American Journal of Epidemiology

Vol. 153, No. 4
Printed in U.S.A.

Coffee Consumption and Serum Lipids: A Meta-Analysis of Randomized Controlled Clinical Trials

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Coffee drinking has been associated with increased serum cholesterol levels in some, but not all, studies. A Medline search of the English-language literature published prior to December 1998, a bibliography review, and consultations with experts were performed to identify 14 published trials of coffee consumption. Information was abstracted independently by two reviewers using a standardized protocol. With a random-effects model, treatment effects were estimated by pooling results from individual trials after weighting the results by the inverse of total variance. A dose-response relation between coffee consumption and both total cholesterol and LDL cholesterol was identified ($p < 0.01$). Increases in serum lipids were greater in studies of patients with hyperlipidemia and in trials of caffeinated or boiled coffee. Trials using filtered coffee demonstrated very little increase in serum cholesterol. Consumption of unfiltered, but not filtered, coffee increases serum levels of total and LDL cholesterol. *Am J Epidemiol* 2001;153:353–62.

clinical trials; coffee; lipids; meta-analysis

Drinking coffee is very common in Western society. In the United States, for example, 52 percent of all persons aged 10 years or older drink coffee (1). Demonstration of the benefits and hazards associated with any such common exposure is important. Some (2–8), but not all (9–11), observational studies have identified a positive association between coffee drinking and higher levels of serum cholesterol. This association was later found to be causal and mediated through a cholesterol-raising effect of oils contained in coffee (12, 13).

Received for publication June 30, 1999, and accepted for publication March 14, 2000.

Abbreviations: CI, confidence interval; HDL cholesterol, high density lipoprotein cholesterol; LDL cholesterol, low density lipoprotein cholesterol.

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In 1965, Bellet et al. (14) reported a clinical trial of the effect of caffeine on the level of fatty acids. Since then, a number of investigations in humans have been published (12, 13, 15–34). Results of these trials have been inconsistent, perhaps because of small sample sizes or other design features. Pooling the results of clinical trials provides a means to explore the basis for heterogeneity in trial outcomes. The objectives of this meta-analysis were to examine the effects of coffee consumption on serum lipids and to assess whether any effect on lipids differs by type of coffee (regular vs. decaffeinated) consumed or method of preparation (boiled vs. filtered).

MATERIALS AND METHODS

Study selection

English-language literature published prior to December 1998 was searched for all reports on the effect of coffee supplementation in humans. Search strategies included 1) a Medline search using the medical subject headings "cholesterol," "lipoprotein," "caffeine," and a text word "coffee"; 2) a review of reference lists from original research and review articles; and 3) a review of the authors' reference files. Twenty-three papers were identified (12–34). These articles were reviewed independently by two authors (S. J. and J. H.) to determine whether they met a series of predetermined criteria for inclusion in our subsequent analyses. Areas of disagreement or uncertainty were adjudicated by consensus. To be included, a study had to have 1) been based on results from human experimentation with random allocation of participants; 2) used coffee drinking as the active treatment intervention; 3) included no intervention difference

between the active treatment and control groups (or periods) other than coffee consumption; and (4) provided data to calculate the differences in serum total cholesterol change and between the active and control treatments and the corresponding variances of this difference.

Fourteen studies met the criteria for inclusion in our analysis. The major reasons for exclusion were 1) nonrandomized treatment allocation (29); 2) a lack of a concurrent control group (29–33); 3) use of coffee oil (such as diterpenes) as the active treatment (12, 13); and 4) insufficient data to calculate the net change in serum lipids and their variances from baseline to the end of follow-up (34).

Data abstraction

From each paper, the following information was abstracted: 1) characteristics of the study population, including sample size, age, sex, proportion with hypercholesterolemia, baseline coffee consumption, and serum lipid levels; 2) study design, including duration of intervention, type of treatment and control, method of coffee preparation (boiled, filtered), coffee additives (cream, sugar, etc.), and cups of coffee consumed per day during the trial; and 3) change in serum lipids and the associated variance. If different protocols were used in the same report, they were analyzed as separate trials, and the effects of coffee intake were calculated as differences between the treatment groups and the no coffee control group. In addition, separate meta-analyses were performed for trials that compared regular coffee use with decaffeinated coffee as well as for trials of boiled versus filtered coffee.

Statistical analysis

For parallel trials, net change in serum lipids was calculated as the mean difference (coffee minus control) of the change (follow-up minus baseline) in serum lipids. For crossover trials, net change was calculated as the mean difference in values between the end of the coffee supplementation and control periods. For calculation of the pooled effects of the interventions, each study was assigned a weight consisting of the reciprocal of its total variance. Because the variances for net changes in serum lipids were not reported directly in most manuscripts, they were calculated from confidence intervals, t statistics, p values, or the individual variances for intervention and control groups (parallel trials) or intervention and control periods (crossover trials). For parallel trials in which the variance of paired differences during the trial was reported separately for each group, we calculated a pooled variance for net change by using standardized methods (35). When the variance of paired differences was not reported, we calculated it from the variance at baseline and at the end of follow-up. To estimate covariance, correlation coefficients between the initial and final measurements of serum lipids from trials of the same duration were used (16–18). We assumed an equal variance during the trial and in the intervention and control groups.

