EPIDEMIOLOGY

Does coffee drinking increase the risk of coronary heart disease? Results from a meta-analysis

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Abstract

Background—The association between coffee drinking and risk of coronary heart disease remains controversial despite many epidemiological studies. A meta-analysis was carried out on these studies to resolve some of the uncertainties. Particular attention was paid to details of study design.

Methods—Eight case-control studies and 15 cohort studies were analysed. Weighted, fixed effects linear regression of log relative risks (or odds ratios) was used to pool the study results. The pooling procedures were performed separately by study design, sex, coronary heart disease end points, smoking habit, and period of study.

Results—The pooled case-control odds ratio (for the effect of drinking five cups of coffee/day *v* none) was 1.63 (95% confidence interval (95% CI) 1.50 to 1.78). The pooled cohort study relative risk (five cups/day *v* none) was 1.05 (95% CI 0.99 to 1.12). The discrepancy between the pooled case-control and cohort study results could not be attributed to differences in the end points chosen, period of study, or to confounding by smoking status or sex.

Conclusions—The cohort study data suggest very little excess risk of coronary heart disease among habitual coffee drinkers. The case-control data do not rule out an increased risk of heart disease among a subgroup of people who acutely increase their coffee intake. Further epidemiological studies are needed to assess the risk of drinking boiled or decaffeinated coffee.

(Br Heart J 1994;72:269-275)

The association between coffee drinking and risk of coronary heart disease (CHD) remains controversial despite many epidemiological studies. A relation of coffee drinking to CHD was first suspected because of the role of caffeine in inducing cardiac arrhythmias, and increases in plasma renin activity, catecholamine concentrations, and blood pressure.^{1,2} Although it seems now that these effects are not clinically significant in most

habitual drinkers,³ renewed concern has arisen from cross sectional findings of an association between coffee drinking and serum total cholesterol concentrations.⁴⁻⁹

The inconsistent findings of epidemiological studies—for example, comparing the results of LaCroix *et al*¹⁰ with those of Grobbee *et al*¹¹—have resulted in conflicting policy advice.¹² To resolve some of the existing uncertainties, we applied the techniques of meta-analysis to all published epidemiological studies of coffee consumption and CHD, paying particular attention to details of study design.

Patients and methods**METHODS***Selection of studies*

Epidemiological studies of coffee consumption and heart disease were identified by a computer aided literature search, as well as by bibliographical searches of review articles¹³ and previous meta-analysis.^{12,14}

Early case-control studies¹⁵⁻¹⁷ were excluded from the meta-analysis as these reports included insufficient information to permit calculations of relative risks and SEMs. Two studies^{18,19} were excluded on the basis that they examined prevalence of heart disease only. Wherever more than one published report was generated with the same cohort or case-control study,²⁰⁻²³ the most updated data were included in the meta-analysis.²⁴⁻²⁷ In the case of the Framingham study the original report by Dawber *et al*²⁸ examined non-fatal myocardial infarction as an end point, whereas the update of the same cohort²⁹ provided data on total cardiovascular disease mortality (including angina, congestive heart failure, and intermittent claudication). We used the more recent Framingham data²⁹ in the overall pooled analysis, although we included the earlier report²⁸ in a subanalysis of studies that used myocardial infarction as an end point. Similarly, in the case of the Seventh Day Adventists' cohort, the original report by Snowdon *et al*²³ assessed fatal CHD in men and women, whereas the updated report²⁷ presented data for men only. We used the more recent data²⁷ in the overall pooled analysis, but included the earlier report²³ subanalyses broken down by sex. A total of eight case-control studies^{25,30-37} (appendix 1)

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Accepted for publication
23 February 1994

and 15 cohort studies^{10 11 24 26 27 29 37-45} (appendix 2) were used in the meta-analysis.

