

Effect of Cocoa and Tea Intake on Blood Pressure

A Meta-analysis

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Background: Epidemiological evidence suggests blood pressure-lowering effects of cocoa and tea. We undertook a meta-analysis of randomized controlled trials to determine changes in systolic and diastolic blood pressure due to the intake of cocoa products or black and green tea.

Methods: MEDLINE, EMBASE, SCOPUS, Science Citation Index, and the Cochrane Controlled Trials Register were searched from 1966 until October 2006 for studies in parallel group or crossover design involving 10 or more adults in whom blood pressure was assessed before and after receiving cocoa products or black or green tea for at least 7 days.

Results: Five randomized controlled studies of cocoa administration involving a total of 173 subjects with a median duration of 2 weeks were included. After the cocoa

diets, the pooled mean systolic and diastolic blood pressure were -4.7 mm Hg (95% confidence interval [CI], -7.6 to -1.8 mm Hg; $P = .002$) and -2.8 mm Hg (95% CI, -4.8 to -0.8 mm Hg; $P = .006$) lower, respectively, compared with the cocoa-free controls. Five studies of tea consumption involving a total of 343 subjects with a median duration of 4 weeks were selected. The tea intake had no significant effects on blood pressure. The estimated pooled changes were 0.4 mm Hg (95% CI, -1.3 to 2.2 mm Hg; $P = .63$) in systolic and -0.6 mm Hg (95% CI, -1.5 to 0.4 mm Hg; $P = .38$) in diastolic blood pressure compared with controls.

Conclusion: Current randomized dietary studies indicate that consumption of foods rich in cocoa may reduce blood pressure, while tea intake appears to have no effect.

Arch Intern Med. 2007;167:626-634

AN INCREASED CONSUMPTION of fruits and vegetables is recommended as a first-line therapeutic approach in current hypertension control guidelines.^{1,2} At least part of the reduction of blood pressure and lowering cardiovascular risk has been attributed to the polyphenols (flavonoids) in fruits and vegetables.³⁻⁵ Tea and cocoa products account for the major proportion of total polyphenol intake in Western countries.^{6,7} However, cocoa or tea are currently not implemented in cardioprotective or anti-hypertensive dietary advice,⁸ although both have been associated with lower incidences of cardiovascular events.⁹⁻¹¹ A recent cross-sectional study suggests considerable hypotensive and cardioprotective effects of cocoa.¹² Observational studies of the association between consumption of black or green tea and blood pressure yielded mixed results; some have reported a reduction of blood pressure,¹³⁻¹⁵ while others found no effects.¹⁶⁻¹⁸ These discrepancies may be due to potential biases and con-

founding factors that are in particular inherent to epidemiological studies of diet and disease.¹⁹ Several randomized controlled trials have also been conducted to answer the question of a causal relationship of cocoa²⁰⁻²⁴ and tea²⁵⁻²⁹ consumption on blood pressure, principally providing higher strength of evidence for an association with a dietary effect.³⁰ We therefore undertook a prospective meta-analysis of randomized controlled trials to quantitatively assess the effect of cocoa or tea intake on blood pressure.

METHODS

LITERATURE SEARCH

To identify randomized controlled studies that report the effects of cocoa or tea intake on blood pressure, we searched the electronic databases MEDLINE, EMBASE, SCOPUS, and Science Citation Index from 1966 to October 2006 as well as the Cochrane Controlled Trials Register for the medical subject headings (MeSH) and text words "cocoa," "chocolate," "tea,"

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“blood pressure,” “hypertension,” “endothelium,” and “cardiovascular.” We also compiled citations from the reference lists of original and review articles. Of the citations identified by the search terms (cocoa OR (chocolate)/ respectively (tea) AND (randomized controlled trial[Publication Type]) OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]), the full articles were retrieved.

STUDY SELECTION

We considered studies in any language that were published as full articles. For inclusion, studies had to fulfill the following criteria: have a randomized controlled parallel group or crossover design; have examined at least 10 normotensive or hypertensive adults (age ≥ 18 years); report means (or differences between means) and standard deviations or 95% confidence intervals (CIs) of systolic blood pressure (SBP) and diastolic blood pressure (DBP) at baseline and after the intervention; and provide type, duration, and amount of the cocoa or tea consumption. Studies were excluded if only abstracts were published; information on cocoa or tea and control interventions was incomplete; allocation of participants to the treatments was not randomized; only supplements of tea or cocoa ingredients were used; or vitamin supplements or polyphenol-rich foods were concomitantly ingested or cocoa and tea intake was mixed with other dietary treatments. Data of multiple published reports from the same study population were included only once. Furthermore, studies with a duration of less than 7 days were excluded from the analysis. This cutoff value was set because shorter assessments (often only administrations of a single dose of cocoa or tea) were considered of questionable clinical relevance, and none of these very short-term studies we retrieved by our search strategy (**Figure 1**) reported changes in blood pressure after ingestion of cocoa or black and green tea.