Estimates of the mean effect of coffee consumption on serum lipids and the corresponding 95 percent confidence intervals were calculated by using both fixed-effects and random-effects models. These approaches yielded similar patterns, but somewhat different effect estimates. Homogeneity of effect size across trials was tested by Q statistics (36). Because there was substantial and significant variation in effect size across trials, we present the results obtained using the random-effects model as developed by DerSimonian and Laird (36). The assumption of heterogeneity implied by the use of the random-effects model is plausible because durations of the trials varied markedly, and they were conducted in samples that differed markedly by age, hypercholesterolemia status, and other covariates. To explore the possible influence of covariates on net change in serum lipids, we conducted a series of prestated subgroup analyses on the basis of plausibility and knowledge of the literature. Finally, univariate and multivariate linear regression models were developed to explore the influence of a series of covariates on net change in serum lipids. The linear regression models were weighted by the inverse of variance for change in serum lipids in each trial. Variables that reached statistical significance in univariate analysis were included in the multivariate models. When information on mean age was missing (one trial), we used an average of the minimum and maximum values for that trial. Information on race was reported in only one trial. For crossover trials, we used mean serum lipid levels during the control period as the baseline values. Variables that reached statistical significance in univariate analysis were included in multivariate analysis. To examine potential publication bias, we plotted the sample sizes of the studies against their corresponding effect size (37) .

RESULTS

Participant and study design characteristics for the 18 comparisons of coffee drinking with no coffee drinking are presented in table 1. The trials, which were conducted between 1985 and 1992, varied in sample size from 12 to 120 participants, with a median of 47 participants per trial. The total number of participants was 885, but 147 (16.6 percent) and 34 (3.8 percent) of them were evaluated twice and three times, respectively, receiving different treatments in separate protocols. All of the trials were conducted on adults, with a range of mean ages of 26–49 years. Nine of the 18 trials included both men and women, while men were the sole participants in the remaining nine trials. Five trials (135 participants) were conducted with hyperlipidemic patients. Persons on lipid-lowering drug therapy were excluded from one study (17). A crossover design was used in six trials, while parallel arm design was used in the remaining 12. All of the trials were single-blind. Average pretreatment total cholesterol ranged from 190.8 to 335.9 mg/dl (median, 213.5 mg/dl).

Characteristics of the intervention in the 18 trials of coffee drinking versus no coffee drinking are given in table 2. The trials varied in length from 21 to 79 days, with a median duration of 56 days. The control group received no coffee in 16 trials. In the remaining two trials (18, 19), the

TABLE 1. Participant and study design characteristics of 18 trials of coffee drinking versus no coffee consumption in English-language literature published prior to December 1998

Author and year (reference no.)	Sample size*	Age (years)		% male	% hyperlipidemic	Study design	Masking	Habitual coffee intake (cups/day)	Baseline lipids (mg/dl)			
		Mean	Range						TC†	HDL cholesterol†	LDL cholesterol†	TG†
Forde, 1985a (15)	8/9	45	35–54	100	100	P†	NA†	7.3	335.9			
Forde, 1985b (15)	8/9	45	35–54	100	100	P	NA	7.3	335.9			
Forde, 1985c (15)	8/9	45	35–54	100	100	P	NA	7.3	335.9			
Aro, 1985 (16)	12	49	35–45	50	0	X†	NA	4.5	193.7	32.7	116.8	30.2
Aro, 1987a (17)	42	49	31–60	50	100	X	NA	6.5	306.3	58.4	227.0	70.4
Aro, 1987b (17)	42	49	31–60	50	100	X	NA	6.5	310.1	58.0	235.9	61.5
Bak, 1989a (18)	33/34	26		54	0	P	Single	5.6	199.3	48.9	126.8	
Bak, 1989b (18)	34/34	26		53	0	P	Single	5.6	195.7	48.0	121.0	
Burr, 1989a (19)	54	35	18–58	65	0	X	Single	3.5				
Burr, 1989b (19)	54	35	18–58	65	0	X	Single	3.5				
Rosmarin, 1990 (20)	11/10	36	22–45	100	0	X	NA	3.9	190.8	37.7	124.9	108.8
Superko, 1991a (21)	62/58	46		100	0	P	Double	4.5	211.5	50.8	141.3	44.1
Superko, 1991b (21)	61/58	46		100	0	P	Double	4.5	213.5	50.1	143.5	59.0
Van Dusseldorp, 1991a (22)	22/21	39	17–57	51	0	P	NA	5.5	206.9	59.9	129.5	40.6
Van Dusseldorp, 1991b (22)	21/21	39	17–57	52	0	P	NA	5.5	204.9	56.1	129.5	44.5
Fried, 1992a (23)	25/25	44	20–60	100	0	P	Open	4.5	201.1	53.0	127.8	47.0
Fried, 1992b (23)	25/25	44	20–60	100	0	P	Open	4.5	201.6	53.9	129.0	39.6
Fried, 1992c (23)	25/25	44	20–60	100	0	P	Open	4.5	201.1	52.4	128.8	42.7

* Active treatment group/control group.
† TC, total cholesterol; HDL cholesterol, high density lipoprotein cholesterol; LDL cholesterol, low density lipoprotein cholesterol; TG, triglyceride; P, parallel arm; NA, not available; X, crossover.