Statistical methods

The pooled method involved a weighted, fixed effects linear regression of the log relative risks (or odds ratios) from the individual studies, with the inverse of the variance of log relative risks as the weights. To convert 95% confidence intervals (95% CIs) into estimates of the variance of the log relative risk (or odds ratio), we transformed the interval to the log scale. The absolute difference between the upper and lower end points was then divided by 3.92 to obtain an approximate SEM. The procedure was modified in reports that gave 90% CIs.⁴⁶ Where the original studies provided no SEMs or CIs for rates or relative risks, these were estimated with procedures described by Greenland.¹⁴ The weighted linear regressions were performed in SAS.⁴⁷ As noted by Greenland,¹⁴ the SEMs computed by this program needed to be corrected by dividing the printed SEMs by the square root of the residual mean square.

Assignment of exposures

Virtually all the studies reported coffee consumption as categories—for example, two to four cups/day, more than five cups/day. We assigned category midpoints to each category. For open ended categories, we used Greenland's suggestion¹⁴ and assigned the mean number of cups/day for a particular category based on the distribution of coffee consumption reported in the Framingham study.²⁸ Thus we assigned 6.5 cups for the category five or more cups/day; 7.4 cups for the category six or more cups/day; 8.5 cups for the category seven or more cups/day; nine cups for the category eight or more cups/day; and so on.

Meta-analyses

The meta-analyses were performed separately for case-control and cohort studies. The stud-

ies used different end points of cardiovascular disease. For the overall pooled analysis, one end point was selected for each study. These were in order of priority: total CHD (fatal CHD and non-fatal myocardial infarction), myocardial infarction (fatal or non-fatal), or fatal CHD (including sudden coronary death). As well as the main pooled analysis, three separate meta-analyses of cohort studies were carried out with CHD death, fatal or non-fatal myocardial infarction, and total CHD as end points. Studies that reported results for all three end points^{24 40} contributed data to each subanalysis.

Sensitivity analyses

We examined the sensitivity of the pooled results to the method of assigning cups/day to the open ended categories used for the highest intake of coffee. In this sensitivity analysis, we assigned the lowest number of cups in a particular category instead of the mean number of cups based on the Framingham distribution. Thus we assigned six cups to the category six or more cups/day (instead of 7.4 cups), and seven cups to the category seven or more cups/day (instead of 8.5 cups).

Two studies reported on total cardiovascular disease events rather than coronary heart disease events.^{29 45} The pooled analyses were repeated both including and excluding these two studies to examine the sensitivity of the results of studies with different end points.

As cigarette smoking is positively associated with coffee consumption,^{48 49} failure to adjust for smoking results in a biased estimate of the risk of coronary heart disease. In our study, we performed a meta-analysis restricted to non-smokers, with data from a subsample of studies that reported data separately for smokers and non-smokers.

We next carried out a pooled analysis of the three case-control studies^{25 32 34} that included data on decaffeinated coffee. Only one cohort study provided data on decaffeinated coffee intake.¹¹ We also carried out separate analyses for men and women to look for any sex differences in the effect of coffee on heart disease.

Results

GENERAL FINDINGS

Appendices to tables 1 and 2 show the characteristics of the case-control and cohort studies included in the meta-analysis. Of the eight case-control studies selected for meta-analysis, seven^{25 30 32-35 37} reported a positive association (or a significant trend in risk) between coffee consumption and coronary heart disease. Of the 15 cohort studies included in the meta-analysis, five^{10 26 27 39 42} reported a positive association between coffee intake and risk of heart disease.

REGRESSION RESULTS

Unless otherwise stated, all the pooled odds ratios (or relative risks) given are for the comparison of five cups of coffee/day *v* none. A log linear assumption was made, in which the

Table 1 Pooled odds ratios (ORs) and relative risks (RRs) (for the effect of drinking five cups/day *v* none) from case-control studies and cohort studies of coffee consumption and CHD

Type of study	No of studies	OR or RR (95% CI)	χ^2 for heterogeneity
Case-control	8	OR 1.63 (1.50 to 1.78) OR * 1.66 (1.52 to 1.81)	10.3
Cohort	15	RR 1.05 (0.99 to 1.12) RR * 1.06 (0.99 to 1.14)	85.4

* Effect of one cup/day *v* none, under sensitivity analysis with conservative assignment of cups/day to open-ended categories (see methods).