DATA EXTRACTION AND QUALITY ASSESSMENT

Data were extracted independently by 2 investigators (D.T. and R.R.) with an interrater agreement³¹ value of $\kappa = 0.94$, and disagreements were resolved by consensus. Methodological quality of the selected studies was assessed independently by 2 reviewers (D.T. and R.R.) ($\kappa = 0.89$), and discrepancies were resolved by consensus. Randomized con-

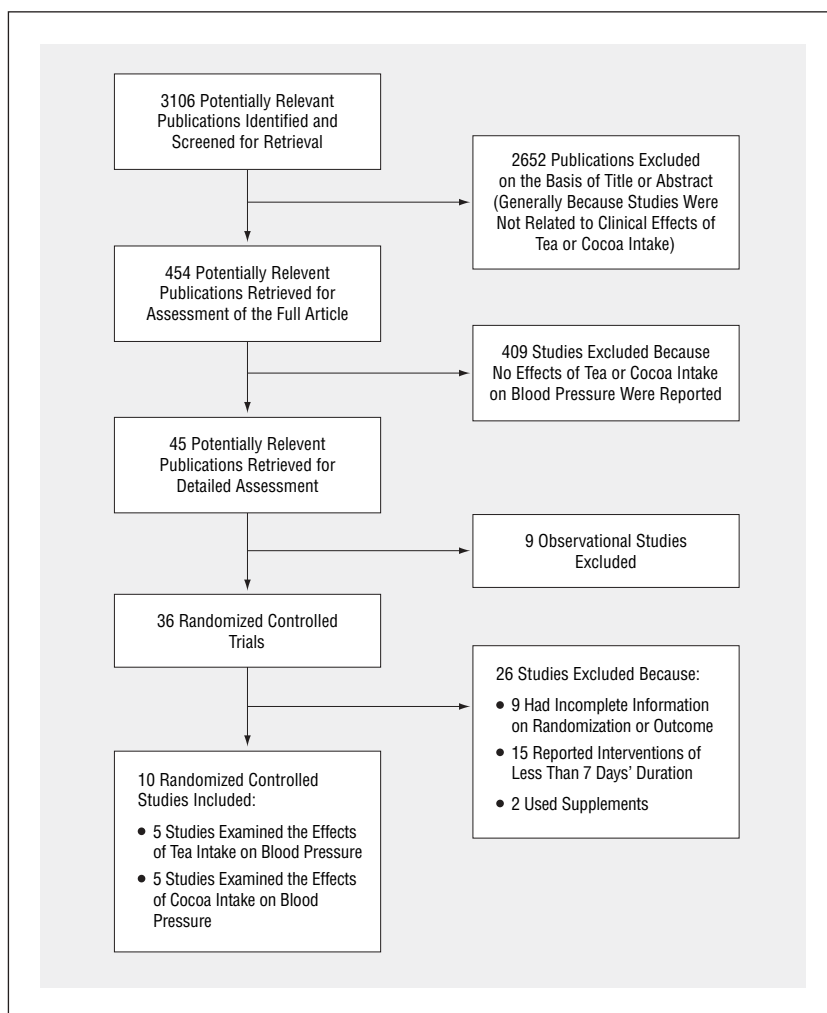


Figure 1. Flow diagram of the study selection process for prospective meta-analysis.

trolled trials were evaluated using the validated Jadad 11-item instrument with a maximum possible score of 13 points.³² Study quality was considered to be good when the score was greater than 9 points and poor when the score was 9 points or lower.

Extracted data include the first author's name; year of publication; country of investigation; number, age, sex, and health status of participants; losses to follow-up; concomitant medications; trial design and duration; Jadad score; funding sources; intervention assessment; and assessment of change in mean \pm SD SBP and DBP.

DATA SYNTHESIS AND ANALYSIS

Changes in SBP and DBP in cocoa or tea and control groups are reported as differences between arithmetic means before and after intervention. If not reported, standard deviations of these differences were estimated by the following equation:

$$SD_{\text{difference}} = \frac{SD_{\text{cocoa/tea}}^2 + SD_{\text{control}}^2 - [2 \times R \times SD_{\text{cocoa/tea}} \times SD_{\text{control}}]}{2}$$

For the 2 studies in which subjects' individual pretreatment and posttreatment blood pressure values were available,^{20,23} we calculated values of the correlation coefficient R of greater than 0.85 for SBP and greater than 0.90 for DBP. To be conservative, we used an imputed value R of 0.68 according to the suggestions of the Cochrane Handbook for Systematic Reviews of Interventions. Crossover trials were incorporated in the meta-analysis as paired analyses if individual data were available. Otherwise, measurements from cocoa or tea and control intervention periods were considered in the same way as parallel group trials of cocoa or tea vs control by imputing the change estimates of the standard deviations.

Interstudy heterogeneity was assessed by the Cochrane Q test; $P < .10$ was considered statistically significant.

Table 1. Characteristics of Randomized Controlled Trials Examining Blood Pressure Changes Due to Cocoa Intake