control group received tea. Regular coffee was used as the active treatment in 15 of the 18 trials, and decaffeinated coffee was used in the other three trials. In five of the 18 trials, coffee was boiled, and in 10, it was filtered. In three trials, it was not specified whether coffee was boiled or filtered, and in one trial, instant coffee was given. The dose of coffee consumption in the active treatment group varied from three to eight cups per day, with a median of six cups per day. Methods of controlling for dietary changes during the trial, weight assessment, and coffee brewing are also given. Information on coffee additives was not available for most studies (18, 21, 25, 30, 31). For studies in which such information was given, several strategies were used. Adjustment was performed for change in the amount of creamer used (23); addition of cream, nondairy additives, or sugar was not permitted (24); aspartame, skim milk, and

TABLE 2. Intervention characteristics of 18 trials of coffee drinking versus no coffee consumption in English-language literature published prior to December 1998

Author and year (reference no.)	Duration (days)	Type of coffee	Cups/day	Control for diet change	BMI*/weight	Brewing method
Forde, 1985a (15)	70	Regular	7.3	Advice†	NA*	50 g ground coffee, 1 liter of boiling water, sit for 10 minutes
Forde, 1985b (15)	70	Regular	7.3	Advice	NA	50 g ground coffee, filtered (Moccamaster, Technivorm type 70)‡
Forde, 1985c (15)	70	Habitual	7.3	Advice	NA	"Habitual"
Aro, 1985 (16)	21	Instant	8.0	Advice	Weight	2 g lyophilized instant coffee, hot water
Aro, 1987a (17)	28	Regular	8.0	Advice	Weight	56 g coffee (8 standard spoonfuls of 7 g each), boiled
Aro, 1987b (17)	28	Regular	8.0	Advice	Weight	56 g coffee (8 standard spoonfuls of 7 g each), filtered
Bak, 1989a (18)	63	Regular	6.0	Fat record	Weight	20 g ground coffee in 0.5 liters of boiling water, sit for 10 minutes
Bak, 1989b (18)	63	Regular	6.0	Fat record	Weight	Drip, filtered
Burr, 1989a (19)	28	Decaffeinated	5.0	Fat record	Weight	NA
Burr, 1989b (19)	28	Regular	5.0	Fat record	Weight	NA
Rosmarin, 1990 (20)	28	Regular	3.6	Monthly diet log	Weight	Filtered
Superko, 1991a (21)	56	Regular	4.0	4-day record	Weight	Drip, standard amounts of ground coffee, filtered
Superko, 1991b (21)	56	Decaffeinated	4.0	4-day record	Weight	Drip, standard amounts of ground coffee, filtered
Van Dusseldorp, 1991a (22)	79	Regular	6.0	1-day recall	Weight	0.5 liter boiling water poured onto 25 g coarse grounds; unfiltered
Van Dusseldorp, 1991b (22)	79	Regular	6.0	1-day recall	Weight	0.5 liter boiling water poured onto 25 g coarse grounds; filtered
Fried, 1992a (23)	56	Regular	3.0	3-day recall	BMI	1,260 ml water, 8 level scoops of coffee, 72 g of caffeinated coffee, filtered
Fried, 1992b (23)	56	Regular	5.0	3-day recall	BMI	1,260 ml water, 8 level scoops of coffee, 72 g of caffeinated coffee, filtered
Fried, 1992c (23)	56	Decaffeinated	5.0	3-day recall	BMI	1,260 ml water, 8 level scoops of coffee, 64 g of decaffeinated coffee, filtered

* BMI, body mass index; NA, not available.
† Advice, advised not to change their diet.
‡ Technivorm, Ameongen, the Netherlands.

nonfat powered dry milk, but no other additives, were permitted (26); and, in a crossover trial, if milk and sugar were used during the coffee period, they were also used during the tea period (17, 20).

Total cholesterol increased in the active treatment group compared with the corresponding control group in 16 (89 percent) of the 18 trials; in nine trials (50 percent), the lower bound of the 95 percent confidence interval was greater than zero (figure 1). Overall, coffee drinking increased total cholesterol by 11.8 mg/dl ($p < 0.001$).

Low density lipoprotein cholesterol (LDL cholesterol) increased in the active treatment group compared with the corresponding control group in 11 (73 percent) of the 15 trials in which it was measured; in four (27 percent) trials, the lower bound of the 95 percent confidence interval was greater than zero (figure 2). The pooled estimate of the effect of coffee drinking on LDL cholesterol was an increase of 6.5 mg/dl ($p = 0.01$, 95 percent CI: 2.0, 11.0).

The overall pooled estimates of the effect of coffee drinking were 0.2 mg/dl for high density lipoprotein cholesterol (HDL cholesterol) ($p = 0.75$), 5.9 mg/dl for triglyceride ($p = 0.02$), 1.2 mg/dl for apolipoprotein A ($p = 0.37$), and 3.9 mg/dl for apolipoprotein B ($p = 0.01$).

There was considerable variation across the 18 trials in the estimate of intervention-related average net change in serum lipids and in the width of the associated 95 percent confidence intervals. Compared with controls, coffee consumption was associated with an average net change in serum lipids that ranged from –0.4 to 58.4 mg/dl for total cholesterol, –3.9 to 5.0 mg/dl for HDL cholesterol, –8.1 to 45.2 mg/dl for LDL cholesterol, and –2.3 to 14.3 mg/dl for triglyceride. Based on a test of homogeneity, the variation in estimated effect size was significant ($p < 0.0001$) for total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride, apolipoprotein A, and apolipoprotein B. The plot of sample size versus effect size was "funnel" shaped with little variation in the effect size for the studies with a larger sample size and an increasing spread of effect size in the studies with a smaller sample size (figure 3). Accordingly, the distribution of effect sizes seen in individual studies was symmetrically distributed around the pooled mean effect size.