Table 2 Pooled relative risks (RRs) (for the effect of five cups/day *v* none) from cohort studies, broken down by CHD

End point	No of studies	PR (95% CI)	χ^2 for heterogeneity
CHD death	10	0.97 * (0.04 to 1.01)	66.2
	8	1.15 † (1.10 to 1.19)	32.7
Myocardial infarction	5	1.16 (1.02 to 1.30)	5.7
Total CHD	5	1.25 (1.08 to 1.46)	4.0

* Including studies by Martin, *et al*²⁵ and Wilson *et al*.²⁹

† Excluding studies by Martin, *et al*²⁵ and Wilson *et al*²⁹ that included data on non-CHD deaths, such as congestive heart failure.

estimated relative risk for five cups/day is the antilog of five times the coefficient for one cup (*v* none) shown on appendices to tables 1 and 2.

The pooled odds ratio for case-control studies was 1.63 (95% CI 1.50 to 1.78). The χ^2 for heterogeneity among case-control studies was 10.3 (degrees of freedom (df) 7, $P > 0.1$). For cohort studies, the pooled relative risk was 1.05 (95% CI 0.99 to 1.12). Due to the extremely high heterogeneity among the cohort studies ($\chi^2 = 85.4$, df 14, $P < 0.0001$), the SEM for the pooled coefficients is almost certainly an underestimate. When the regression procedures were repeated with the more conservative assignment of cups/day in the open ended categories, the pooled odds ratios or relative risks were virtually unchanged (table 1).

We carried out separate pooled procedures for each of the end points: CHD death, myocardial infarction (fatal and non-fatal), and total CHD (table 2). These analyses were done only for cohort studies, as all the case-control studies used myocardial infarction as their end point (with the exception of the study by Hennekens *et al.*,³⁶ which used fatal CHD as the end point). The pooled relative risks were 0.97 (95% CI 0.94–1.01) for CHD death, 1.16 (95% CI 1.02 to 1.30) for myocardial infarction, and 1.25 (95% CI 1.08 to 1.46) for total CHD. These results suggest a possible slight increase in risk of coronary heart disease, although the magnitude of the effect is such that confounding—for example, by smoking—could not be ruled out.

To compensate for confounding by smoking we next performed a pooled analysis restricted to data on non-smokers. Three case-control studies,^{25 34 35} and six cohort studies^{26 37 39 40 42 45} included such data (table 3). Among cohort studies there was no suggestion of increased risk (pooled relative risk = 1.04; 95% CI 0.71 to 1.52). The pooled result among case-control studies was again discrepant from the cohort data with a summary odds ratio among non-smokers of 1.85 (95% CI 1.42 to 2.42).

The pooled odds ratio from the three case-

control studies that examined decaffeinated coffee was 1.42 (95% CI 1.01 to 1.99, χ^2 for heterogeneity = 0.9). This point estimate was not substantially different from the pooled odds ratio for caffeinated coffee (odds ratio = 1.65, 95% CI 1.52 to 1.81).

We performed separate pooling procedures for men and women (table 4). The results for both case-control and cohort studies indicated similar magnitudes of effect of coffee drinking on risk of heart disease for men and women. The discrepancy between the results of case-control and cohort studies persisted.

Discussion

Our meta-analysis supersedes previous studies^{12 14} because it includes case-control studies (omitted in the study of Myers and Basinski¹²); pools data from a more comprehensive set of studies (15 cohort studies compared with 11 analysed in Myers and Basinski,¹² and five by Greenland¹⁴); and stratifies the analyses by disease end point, smoking, and sex.

ASSESSMENT OF CAUSALITY

Bradford Hill proposed a set of criteria by which to assess causality—namely, the strength, consistency, and specificity of the association found, the time relation between exposure and outcome, the existence of a biological gradient, and biological plausibility.⁵⁰ We consider each of these in turn.