Source	Study Design, Duration (Subjects' Health Status), Concomitant Medication	No. of Participants Enrolled (Men/Women), Mean Age (Range), y*	Study Quality: Jadad Score, Funding Sources	Intervention	SBP, Mean (SD), mm Hg, Before/After Cocoa Intervention vs Control	DBP, Mean (SD), mm Hg, Before/After Cocoa Intervention vs Control
Taubert et al, ²⁰ 2003, Germany	Crossover, 14 d/phase (isolated systolic hypertension stage I), no medication	13 (6/7), 58.8 (55-64)	10, No funding	Dark chocolate (100 g/d containing 500 mg of polyphenols) vs polyphenol-free white chocolate; energy: 480 kcal/d	Cocoa: 153.3 (4.4)/148.6 (2.4); Control: 153.6 (4.4)/154.0 (3.6)	Cocoa: 84.5 (4.6)/82.9 (4.6); Control: 84.2 (4.2)/84.5 (4.3)
Engler et al, ²¹ 2004, United States	Parallel group, 2 wk (healthy, normotensive subjects), no medication	21 (11/10), 32.1 (21-55)	10, Institutional grant: University of California, San Francisco, School of Nursing. Cocoa Research Institute, Vienna, Va	High-flavonoid chocolate (46 g/d containing 213 mg of procyanidins) vs low-flavonoid chocolate; energy: 240 kcal/d	Cocoa: 121.0 (5.4)/120.0 (4.0); Control: 112.8 (2.8)/110.0 (2.0)	Cocoa: 68.1 (2.5)/69.0 (2.0); Control: 66.1 (1.7)/66.0 (2.0)
Grassi et al, ²² 2005, Italy	Crossover, 15 d/phase (healthy, normotensive subjects), no medication	15 (7/8), 33.9 (SD, 7.6)	9, No funding	Dark chocolate (100 g/d containing 500 mg of polyphenols) vs polyphenol-free white chocolate; energy: 480 kcal/d	Cocoa: 109.3 (8.4)/102.7 (6.4); Control: 109.7 (7.7)/109.3 (7.2)	Cocoa: 71.6 (5.1)/67.5 (4.2); Control: 71.6 (5.2)/71.0 (4.8)
Grassi et al, ²³ 2005, Italy	Crossover, 15 d/phase (essential hypertension grade I), no medication	20 (10/10), 43.7 (SD, 7.8)	9, No funding	Dark chocolate (100 g/d containing 500 mg of polyphenols) vs polyphenol-free white chocolate; energy: 480 kcal/d	Cocoa: 135.5 (5.8)/123.6 (6.3); Control: 135.6 (5.5)/134.7 (4.7)	Cocoa: 88.0 (4.1)/79.6 (5.4); Control: 87.6 (4.3)/87.5 (4.6)
Fraga et al, ²⁴ 2005, Argentina	Crossover, 14 d/phase (healthy, normotensive subjects), no medication	28 (28/0), 18 (18-20)	8, Institutional grant: University of Buenos Aires and Agencia Nacional de Promoción Científica y Tecnológica (ANPCYT), Buenos Aires, Argentina	Flavanol-containing milk chocolate (105 g/d with 294 mg of flavanols and procyanidins) vs cacao butter chocolate (containing <5 mg of flavanols); energy intake: 544 kcal/d (value provided by Mars Inc, McLean, Va)	Cocoa: 123 (3)/117 (2); Control: 123 (3)/121 (2)	Cocoa: 72 (2)/67 (2); Control: 71 (2)/70 (2)

Abbreviations: DBP, diastolic blood pressure; SBP, systolic blood pressure.

*If age range was not reported, standard deviation is given. There were no dropouts except in the study by Engler et al²¹ (1 dropout [per-protocol analysis]).

The magnitude of heterogeneity was evaluated by the I^2 statistic that describes the proportion of total variation in study estimates that is due to heterogeneity.³³

To account for interstudy heterogeneity, the pooled estimates of the mean differences in SBP and DBP between control and intervention and the corresponding 95% CIs were calculated by the random effects model according to DerSimonian and Laird.³⁴

Potential publication bias in the meta-analyses was assessed by the funnel plots of each trial's effect size against the inverse standard error. Funnel plot asymmetry was evaluated by the Egger regression test requiring a minimum of 5 trials to reliably detect a bias ($P < .10$).³⁵ Adjusted estimates of the pooled changes in blood pressure and the overall 95% CIs were calculated by the trim-and-fill method according to Duval and Tweedie.³⁶

To test whether any one study was exerting excessive influence on the results, we conducted a sensitivity analysis by systematically excluding each study and then reanalyzing the remaining data. Additional sensitivity analyses were done to test the influence of alternative values (0 and 1) of the imputed correlation coefficient R on the pooled estimates.

The statistical analyses were performed with Cochrane Review Manager 4.2 (Cochrane Library Software, Oxford, England) and MIX version 1.4 software (Department of Medical Informatics, Kitasato University, Kanagawa, Japan).

RESULTS

We identified 10 studies that met the inclusion criteria, with 5 addressing the relation between cocoa (**Table 1**)

and 5 the relation between tea (**Table 2**) intake and blood pressure. Most studies were excluded because of short duration (<7 days) or missing information of randomization, withdrawals, or outcome (Figure 1). Two studies were excluded because supplements of cocoa or tea extracts were applied.^{37,38} One study²⁶ assessed black tea and green tea in the same subjects in subsequent interventions. Because of the lack of independency between these studies and since black tea and green tea did not differ in their effects on blood pressure, we entered only the data of the black tea intervention. The cocoa studies had a combined total of 173 individuals allocated to cocoa ($n=87$) and control ($n=86$) arms, and the tea studies had a combined total

Table 2. Characteristics of Randomized Controlled Trials Examining Blood Pressure Changes Due to Tea Intake