Table 3 summarizes the pooled estimates of treatment effect in subgroups of trials defined according to partici-

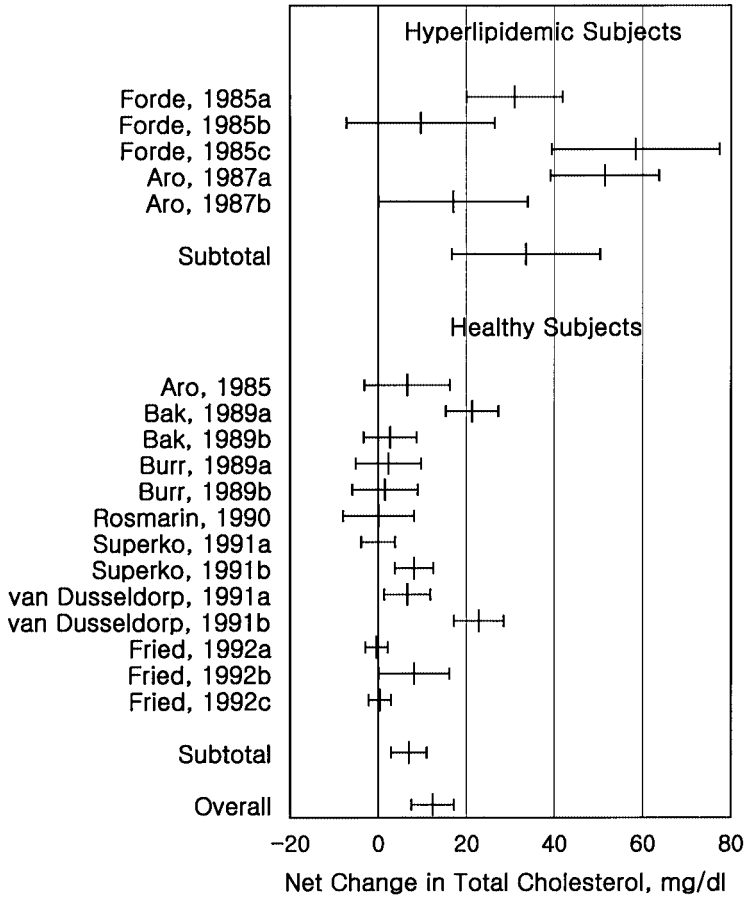

FIGURE 1. Net change and 95% confidence intervals in total cholesterol associated with coffee drinking in 18 clinical trials published in English-language literature prior to December 1998. The overall effect is weighted by the inverse of the total variance of each trial.

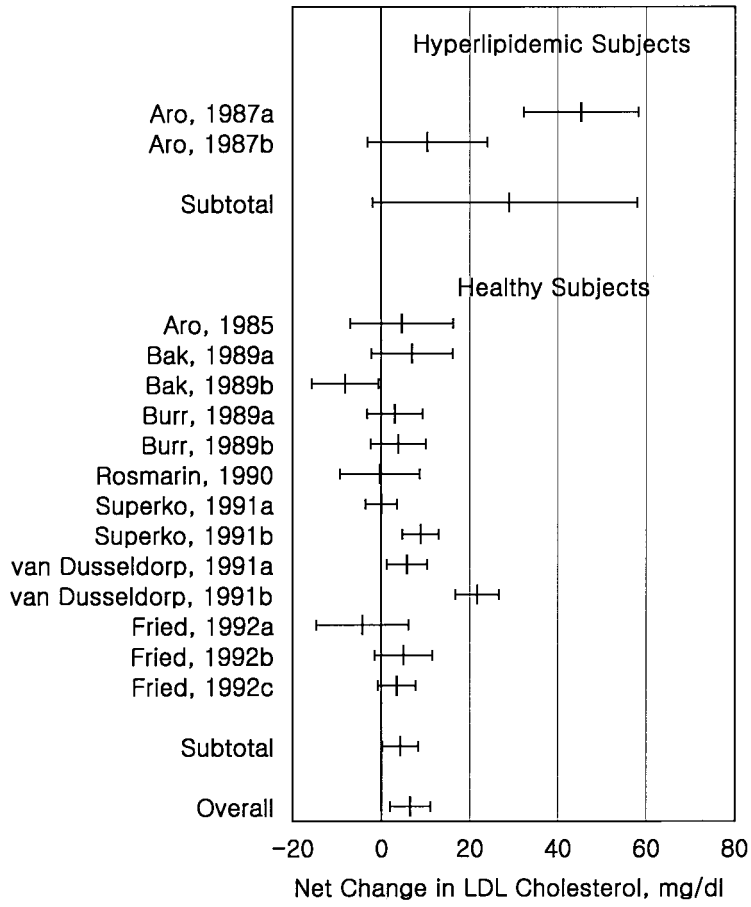

FIGURE 2. Net change and 95% confidence intervals in low density lipoprotein cholesterol (LDL cholesterol) associated with coffee drinking in 15 clinical trials published in English-language literature prior to December 1998. The overall effect is weighted by the inverse of the total variance of each trial.