Strength of association

The pooled cohort study data suggest, at most, a very weak association (relative risk < 1.2) between coffee intake and risk of CHD. Even the pooled case-control data do not suggest a relative risk of CHD greater than about 1.6 for drinking five or more cups/day. Relative risks of this magnitude could easily arise from residual confounding by factors such as smoking, diet, and other cardiovascular risk factors.⁵⁰ Coffee drinkers are more likely to smoke than those who do not drink coffee.^{48 49} Failure to adjust for cigarette smoking may thus lead to spurious associations between coffee drinking and CHD. Among studies that adjusted for smoking, sometimes substantial differences have been found between the crude age adjusted relative risks and the multivariate relative risks. For example, in the study by LaVecchia *et al.*,³² the age adjusted odds ratio for drinking four or more cups/day was 2.65 (95% CI 1.56 to 4.52) compared with 1.72 (95% CI 0.92 to 3.23) after adjustment for smoking and a range of other CHD risk factors.

Some of the earlier case-control studies that reported a positive association between coffee intake and CHD did not control for smoking—for example, those of Jick *et al.*,³⁰ the Boston collaborative drug surveillance program,³⁵ and Mann and Thorogood.³³ Alternatively, failure to control for smoking cannot entirely account for the discrepancy between the pooled case-control and cohort study results, as the analyses restricted to data

Table 3 Pooled odds ratios (ORs) and relative risks (RRs) (for the effect of five cups/day *v* none) from case-control and cohort studies of coffee consumption and CHD, restricted to non-smokers

Type of study	No of studies	OR or RR (95% CI)	χ^2 for heterogeneity
Case-control	3	1.85 (1.42 to 2.42)	7.2
Cohort	6	1.04 (0.71 to 1.52)	11.2

Table 4 Pooled odds ratios (ORs) and relative risks (RRs) (for the effect of five cups *v* none) from case-control studies and cohort studies of coffee consumption and CHD, by sex

Type of study	No of studies	OR or RR (95% CI)	χ^2 for heterogeneity
Case-control			
Men only	3	1.69 (1.50 to 1.90)	4.3
Women only	3	1.54 (1.33 to 1.77)	2.6
Men and women	2	1.79 (1.49 to 2.14)	0.1
Cohort			
Men only	13	1.15 (1.07 to 1.25)	40.9
Women only	4	1.21 (0.90 to 1.63)	4.4
Men and women	7	0.91 (0.83 to 0.99)	38.7

on non-smokers continued to show an excess risk among case-control studies (pooled odds ratio = 1.85, 95% CI 1.42 to 2.42) but no increased risk among cohort studies (pooled risk ratio = 1.04, 95% CI 0.71 to 1.52).

Consistency of the association

The cohort studies included in our meta-analysis were consistent in suggesting a lack of (or, at most, a very weak) association between coffee intake and risk of coronary heart disease. By contrast, the case-control studies consistently pointed to an excess risk. Among the possible explanations for this discrepancy is that some earlier hospital based case-control studies included patients among the controls who may have reduced their intake of coffee after a diagnosis of chronic illness—for example, digestive diseases.^{30 35} Rosenberg *et al* examined the extent of this bias by including two types of control subjects in a hospital based case-control study: those admitted with acute emergencies and those with chronic diseases.^{20 25} Coffee intake was significantly lower among patients admitted to hospitals with chronic compared with acute conditions. Thus case-control studies that included control patients admitted for chronic conditions may have overestimated the association between coffee consumption and risk of heart disease.^{30 35}

Specificity of the association

With one exception,³⁶ all of the case-control studies used non-fatal myocardial infarction as the disease end point. By comparison, cohort studies looked at various end points, including non-fatal myocardial infarction, fatal CHD, and angina. When we stratified the cohort data according to type of end point (table 2) there was no evidence to suggest that the effect of coffee drinking was specific to a particular category of CHD. Moreover, the discrepancy between the results of case-control studies and cohort studies could not be explained by differences in the choice of end points. The pooled odds ratio for case-control studies with myocardial infarction as the end point was 1.66 (95% CI 1.52 to 1.81); whereas the pooled relative risk for cohort studies with myocardial infarction as the end point was 1.16 (95% CI 1.02 to 1.30).

Time relation between exposure and outcome

Retrospective ascertainment of exposure in case-control studies may pose a problem in the form of recall bias—that is, the experience of having had a coronary event selectively affects patients' recall of coffee consumption and smoking habit before the event.³⁷ This problem is compounded by ascertainment of coffee intake by interviewers who were not blinded with respect to the case-control state of patients.^{30 32 33} In theory, a prospective study design is more capable of making reliable assessments of both coffee intake and smoking habits.