Source	Study Design, Duration (Subjects' Health Status), Concomitant Medication	No. of Participants Enrolled (Men/Women), Mean Age (Range), y,* Loss to Follow-up	Study Quality: Jadad Score, Funding Sources	Intervention	SBP, Mean (SD), mm Hg, Before/After Tea Intervention vs Control	DBP, Mean (SD), mm Hg, Before/After Tea Intervention vs Control
Bingham et al, 1997, ²⁵ United Kingdom	Crossover, 4 wk/phase (healthy, normotensive subjects), no medication	65 (31/34), 40.7 (20-73), 15 dropouts (intention-to-treat analysis)	10, Tea Packers Association, London, England	Black tea (minimum of 6 cups/d) vs placebo (matched to water, milk, sugar, and caffeine intake); polyphenol and energy intake: NR	Tea: 119.9 (14.0)/119.9 (12.7); Control: 119.9 (14.0)/120.1 (12.9)	Tea: 76.6 (7.8)/74.0 (8.4); Control: 76.6 (7.8)/75.1 (8.4)
Hodgson et al, 1999, ²⁶ Australia	Crossover, 7 d/phase (mild systolic hypertension), no medication	13 (13/0), 59.8 (25-72), no dropouts	9, Institutional grant: National Heart Foundation and National Health and Medical Research Council, Canberra, Australia	Black tea (5 cups/d) vs hot water with caffeine (matched to tea content, 180 mg/d); polyphenol and energy intake: NR	Tea: 136.6 (3.3)/136.1 (5.5); Control: 136.6 (3.3)/135.5 (5.5)	Tea: 76.2 (2.5)/76.9 (2.5); Control: 76.2 (2.5)/77.5 (2.8)
Duffy et al, ²⁷ 2001, United States	Crossover, 4 wk/phase (coronary artery disease and hypertension in 52%), aspirin and antihypertensive drugs	50 (39/11), 55 (SD 8), 16 dropouts (per-protocol analysis)	10, North American Tea Trade Health Research Association and Lipton Inc, Englewood Cliffs, NJ	Black tea (900 mL/d, containing 1350 mg of polyphenols) vs water (900 mL/d); energy intake: NR	Tea: 137 (17)/136 (19); Control: 137 (17)/137 (17)	Tea: 78 (7)/77 (9); Control: 78 (7)/77 (8)
Hodgson et al, ²⁸ 2002, Australia	Parallel group, 4 wk, (mild elevation of serum cholesterol or triglycerides), no medication	21 (16/5), 59.1 (NR), no dropouts	10, Institutional grant: National Heart Foundation, Australia. Tea Trade Health Research Association, Toronto, Ontario	Black tea (5 cups/d) vs hot water; polyphenol and energy intake: NR	Tea: 123 (5)/120 (5); Control: 127 (5)/123 (4)	Tea: 73 (2)/71 (2); Control: 75 (3)/73 (2.6)
Fukino et al, 2005, ²⁹ Japan	Parallel group, 2 mo (high-normal blood pressure and borderline diabetes mellitus), no medication	66 (53/13), 53.5 (32-73), 4 dropouts (per-protocol analysis)	8, Institutional grant: Ministry of Education, Culture, Sports, Science, and Technology, Japan. Taiyou Kagakou Co Ltd Yokkaichi, Japan	Green tea (1 packet/d, containing 544 mg of polyphenols) vs no tea; energy intake: NR	Tea: 139.3 (15.7)/131.6 (20.8); Control: 138.6 (18.2)/129.2 (19.0)	Tea: 92.5 (11.1)/83.3 (12.6); Control: 87.8 (11.5)/83.2 (15.3)

Abbreviations: DBP, diastolic blood pressure; NR, not reported (the energy intake with the tea interventions was not reported; it depended on the addition of sugar, milk, and lemon); SBP, systolic blood pressure.

*If age range was not reported, standard deviation is given.

of 343 individuals allocated to tea (n=171) and control (n=172) arms. The median duration of the interventions in the cocoa studies was 2 weeks, and in the tea studies, 4 weeks. Of the cocoa and tea study participants, 63.9% and 70.7%, respectively, were men and 34.0% and 48.8%, respectively, had hypertension or high-normal blood pressure.

Of 5 cocoa studies, 4 reported a reduction of SBP and DBP after cocoa consumption. Compared with the cocoa-free control, the pooled decrease was -4.7 mm Hg (95% CI, -7.6 to -1.8 mm Hg; P=.002) in SBP and -2.8 mm Hg (95% CI, -4.8 to

-0.8 mm Hg; P=.006) in DBP for cocoa intake (**Figure 2**). Of the 5 studies on tea consumption, none was associated with significant alterations in blood pressure. Compared with control, the pooled change was 0.4 mm Hg (95% CI, -1.3 to 2.2 mm Hg; P=.63) in SBP and -0.6 mm Hg (95% CI, -1.5 to 0.4 mm Hg; P=.38) in DBP for tea intake (**Figure 3**).

There was evidence of considerable heterogeneity between the cocoa studies with respect to SBP (Q₄=32.33; P<.001; I²=87.6%) as well as DBP (Q₄=32.18; P<.001; I²=87.6%). In contrast, there was no

indication of heterogeneity between the tea studies (SBP: Q₄=0.61; P=.96; I²=0%; and DBP: Q₄=3.29; P=.51; I²=0%). Exclusion sensitivity analysis showed that heterogeneity was due to the studies by Engler et al²¹ and Grassi et al.²³ Omitting these studies had little impact on the pooled estimates for changes in SBP (-4.5 mm Hg [95% CI, -5.5 to -3.5 mm Hg]; P<.001) and DBP (-3.1 mm Hg [95% CI, -3.8 to -2.3 mm Hg]; P<.001).