pant characteristics and study design features. As also noted in figure 1, the results were more marked in trials of persons with hypercholesterolemia; cholesterol increased by 33.5 mg/dl (95 percent CI: 16.7, 50.4) in the coffee-drinking groups compared with controls in such patients. In trials that excluded persons with hypercholesterolemia, the average change in cholesterol was 6.1 mg/dl (95 percent CI: 2.1, 10.1). However, the most notable finding in

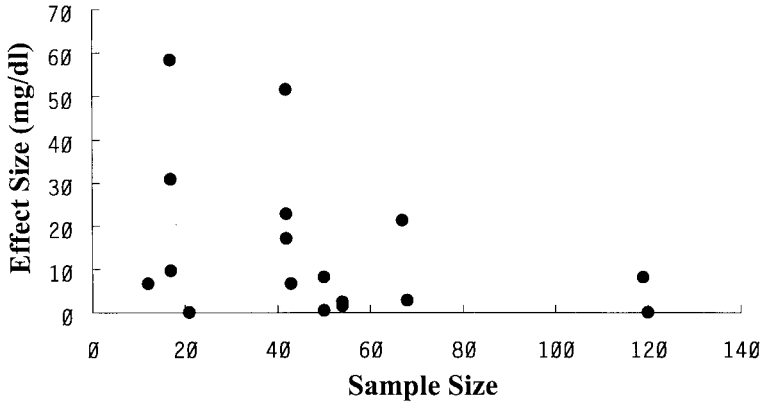

FIGURE 3. Plot of effect on total cholesterol (mg/dl) by sample size in 18 clinical trials of coffee drinking published prior to December 1998.

TABLE 3. Net change in total and LDL cholesterol† by study characteristics of 18 trials of coffee versus no coffee consumption in English-language literature published prior to December 1998

Variables	Total cholesterol (mg/dl)				LDL cholesterol (mg/dl)			
	No.	Net change (95% CI†)	*p* value*	*p* value**	No.	Net change (95% CI)	*p* value*	*p* value**
Overall	18	11.8 (6.8, 16.0)	<0.001		15	6.5 (2.0, 11.0)	0.002	
Sample size								
<43	9	21.8 (10.7, 32.6)	<0.001	0.052	6	1.6 (–5.6, 8.7)	0.336	0.24
≥43	9	8.6 (1.7, 10.6)	0.011		9	7.1 (2.2, 12.1)	0.003	
Age(years)								
<50	8	8.2 (1.5, 14.8)	0.008	0.17	8	4.9 (–1.8, 11.6)	0.075	0.50
≥50	10	15.2 (8.3, 22.1)	<0.001		7	8.2 (1.6, 14.8)	0.007	
Hyperlipidemic participants								
No	13	6.1 (2.1, 10.1)	<0.0001	0.01	13	4.3 (0.3, 8.3)	0.019	0.15
Yes	5	33.5 (16.7, 50.4)	0.025		2	27.9 (–2.1, 57.9)	0.033	
Design								
Parallel	12	11.7 (6.1, 17.2)	<0.001	0.99	9	4.8 (–0.4, 9.9)	0.035	0.36
Crossover	6	12.5 (–0.6, 25.6)	0.031		6	10.3 (0.1, 20.6)	0.024	
Duration of intervention (weeks)								
<8	6	12.5 (–0.6, 25.6)	0.031	0.99	6	10.3 (0.1, 20.6)	0.024	0.36
≥8	12	11.7 (6.1, 17.2)	<0.001		9	4.8 (–0.4, 9.9)	0.035	
Type of coffee								
Regular	15	14.2 (7.8, 20.7)	<0.001	0.02	12	7.0 (0.9, 13.1)	0.012	0.69
Decaffeinated	3	3.6 (–1.9, 9.0)	0.100		3	5.5 (1.6, 9.4)	0.004	
Filtered								
Yes	10	3.2 (0.6, 5.8)	0.01	0.004	9	2.6 (–0.8, 6.0)	0.067	0.07
No	8	23.0 (11.9, 34.9)	<0.001		3	13.6 (3.4, 23.9)	0.005	
Amount of coffee (cups)								
<6	8	2.0 (–0.4, 4.4)	0.0548	<0.001	8	3.2 (0.5, 6.0)	0.011	0.13
≥6	10	21.6 (12.5, 30.7	<0.001		7	11.9 (1.7, 22.1)	0.011	

* Within strata *p* value.
** Test of homogeneity between strata.
† LDL cholesterol, low density lipoprotein cholesterol; CI, confidence interval.