Empirical evidence needs to be gathered to quantify the degree of recall bias, if any, in

retrospective assessments of coffee intake. Data from cohort studies have shown the existence of recall bias when intake of other beverages (such as alcohol) are assessed retrospectively in relation to the onset of disease.⁵¹

One limitation of the prospective study design is the lag time between exposure assessment and outcome, which might potentially obscure acute effects of coffee intake on risk of heart disease.¹⁴ In cohort studies with repeated measurements of exposure assessment, the association between heart disease and coffee intake was strongest when the exposure measurement used was nearest to the outcome.^{10 42} In the study by LaCroix *et al* the relative risk for five or more cups/day compared with none increased from 1.8 (95% CI 0.8 to 4.0) when intake was assessed 10 or more years previously, to 2.5 (95% CI 1.1 to 5.8) when the intake within the past five years was used.¹⁰ Grobbee *et al* however, found no association between coffee intake and risk of heart disease, even though the mean lag time between exposure assessment and outcome was less than two years.¹¹

Evidence from the Nurses' Health Study suggests that coffee intake in an individual subject stays stable over time.⁵² In this study, which assessed the reproducibility of food and beverage intake nine months apart, the Spearman correlation coefficient for coffee intake was 0.71, the highest recorded of all the items in the diet.

Biological gradient

The case-control data consistently suggest a monotonic dose-response gradient between daily coffee intake and risk of myocardial infarction. Compared with non-drinkers, those who drink five or six cups of coffee have about double the risk of myocardial infarction (relative risks of 2.2 reported by Rosenberg *et al*²⁴; 2.1 by Rosenberg *et al*²⁵; 2.2 by Jick *et al*³⁰; 2.1 by the Boston collaborative drug surveillance program³⁵; and 1.86 by Mann and Thorogood³³). In contrast, there was no overall suggestion of a biological gradient in the cohort data. In their meta-analysis of 11 cohort studies Myers and Basinski reported relative risks of 1.01 among drinkers of one to four cups/day, 1.01 for four to six cups/day, and 1.09 for six or more cups/day (with drinkers of less than one cup/day as the reference category).¹²

Biological plausibility

The biological plausibility of the association between coffee drinking and CHD is based, in part, on the effects of caffeine on the cardiovascular system. The available evidence, however, fails to implicate caffeine as such as a significant contributor to risk of cardiovascular disease.³ Although the acute effects of caffeine on the cardiovascular system are well documented, it is doubtful that these are of sufficient clinical significance to produce CHD. Clinical data indicate that moderate caffeine consumption (< 500 mg/day—equivalent to four to six cups of coffee) does not increase the frequency or severity of car-

diac arrhythmias, even among people with ischaemic heart disease or patients with pre-existing ventricular extrasystoles.⁵³ Nor does regular ingestion of caffeine seem to lead to an increase in blood pressure (although infrequent use among people who have not developed tolerance does seem to cause a small, but clinically unimportant rise in blood pressure).^{3 54}

Clinical trial evidence suggests that caffeine itself is unrelated to adverse effects on lipids.^{55 56} No studies to date have shown a positive association between tea intake and CHD even though tea contains caffeine (64 mg/cup of tea, compared with 136 mg/cup for coffee).^{11 30 36 39}

Both the prospective data by Grobbee *et al*,¹¹ and a pooled analysis of the three case-control studies that included data on decaffeinated coffee, suggest a marginally increased risk of CHD with decaffeinated coffee consumption. In the study by Grobbee *et al* the relative risk of total CHD with four or more cups of decaffeinated coffee consumed/day was 1.63 (95% CI 1.02 to 2.60), which may be attributable to an adverse effect of decaffeinated coffee on serum lipids.¹¹ In one randomised trial, the consumption of three to six cups of decaffeinated coffee/day raised the concentrations of low density lipoprotein cholesterol.⁵⁷