Additional sensitivity analysis demonstrated that the values for the pooled changes in blood pressure with corresponding CIs and

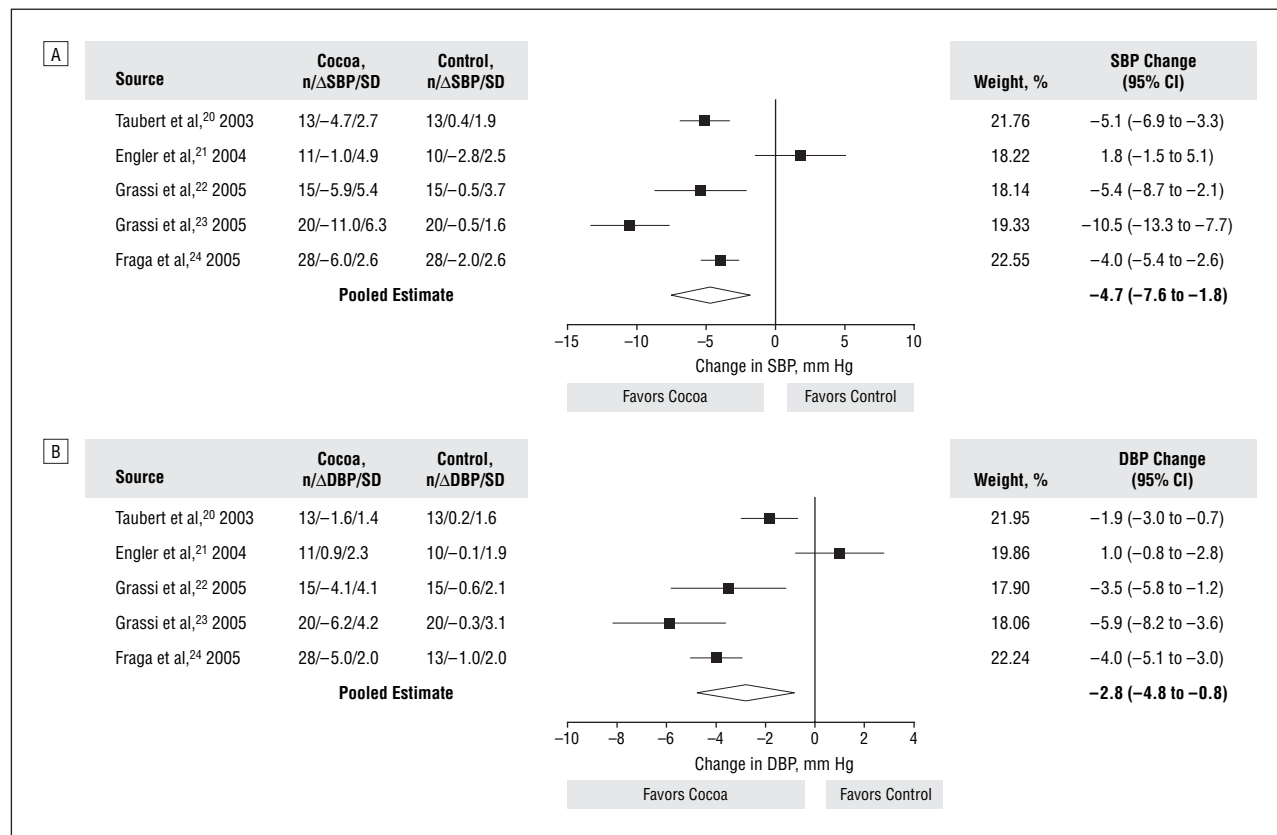


Figure 2. Individual and pooled changes in systolic blood pressure (SBP) (A) and diastolic blood pressure (DBP) (B) due to cocoa intake in controlled randomized studies. Square sizes are proportional to the weight of each study in the meta-analysis. n Indicates number of participants in cocoa and control regimes; Δ SBP/ Δ DBP, difference in SBP/DBP before and after intervention; and SD, standard deviation of blood pressure differences.

P values were not altered with the exclusion of any individual study or the imputation of other values of R.

The funnel plots and the Egger regression test suggested no significant asymmetry in the 4 meta-analyses (Figure 4). Furthermore, the trim-and-fill computation using the symmetry estimator L_0 revealed that there were no missing trials, indicating that no publication bias was present.

The methodological quality score (Jadad scale) of cocoa and tea studies ranged from 8 to 10 (Table 1 and Table 2), with a mean (SD) of 9.2 (0.8) and 9.4 (0.9), respectively. With the exception of 1 study,²¹ participants were not reported to be blinded to the intervention. However, this problem is inherent to most dietary interventions. Further methodical deficiencies included failures to describe the methods to generate the sequence of randomization or to assess adverse effects and missing justification of the sample size. We found no indi-

cation that industrial or institutional funding affected the study outcomes with respect to blood pressure (Table 1 and Table 2). The concurrent administration of antihypertensive drugs along with black tea in the investigation by Duffy et al²⁷ may have offset any antihypertensive effect of the tea; however, blood pressure-lowering effects of polyphenols have also been observed in normotensive subjects.

In the 4 cocoa studies, which were associated with blood pressure reductions, similar amounts of cocoa were applied to different study populations. The results suggest that younger subjects with mild essential hypertension experience the highest decrease in SBP and DBP, whereas elderly hypertensive subjects and younger normotensive subjects show smaller reductions (Table 1). Moreover, it appears that the amount of the ingested cocoa phenols is essential for the magnitude of the blood pressure reduction, since in the study by Engler et al,²¹ administration of about half of the cocoa phenols over the

same 2-week period did not affect blood pressure.