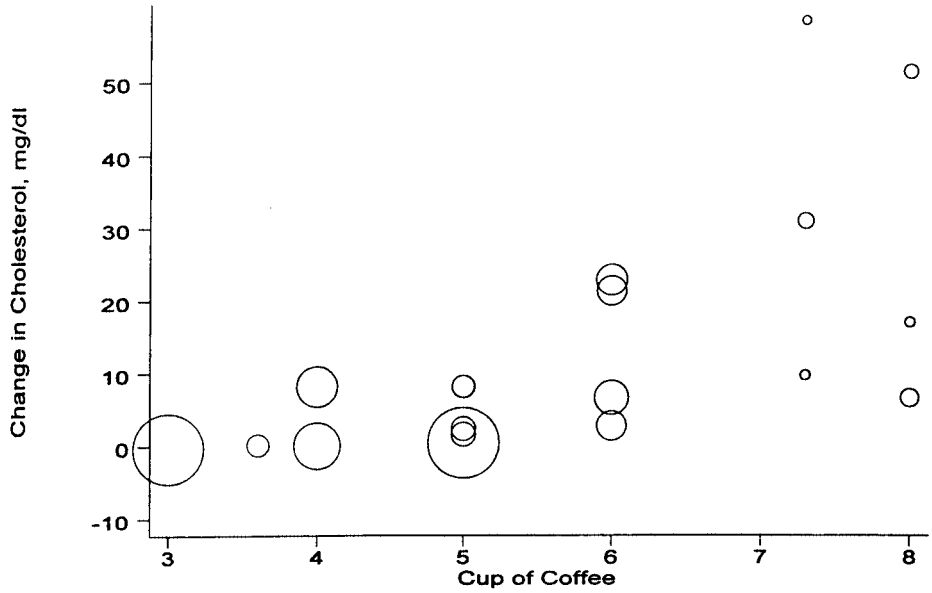

FIGURE 4. Net change in total cholesterol by amount of coffee supplementation in 18 trials published before December 1998. Diameter of circles is proportional to the inverse of the total variance of each trial.

TABLE 4. Participant and study design characteristics of 14 trials comparing boiled with filtered coffee (n = 6) or caffeinated with decaffeinated coffee (n = 8) in English-language literature published prior to December 1998

Author and year (reference no.)	Sample size*	Age (years)		% male	% hyper-lipidemic	Study design*	Masking	Baseline coffee intake (cups/day)	Baseline cholesterol (mg/dl)			
		Mean	Range						TC†	HDL cholesterol†	LDL cholesterol†	TG†
Forde, 1985 (15)	8/8	45	35–54	100	100.0	P†	NA†	7.3				
Aro, 1987 (17)	42	49	35–45	50	0	X†	NA	4.5	310.1	57.0	235.9	61.5
Burr, 1989 (19)	54	35	18–58	65	0	X	Single	3.5				
Bak, 1989 (18)	33/34	26		54	0	P	Single	5.6	194.5	45.6	118.3	
Aro, 1990 (24)	20/21	45	23–61	46	0	X	NA	5.7				
van Dusseldorp, 1990 (25)	45	38	25–45	49	0	X	Double	4–6	215.0	58.8		
Superko, 1991 (21)	52/61	46		100	0	P	Double	4.5	215.8	49.9	145.0	46.4
van Dusseldorp, 1991 (22)	21/22	39	17–57	51	0	P	NA	5.5	204.9	54.1	131.5	
Ahola, 1991 (26)	11/9	45		85	0	X	NA	7.0	216.6	146.9	146.9	34.8
Fried, 1992a (23)	25/25	44	20–60	100	0	P	Open	4.5	204.6	54.5	127.6	
Fried, 1992b (23)	25/25	44	20–60	100	0	P	Open	4.5	204.6	54.5	127.6	
Wahrburg 1994a (27)	39/39	25		51	0	P	NA	3–6	209.5	60.3	131.1	39.8
Wahrburg, 1994b (27)	39/38	25		51	0	P	NA	3–6	209.5	60.3	131.1	39.8
Sanguigni, 1995 (28)	49	23	21–28	51	0	X	Double	>5.0	173.6	38.7	104.4	

* Active treatment group/control group.
† TC, total cholesterol; HDL cholesterol, high density lipoprotein cholesterol; LDL cholesterol, low density lipoprotein cholesterol; TG, triglyceride; P, parallel arm; NA, not available; X, crossover.

subgroup analyses was greater intervention-related increases compared with controls in total cholesterol ($p < 0.001$) and LDL cholesterol ($p = 0.03$) in the trials that used nonfiltered coffee as the active treatment compared with those that used filtered coffee. There was also a greater effect on total cholesterol in trials that used regular coffee as the active intervention compared with the few trials with decaffeinated coffee as the active treatment. Total cholesterol increased to a larger extent in trials in which six cups or more of coffee were consumed compared with those in which the participants drank fewer than six cups of coffee per day. Figure 4 displays the net change in total cholesterol by cups of coffee consumed. A dose-response relation was seen with trials that administered higher doses of coffee, demonstrating larger increases in serum cholesterol.

Tables 4 and 5 display participant, study design, and intervention characteristics of the 14 trials that tested intake of boiled versus filtered coffee or regular versus decaffeinated coffee drinking. Some of the treatment arms are the same as those listed in table 1, but the comparison groups differ (15, 17–19, 21, 23). These trials, which were conducted between 1985 and 1995, varied in sample size from 17 to 113 participants, with a median of 50 persons per trial. Table 6 displays pooled results from these trials. In the eight trials of regular versus decaffeinated coffee, there was no difference in the effect of the two treatments on serum lipid values. In contrast, pooled results of six trials that compared the effects of boiled with filtered coffee showed significantly greater increases in serum lipoprotein levels in the participants who drank boiled coffee than in those who drank filtered coffee.