Boiled v filtered coffee

A biologically plausible hypothesis, not assessed by any of the epidemiological studies to date, is that the method of preparing coffee (boiling v filtering) affects the risk of cardiovascular disease. In a meta-analysis of 21 cross sectional studies, Bak found that filtered coffee was associated with an average increase in total cholesterol of 0.008 mmol/l/daily cup consumed, compared with an increase of 0.038 mmol/l for boiled (unfiltered) coffee.⁵⁴

The studies from Sweden⁴⁰ and Norway⁴² present an interesting comparison in this regard. In Norway, boiled coffee is the most common form of preparation, whereas in Sweden the predominant method of preparation is filtration. The Norwegian study by Tverdal *et al* found relative risks of CHD death (comparing more than nine v less than one cup/day) of 2.2 (95% CI 1.1 to 4.5) for men, and 5.1 (95% CI 0.4 to 60.3) for women.⁴² By contrast, the Swedish study reported a relative risk of CHD death (again comparing more than nine v less than one cup/day) of 1.1 (95% CI 0.5 to 2.4) for men.⁴⁰ (A Norwegian cohort study that found no association between coffee drinking and CHD death has also been reported.⁴⁴ Unlike the study by Tverdal *et al*⁴² this failed to exclude CHD cases at baseline; also, mortality data were obtained solely by linkage to the Norwegian Bureau of Statistics).

The adverse effect of coffee consumption on the lipid profile is now believed to stem from an as yet unidentified lipid soluble substance that is present in boiled preparations, but seems to be removed during the filtering process.⁵⁸ Thus the precise measurement of coffee intake may be less relevant than the

ascertainment of brewing method (filtered v boiled) in future epidemiological investigations of coffee intake and CHD.

Secular trends in coffee preparation method

In the USA, there has been a considerable shift in the method of coffee preparation from percolated to filtered between 1975 and 1985. In 1975, 75% of Americans drank percolated coffee and only 20% filtered, whereas by 1985, 25% drank percolated coffee and 66% filtered (International Coffee Organization, 1989—quoted by Bak⁵⁴). Percolation involves boiling coffee, which has been shown to have adverse effects on serum lipids.⁵⁴

The secular trends in method of coffee preparation may be consistent with the generally positive associations between coffee intake and heart disease found in the United States case-control studies, all but one of which were completed during the 1970s—Jick *et al* in 1972³⁰; Boston collaborative drug surveillance program in 1972³⁵; and Rosenberg *et al* (female subjects) between 1976 and 1979.²⁵ Conversely, among cohort studies, there seems to be no consistent pattern whereby studies conducted before 1975 (the period during which there was relatively high prevalence of percolated coffee consumption) show a positive association between coffee intake and heart disease. The seven studies completed before 1975 show no association between coffee drinking and heart disease (pooled relative risk = 1.03, 95% CI 0.94 to 1.12); whereas the four studies that assessed coffee drinking during the 1980s reported a slightly positive association (pooled relative risk = 1.21, 95% CI 1.05 to 1.40).

In conclusion the pooled cohort data suggest very little association between coffee intake and risk of CHD. The pooled case-control data suggest an excess risk of the order of 60% for drinking five cups/day. The higher risk estimates from individual case-control studies may have resulted from a combination of bias in control selection^{30 35}; recall bias; or be confounded by cigarette smoking^{30 33 35}; although it is unlikely that the discrepancy between cohort and case-control data could be wholly explained by bias and confounding. It is possible that cohort studies may have missed an acute effect of coffee drinking on CHD risk, although the evidence for this hypothesis is sparse and inconsistent. Further studies are needed to assess the risk of drinking boiled coffee and decaffeinated coffee, as there are biologically plausible reasons to hypothesise an association with CHD.

Preparation of this report was supported in part by the National Coffee Association. IK was the recipient of an overseas research fellowship of the Health Research Council of New Zealand during the early stages of this study.