The negative outcome of the tea interventions was independent of subjects' age, the presence of hypertension, or study duration (between 1-8 weeks). Furthermore, the reported cocoa and tea studies provided no indication that ethnicity, sex, or body weight affected outcome.

COMMENT

In our meta-analysis of randomized controlled trials in adults, diets rich in cocoa were associated with statistically significant reductions in SBP and DBP, whereas black or green tea did not lead to apparent changes in blood pressure. The magnitude of the hypotensive effects of cocoa is clinically noteworthy; it is in the range that is usually achieved with monotherapy of β -blockers or angiotensin-converting enzyme inhibitors.³⁹ At the population level, a reduction of 4 to 5 mm Hg in SBP and 2 to 3 mm Hg in DBP would be ex-

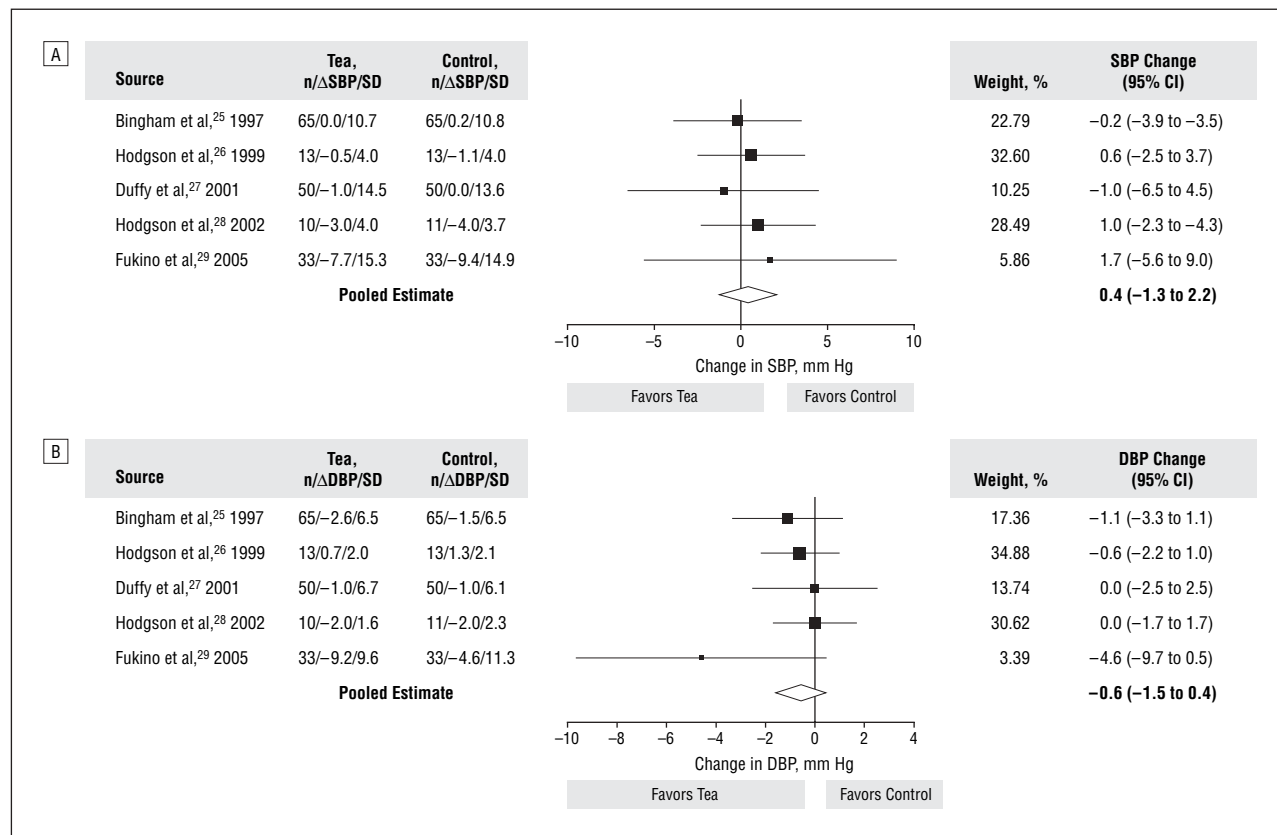


Figure 3. Individual and pooled changes in systolic blood pressure (SBP) (A) and diastolic blood pressure (DBP) (B) due to tea intake in controlled randomized studies. Square sizes are proportional to the weight of each study in the meta-analysis. See Figure 2 for abbreviations.

pected to substantially reduce the risk of stroke (by about 20%), coronary heart disease (by 10%), and all-cause mortality (by 8%).⁴⁰

The blood pressure-lowering effects of cocoa have a biological basis. Cocoa is a rich source of polyphenols.⁴¹ In mechanistic studies, cocoa extracts have been shown to cause arterial vasodilation by increasing endothelial production of nitric oxide.⁴² In clinical studies in healthy subjects, infusion of the nitric oxide synthase inhibitor N^G-nitro-L-arginine methyl ester (L-NAME) caused doubling of SBP and DBP responses after only 4 days of ingestion of cocoa.⁴³ These studies suggest that the polyphenols in cocoa-containing foods are likely to be responsible for the reduction in blood pressure and also the improvement of endothelial function⁴⁴ and platelet inhibition⁴⁵ by inducing local synthesis of the vasodilatory signaling molecule nitric oxide.