In multiple linear regression analysis, the number of cups of coffee administered was independently associated with change in total cholesterol and LDL cholesterol (table 7). Older age was independently associated with a greater net change in LDL cholesterol. Substantially greater effects of coffee consumption on both total cholesterol and LDL cholesterol were reported in trials in which the participants drank boiled coffee. Approximately 88.1 percent of the variance in total cholesterol and 86.2 percent of the variance in LDL cholesterol-related treatment effect size could be explained by the five variables included in the multivariate model.

DISCUSSION

To the best of our knowledge, this is the first quantitative review of randomized clinical trials yielding information on the effect of coffee consumption on serum lipids. It demonstrates that, on average, drinking six cups of coffee was significantly associated with an increase in total cholesterol (11.8 mg/dl), LDL cholesterol (6.5 mg/dl), and triglyceride (5.9 mg/dl), but not HDL cholesterol (0.2 mg/dl) levels. The relation between coffee intake and serum lipids persisted after controlling for the mean age of the study participants and the method of coffee preparation. The effect of coffee drinking on total cholesterol was mediated almost solely through its effect on LDL cholesterol and was more pronounced in trials in which the participants drank boiled coffee, had hyperlipidemia, drank more coffee, and were, on average, older. Pooled results of the trials that used filtered coffee demonstrated only minimal effects of coffee on serum cholesterol levels. These results are reassuring for the vast majority of Americans who drink filtered coffee.

Heavy consumption of caffeine or coffee has long been suspected to have a cholesterol-raising effect, but cross-sectional studies investigating the associations have yielded conflicting results (2–4, 38–45). These inconsistencies may reflect variation in the choice of the comparison group (no coffee vs. decaffeinated coffee), variation in methods of cof-

TABLE 5. Intervention characteristics of 14 trials comparing boiled with filtered coffee (n = 6) or caffeinated to decaffeinated coffee (n = 8) in English-language literature published prior to December 1998

Author and year (reference no.)	Duration (days)	Active	Control	Amount (cups)	Control for dietary change	BMI*/weight	Brewing method
Forde, 1985 (15)	70	Boiled	Filtered	7.3	Advice†	NA*	50 g ground coffee added to 1 liter boiling water, sit for 10 minutes (Moccamaster, Technivorn type 70)‡
Aro, 1987 (17)	21	Boiled	Filtered	8.0	Advice	Weight	56 g coffee (8 standard spoonfuls of 7 g each)
Burr, 1989 (19)	28	Caffeinated	Decaffeinated	5.0	Fat record	Weight	NA
Bak, 1989 (18)	63	Boiled	Filtered	6.0	Fat record	Weight	20 g ground coffee, 0.5 boiling water, sit for 10 minutes
Aro, 1990 (24)	28	Boiled	Filtered	5.7	Advice	Weight	Standard spoonful (7 g) of ground coffee placed in hot water for 5–10 minutes
van Dusseldorp, 1990 (25)	54	Caffeinated	Decaffeinated	5.0	7-day recall	BMI	5.4 g of coffee or 5.1 g decaffeinated coffee in 110–150ml hot water
Superko, 1991 (21)	56	Caffeinated	Decaffeinated	4.0	4-day record	Weight	Drip-brewing technique (paper filter) using standard amounts of ground coffee
van Dusseldorp, 1991 (22)	79	Boiled	Filtered	6.0	1-day recall	Weight	0.5 liter boiling water poured 25 g onto coarse pounds
Ahola, 1991 (26)	28	Boiled	Boiled Filtered	6.0	Advice	Weight	Boiled for 5–10 minutes
Fried, 1992a (23)	56	Caffeinated	Decaffeinated	3.0	3-day recall	BMI	1,260 ml water, 8 level scoops of coffee, 72 g of caffeinated coffee
Fried, 1992b (23)	56	Caffeinated	Decaffeinated	5.0	3-day recall	BMI	1,260 ml water, 8 level scoops of coffee, 72 g of caffeinated coffee
Wahrburg, 1994a (27)§	42	Caffeinated	Decaffeinated (arabica)	5.8	3-day record	Weight	50 g of coffee in 1.1 liter water using an electric coffeemaker with paper filter
Wahrburg, 1994b (27)§	42	Caffeinated	Decaffeinated (arabica/robusta)	5.8	3-day record	Weight	50 g of coffee in 1.1 liter water using an electric coffeemaker with paper filter
Sanguigni, 1995 (28)	70	Caffeinated	Decaffeinated	3.0	7-day recall	NA	6.25 g coffee and water to produce 40–50 ml of coffee; 100 seconds contact time

* BMI, body mass index; NA, not available.
† Advice, advised not to change their diet.
‡ Technivorn, Ameogen, the Netherlands.
§ Wahrburg: a, decaffeinated arabica coffee; b, decaffeinated arabica/robusta coffee.

fee preparation between the studies, or confounding. One prospective study has found a lipid-raising effect for habitual coffee consumption (7). In that investigation, drinking one cup of regular coffee a day was associated with about a 2-mg/dl increase in total cholesterol over 16.7 months of follow-up after adjustment for age and changes in other potential confounders. This result is similar to the effect observed in this quantitative summary of clinical trials (11.8 mg/dl higher serum cholesterol with ingestion of six cups per day). In observational studies, the association between coffee consumption and higher serum cholesterol levels might be due to an effect of coffee additives, such as milk and cream, rather than to coffee consumption per se. This is not the case in the clinical trials used in our meta-analysis, however, because use of additives was controlled in almost all trials.