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Appendix 1: Summarised characteristics of the case-control studies used in the meta-analysis

Author	No cases (sex/age)	Outcomes	Coefficient (SEM)*	Adjustments
Jick, et al ³⁰	440 (M + F/20-75)	MI	0.120 (0.022)	Age, sex
LaVecchia, et al ³²	262 (F/24-69)	MI	0.061 (0.048)	Age, sex, DM, BP, CHOL, DM, ALC, BMI, other
Rosenberg, et al ^{20, 25}	491 (F/30-44)	MI	0.068 (0.021)	Age, SMK, DM, BP, CHOL, BMI, other
Mann and Thorogood ³³	64 (F/ < 45)	MI	0.0001 (0.070)	Age
Rosenberg, et al ³⁴	1,867 (M/ < 55)	MI	0.103 (0.015)	Age, SMK, DM, BP, CHOL, BMI, ALC, other
Boston Collaborative Drug Surveillance Program ³⁵	276 (M + F)	MI	0.108 (0.032)	Age, sex
Hennekens, et al ³⁶	649 (M/30-70)	Fatal CHD	0.030 (0.043)	Age, SMK, BP, DM, other
Wilhelmsen, et al ³⁷	230 (M/40-57)	MI	0.131 (0.023)	SMK, BP, CHOL, ALC

* Coefficient for one cup v none (SEM).

SMK, smoking; DM, diabetes mellitus; BP, blood pressure; CHOL, serum cholesterol concentration; BMI, body mass index; ALC, alcohol intake; MI, myocardial infarction.

Appendix 2: Summarised characteristics of the cohort studies used in the meta-analysis

Author	Cohort (sex/age)	Outcomes	Coefficient (SEM) *	Adjustments
Yan, <i>et al</i> ²¹	7,705 (M/46–65)	MI CHD death Total CHD	0.016 (0.039) 0.049 (0.070) 0.058 (0.026)	Age, sex
Wilhelmsen, <i>et al</i> ²⁷	834 (M/50)	Total CHD	0.113 (0.153)	Age, sex, CHOL, BP, ALC
Murray, <i>et al</i> ⁴¹	16 911 (M/ >35)	CHD death	– 0.008 (0.017)	Age, SMK, other
LaCroix, <i>et al</i> ¹⁰	1130 (M/19–49)	Total CHD	0.103 (0.043)	Age, SMK, BP, CHOL
Jacobsen, <i>et al</i> ⁴⁴	16 555 (M + F)	CHD death	– 0.023 (0.016)	Age, sex
LeGrady, <i>et al</i> ⁶	1910 (M/40–56)	CHD death	0.119 (0.031)	Age, SMK, BP, CHOL
Martin, <i>et al</i> ⁴⁵	10 064 (M + F/30–69)	Total CVD	– 0.051 (0.40)	Age, sex, race
Grobbee, <i>et al</i> ¹¹	45 589 (M/40–75)	Total CHD	0.004 (0.032)	Age, SMK, BMI, ALC, DIET, DM, other
Tverdal, <i>et al</i> ⁴²	38 564 (M + F/35–54)	CHD death	0.104 (0.055)	Age, SMK
Rosengren, Wilhelmsen ⁴⁰	6765 (M/51–59)	MI CHD death Total CHD	0.050 (0.036) 0.010 (0.042) 0.035 (0.030)	Age, SMK, BP, BMI ALC, DM, other
Lindsted, <i>et al</i> ²⁷	9484 (M/ > 30)	CHD death	0.090 (0.022)	SMK, BMI, BP, DIET, other
Klatsky, <i>et al</i> ³⁸	464 (M + F/59)	MI	– 0.007 (0.023)	Age, sex, SMK, race, BP, CHOL, other
Klatsky, <i>et al</i> ³⁹	101 774 (M + F)	MI	0.062 (0.021)	Age, sex, SMK, race, ALC, other
Wilson, <i>et al</i> ²⁹	6214 (M + F/30–67)	Total CHD	– 0.094 (0.018)	Age
Heyden, <i>et al</i> ⁴³	2530 (M + F)	CHD death	0.022 (0.088)	Age

* Coefficient for one cup *v* none (SEM).

SMK, smoking; DM, diabetes mellitus; BP, blood pressure; CHOL, serum cholesterol concentration; BMI, body mass index; ALC, alcohol intake; MI, myocardial infarction.