The lack of effects of tea on blood pressure appears less plausible. Tea is also rich in polyphenols,⁴⁶ and the total polyphenol doses that were in-

gested with the tea diets were not lower compared with the cocoa diets (Table 1 and Table 2). Moreover, tea and cocoa studies showed no major differences in baseline characteristics of the participants or study duration. It is also unlikely that the dilator responses of the tea polyphenols are outweighed by pressor effects of the tea caffeine, since administration of caffeine-matched control beverages had no sustained impact (ie, lasting more than 60 minutes after consumption) on blood pressure.^{25,26} However, the composition of the polyphenols differs between cocoa and tea. The main polyphenol monomers in black and green tea are flavan-3-ols (in particular epicatechin gallates) and gallic acid^{46,47}; the main polymers are condensed catechins (in particular, thearubigins and theaflavins) that dominate in black tea.^{47,48} The flavan-3-ols epicatechin and catechin are also present in cocoa, but the main cocoa polyphenols are procyanidins.^{41,49} Whereas the flavanols or gallic acid were found to exhibit no or only modest vasodilatory or ni-

tric oxide-stimulating effects in different experimental settings⁵⁰⁻⁵⁴ and there are no data on vascular effects of thearubigins and theaflavins, the fraction of oligomeric procyanidins demonstrated a strong vasodilation.^{52,53} Furthermore, in humans, bioavailability of phenolic compounds from cocoa has been reported not only for the monomeric flavanols but also for the procyanidin oligomers.⁵⁵ This suggests that the different plant phenols must be differentiated with respect to their blood pressure-lowering potential and thus cardiovascular disease prevention, supposing that the tea phenols are less active than cocoa phenols. In support of this conclusion, results of a component-based epidemiological study have shown that dietary flavanol intake was not associated with the incidence of myocardial infarction and stroke,⁵⁶ while other flavonoids were found to be protective.^{57,58}

We pooled the data of black and green tea interventions in a single meta-analysis because the principal polyphenol components are al-

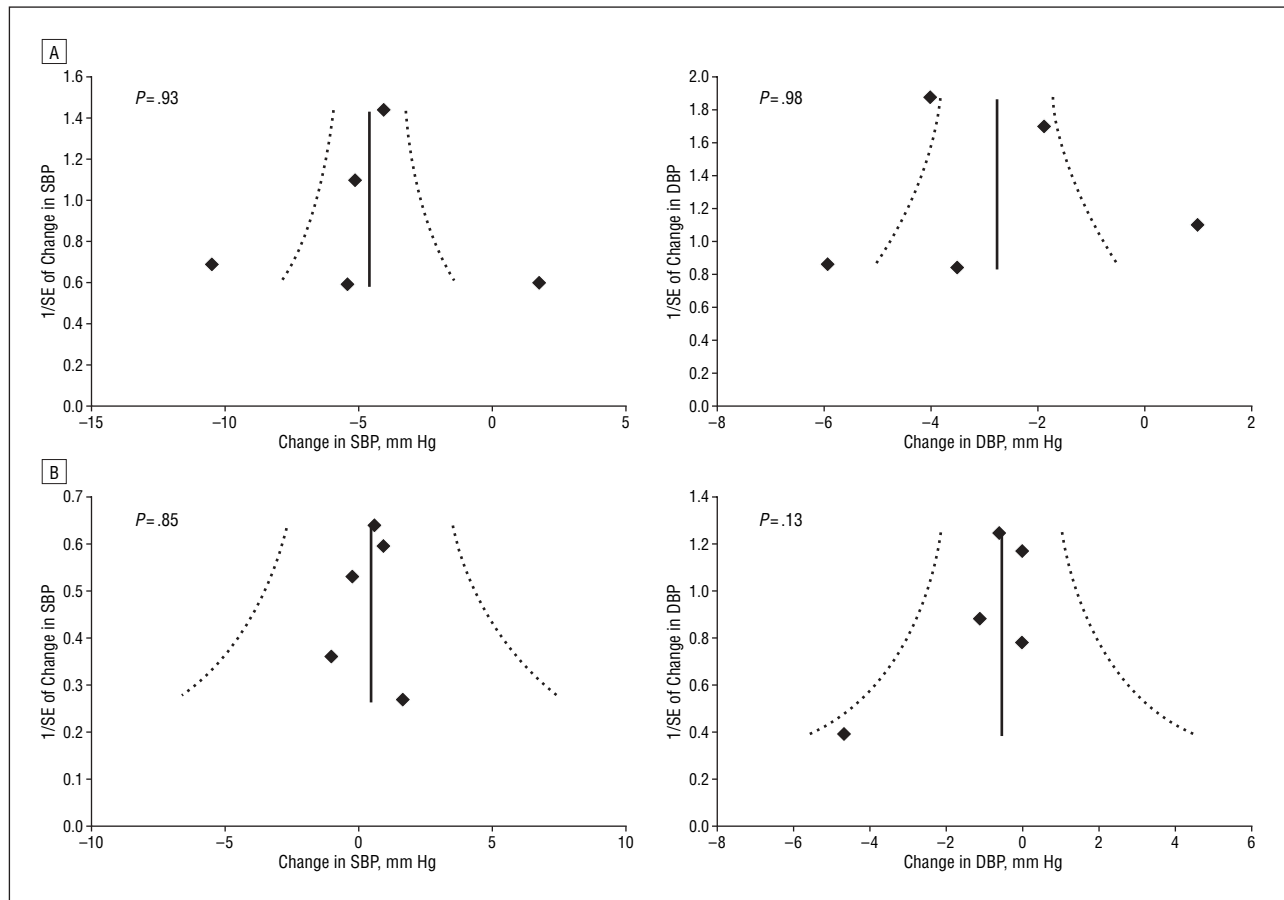


Figure 4. Funnel plots of blood pressure changes in cocoa (A) and tea (B) studies. SBP indicates systolic blood pressure; DBP, diastolic blood pressure; and 1/SE, inverse standard error. The vertical line represents the pooled mean effect size.