In this summary, trials using a control group that consumed decaffeinated coffee identified no effect of drinking regular coffee on serum cholesterol. This suggests that the cholesterol-raising effect of coffee is not due to the caffeine itself but to another ingredient of coffee (46, 47). The lipid-raising effects of coffee drinking have been reported to be primarily due to coffee oils, such as cafestol and kahweol (12, 13), that increase the synthesis of cholesterol by decreasing excretion of bile acids and neutral sterols (48). Boiled coffee has a higher concentration of coffee oils because of the higher temperatures used during its preparation (17) and the longer contact time between the coffee grounds and water (17, 38). Filtration of coffee through a paper filter removes the cholesterol-raising fraction from the coffee extract (22, 32). Consistent with these observations, trials using boiled or nonfiltered coffee had a stronger cholesterol-raising effect than did those using filtered coffee (table 3).

Several lines of evidence favor the presence of a causal relation between coffee drinking and higher levels of total cholesterol and LDL cholesterol serum lipids. The 95 percent confidence intervals around the estimate of effect size make it unlikely that the associations noted reflect a chance finding. Another finding favoring causality is the presence of a dose-response relation between coffee and serum lipids. Similarly important is replication of the relation in studies conducted in different populations and with different study designs. Finally, the association is biologically plausible.

A limitation of our approach is that only articles published in the English language were included. Limited resources prevented us from including articles published in other languages. Studies in the English-language literature may show a greater intervention effect than does research that is never published or is published in languages other than English. From analysis of the funnel plot, however, there was no evidence that publication bias contributed to the observed results.

In summary, our findings provide support for a causal relation between intake of unfiltered coffee and a higher cholesterol level. The average effect size noted in the trials comparing unfiltered with filtered coffee was relatively large and may have therapeutic importance. These

TABLE 6. Net change in serum lipid levels in trials comparing regular versus decaffeinated coffee or boiled versus filtered coffee in English-language literature published prior to December 1998

Outcome	Regular vs. decaffeinated coffee				Boiled vs. filtered coffee			
	Sample size	Net change	95% confidence interval	*p* value	Sample size	Net change	95% confidence interval	*p* value
Total cholesterol (mgl/dl)	8	1.4	–4.2 to 7.0	0.63	6	18.2	12.4 to 24.0	<0.001
HDL cholesterol* (mg/dl)	8	1.4	–0.5 to 3.2	0.19	5	–0.6	–1.0 to –0.2	0.04
LDL cholesterol* (mg/dl)	8	–0.7	–3.1 to 1.7	0.59	5	17.8	11.1 to 24.5	0.003
Triglyceride (mg/dl)	4	–0.9	–2.5 to 1.0	0.36	4	9.6	3.6 to15.6	0.01
Apo A* (mg/dl)	5	–0.5	–2.6 to 1.8	0.70	5	4.6	–0.5 to 9.7	0.14
Apo B* (mg/dl)	5	–1.0	–5.1 to 3.8	0.65	5	6.3	0.5 to 12.1	0.09

* HDL cholesterol, high density lipoprotein cholesterol; LDL cholesterol, low density lipoprotein cholesterol; apo A, apolipoprotein A; apo B, apolipoprotein B.

TABLE 7. Characteristics associated with average net change in total cholesterol and LDL cholesterol* in 18 coffee consumption trials, multiple linear regression analysis in English-language literature published prior to December 1998

	Total cholesterol (n = 14)						LDL cholesterol (n = 12)					
	Model 1 (R^2 = 0.85)			Model 2 (R^2 = 0.88)			Model 1 (R^2 = 0.83)			Model 2 (R^2 = 0.86)		
	Net change	SE*	*p* value	Net change	SE	*p* value	Net change	SE	*p* value	Net change	SE	*p* value
Intercept	–43.4	7.5	<0.001	–43.0	9.5	<0.001	–65.3	9.8	<0.001	–57.0	11.0	<0.001
Age (years)	0.3	0.1	0.016	0.2	0.2	0.363	0.9	0.2	<0.001	0.7	0.2	0.003
Amount of coffee (cups)	2.4	0.6	<0.001	1.6	0.9	0.091	3.0	1.0	0.006	2.7	1.3	0.051
Method of preparation (boiled vs. filtered)	21.4	2.4	<0.001	19.7	2.6	<0.001	18.0	2.7	<0.001	18.7	2.7	<0.001
Type (regular vs. decaffeinated)				0.5	1.8	0.794				–3.5	2.0	0.105
Hyperlipidemic participants				10.3	5.2	0.062				3.7	7.0	0.888

* LDL cholesterol, low density liproprotein cholesterol; SE, standard error.

results confirm that coffee should be filtered prior to drinking.

ACKNOWLEDGMENTS

This study received partial support from National Institutes of Health, National Institute on Aging grant AG01760 and Outpatient General Clinical Research Center grant 5M01RR00722 from the National Institutes of Health. Computational assistance was received from National Institutes of Health grant RR00035. Dr. Jee was supported by a Post Doctoral Fellowship Award from the World Health Organization. Dr. He was supported by grant R29HL58458–01 from the National Institutes of Health, National Heart, Lung, and Blood Institute.

The authors thank Roxanne Stambaugh for her expert editorial assistance in the preparation of this manuscript.

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