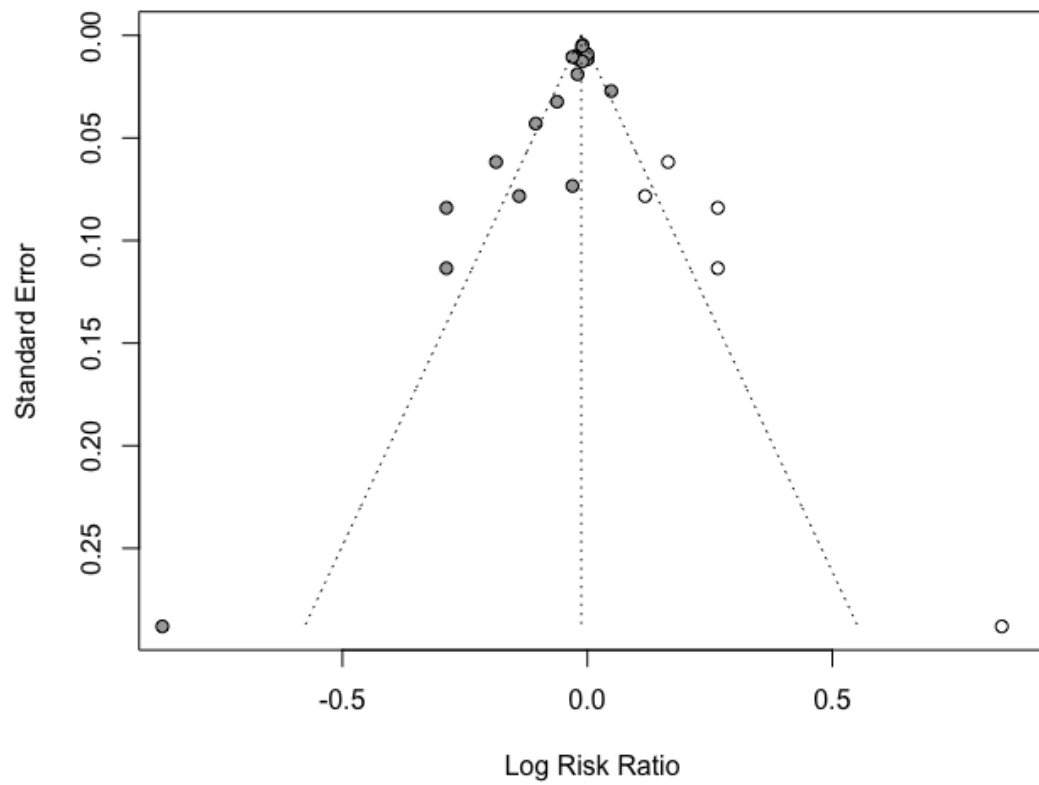
Observed 21 studies: pooled relative risk=0.98, 95% confidence interval: 0.975, 0.99; P value=0.0001
Observed (21) + Filled (5) studies: pooled relative risk=0.988, 95% confidence interval: 0.976, 0.9995); P value =0.042