most identical in black and green tea, and, although the relation of these components may vary between black and green tea, total polyphenols are in a similar concentration range.⁴⁷

The present study provides robust effect estimates. The prospective design of the meta-analysis minimizes selection and recall biases. Despite residual statistical heterogeneity between the cocoa studies, the adjustments made by sensitivity analyses revealed no significant changes in pooled outcome measures.

Our findings have several potential limitations. First, as with any meta-analysis the internal validity relies on the quality of the individual studies. Although all studies were randomized and described adverse events or withdrawals, the lack of blinding of participants or investigators to the intervention in most of the studies reviewed increased the risk of expectation bias.

Second, our meta-analysis involved only a few studies with small

sample sizes, which makes the estimates especially susceptible to publication bias and to overestimation of treatment effects; consequently, accuracy and statistical power of the outcome estimates were limited.⁵⁹ Although the Egger regression test and trim-and-fill computation provided no indication of publication bias, this cannot be ruled out because these tests lacked sensitivity, with the inclusion of only 5 studies in our meta-analysis.

Third, the studies reviewed had only a short duration. Thus, their results cannot simply be translated into long-term outcomes, that is, the prediction of beneficial treatment effects. In particular, it has to be considered that the short-term administration and the calorie-balanced study design prevented a potential weight gain with the high-caloric cocoa diets (Table 1); however, a concurrent increase in body weight may reverse any blood pressure reductions during long-term habitual intake of cocoa products.⁶⁰ Although

outcome evidence from long-term randomized trials is ideal, those studies with dietary interventions are difficult to implement on a practical basis. It is therefore instructive to compare the data of our meta-analysis with the results of long-term observational studies.

A recent cross-sectional study that assessed habitual cocoa intake and blood pressure in 470 elderly men over 5 years found a -3.7 mm Hg (95% CI, -7.1 to -0.3 mm Hg) lower mean SBP and a -2.1 mm Hg (95% CI, -4.0 to -0.2 mm Hg) lower mean DBP in the highest tertile of cocoa intake compared with the lowest tertile.¹² This is close to the pooled estimates we derived from the randomized trials but was observed with one tenth of the daily cocoa amount compared with the intake in the randomized trials. Hence, the long-term effects of high cocoa consumption on blood pressure may be underestimated by the presented meta-analysis of short-term trials. Moreover, the high degree of risk re-

duction of about 50% in cardiovascular and all-cause mortality associated with regular cocoa intake¹² suggests that cocoa phenols also confer genuine cardiovascular protection beyond blood pressure reduction, possibly due to protective nitric oxide-mediated effects on endothelium or platelets.^{44,45}

In contrast, long-term epidemiological studies of tea intake and blood pressure reported either no blood pressure-lowering effects of habitual tea consumption¹⁶⁻¹⁸ or only small reductions of approximately -2 mm Hg in SBP and -1 mm Hg in DBP,¹³⁻¹⁵ which is consistent with the nonsignificant effects in the short-term randomized trials. Accordingly, a meta-analysis of observational studies on tea consumption in relation to cardiovascular disease conducted in 2001 found only a small, nonsignificant reduction of myocardial infarction incidence with an increase in tea consumption of 3 cups per day (relative risk, 0.89; 95% CI, 0.79 to 1.01).⁹ Subsequent population studies also reported no⁶¹ or similar modest inverse associations⁶² of regular tea intake and cardiovascular diseases.

In conclusion, controlled data from short-term randomized and long-term observational studies suggest clinically relevant reductions of SBP and DBP with the use of cocoa products, supported by the biological plausibility and consistent laboratory data of the vasodilator activity of cocoa phenols. In contrast, cumulative evidence does not support substantial effects of tea consumption on blood pressure. The findings of favorable hypotensive cocoa actions should, however, not encourage common recommendations to consume more cocoa. We believe that any dietary advice must account for the high sugar, fat, and calorie intake with most cocoa products. On the basis of the limitations of current dietary studies, it appears reasonable to allow phenol-rich cocoa products such as dark chocolate for calorie-balanced substitution of high-fat dairy products, sugar confectionary, or cookies of the usual diet. Rationally applied, cocoa products might be considered part of dietary approaches to lower hypertension risk.

Accepted for Publication: December 18, 2006.

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Author Contributions: Dr Taubert had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Taubert. *Acquisition of data:* Taubert and Roesen. *Analysis and interpretation of data:* Taubert, Roesen, and Schömig. *Drafting of the manuscript:* Taubert. *Critical revision of the manuscript for important intellectual content:* Taubert, Roesen, and Schömig. *Statistical analysis:* Taubert. *Administrative, technical, and material support:* Schömig. *Study supervision:* Taubert. **Financial Disclosure:** None reported.

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