

An evidence-based nutrition
statement from the National Heart
Foundation of New Zealand's
Nutrition Advisory Committee

coffee & caffeine

Author:

D Roberts BPhEd.BSc.PGDipDiet.NZRD
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**Heart
Foundation**

The Heart of Our Nation

coffee & caffeine

contributors

committee members

Professor J Mann PhD, MD, FRACP, FRSNZ. Professor of Human Nutrition and Medicine, University of Otago, Dunedin, New Zealand.

Dr A Chisholm DipHSc, MCApSc, PhD, NZRD. Research Dietitian, Department of Human Nutrition, University of Otago, Dunedin, New Zealand.

Associate Professor L Eyres PhD, MBA. Technical and Developments General Manager, New Zealand Dairy Foods, Auckland, New Zealand.

M McKerchar DipSc, PGDipSc (Com Nutr), NZRD. Maori Health Promoter, Southern Public Health Services, Invercargill, New Zealand.

J Reid BSc (Hons), PGDipDiet, MPH, NZRD. Nutrition Advisor, Ministry of Health, Wellington, New Zealand.

D Roberts BPhEd, BSc, PGDipDiet, NZRD. National Dietitian, the National Heart Foundation of New Zealand, Auckland, New Zealand.

Associate Professor B Swinburn MB ChB, FRACP, MD. Medical Director, the National Heart Foundation of New Zealand, Auckland, New Zealand.

A Tuffin BA, DipTchg. Senior Lecturer Health Education, College of Education, Massey University, Palmerston North, New Zealand.

L Young BHSc, PGDipSc (Com Nutr), NZRD. Food Industry Manager, the National Heart Foundation of New Zealand, Auckland, Zealand.

other contributors

J Bremer DipHSc, NZRD. Consulting Dietitian, Christchurch, New Zealand.

S Mackay BCAPSc, PGDipPH, MSc. Nutritionist, Nelson, New Zealand.

M Seddon MB ChB, MPH. Public Health Registrar, the National Heart Foundation of New Zealand, Auckland, New Zealand.

reviewing organisations

The Ministry of Health, Wellington, New Zealand.

The Nutrition and Metabolism Advisory Committee of the National Heart Foundation of Australia, Canberra, Australia.

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section summary

Coffee and caffeine have been associated with heart rhythm disturbances (cardiac arrhythmias), raised blood pressure and raised blood cholesterol.

For the general population

Limit the consumption of high-caffeine containing beverages, such as coffee, tea, cola products and high-caffeine soft drinks, to the equivalent of five cups of coffee per day.

Traditional Scandinavian and Turkish-style coffees, and unfiltered coffee that is brewed in a plunger pot or boiled using coarse grounds, raise blood cholesterol more than filtered, percolated or instant coffee varieties.

For those at high risk of cardiovascular disease

As for the general population.

Explanatory notes

- The method of brewing coffee will often be the determining factor when describing its association with CVD risk factors (Level of evidence B).
- The consumption of boiled or plunger coffee raises total blood cholesterol primarily through an increase in blood LDL-C. This is a dose-dependent relationship (Level of evidence A).
- Two lipid-containing substances, cafestol and kahweol, have been implicated as the components in coffee responsible for its hypercholesterolaemic effects (Level of evidence B).
- Cessation of caffeine consumption or a change to decaffeinated coffee in habitual caffeine consumers may lower ambulatory blood pressure levels among normotensive individuals (Level of evidence A). The evidence is less clear for borderline hypertensive individuals, and a recommendation cannot be made until further RCT's are conducted within this high-risk population group.
- The trials examining caffeine and arrhythmias are conflicting. Until larger RCT's are conducted, a conservative approach would be to recommend that people with arrhythmias limit their consumption of caffeine-containing beverages (Level of evidence E).

background paper

Examination of the evidence

Introduction

The association between coffee drinking and risk of CVD remains controversial despite many epidemiological studies. A relation of coffee drinking to CVD was first suspected because of the role of caffeine in inducing cardiac arrhythmias, and increases in blood renin activity, catecholamine concentrations, and blood pressure. Although it seems now that at least some of these effects are not clinically significant in habitual drinkers, renewed concern has arisen from cross-sectional findings of an association between coffee drinking and total blood cholesterol concentrations^{1,2,3}.

Observational studies

Prospective data from the Precursors Study was used to determine the association between coffee consumption and the incidence of CHD in 1,130 white, male, medical students⁴. Follow-up ranged from 19-35 years. At 30-year follow-up, there were 47 reported coronary events.

Subjects who drank at least 5 cups.d⁻¹ of coffee had the highest cumulative incidence of CHD (10.7%), as compared with subjects who drank 3-4 cups.d⁻¹ (8.8%), 1-2 cups.d⁻¹ (5.1%), or no coffee (1.6%). Relative risks comparing non-coffee drinkers and heavy coffee drinkers (at least 5 cups.d⁻¹) were 2.77 and 2.49 respectively for average and most recent coffee consumption.

Supporting the role of coffee in the development of CHD, Tverdal et al reported that an increase of 2 cups.d⁻¹ coffee was associated with the same relative risk in men as an increase of 4.3 cigarettes per day, 6.9 mm Hg SBP, 0.47 mmol.L⁻¹ total blood cholesterol or a decrease of 0.24 mmol.L⁻¹ HDL-C⁵. In women, the same increase in coffee consumption was reported to be equal to an increase of 3.5 cigarettes per day, 11.2 mm Hg SBP, 0.47 mmol.L⁻¹ total blood cholesterol or 0.39 mmol.L⁻¹ HDL-C.

Despite these findings, these earlier studies have been criticised because they often failed to control for other lifestyle factors, the most important being an atherogenic diet which has been shown to be more common in people who drink larger amounts of coffee, particularly men⁶. In addition, heavy coffee consumption may occur more frequently in combination with a number of risk - producing habits or exposures, such as a sedentary lifestyle or high levels of occupational stress. The lack of sufficient numbers of coronary events in the Precursors Study, 47, and with only 21 cases of MI also means that confidence intervals around the estimates of relative risk were very large.

More recently a meta-analysis examined the inter-relationship between many of these studies⁷. Eight case-control and 15 cohort studies were examined to determine if coffee consumption did increase the risk of CHD. The difficulty with pooling such data was that many cohort and case-control studies used different end points, typically MI in case control, and CHD death, MI (fatal or non fatal) and total CHD in cohort studies.

Using the comparison of 5 cups.d⁻¹ versus none, the pooled relative risk for case control studies was 1.63 (95% CI 1.50 to 1.78) and for cohort studies 1.05 (95% CI 0.99 to 1.12) from this meta-analysis.

Separating out the different end points from the cohort studies, the authors reported that pooled relative risks were 0.97 (95% CI 0.94 to 1.01) for CHD deaths, 1.16 (95% CI 1.02 to 1.30) for MI, and 1.25 (95% CI 1.08 to 1.46) for total CHD. These results suggested a slight increase in risk of CHD, although the magnitude of effect is such that confounding could not be ruled out. Failure to control for smoking proved to explain much of the strength of association illustrated by the cohort studies (pooled relative risk 1.04 95% CI 0.71 to 1.52) and other confounding factors such as, recall bias and the presence of acute or chronic disease, accounted for the discrepancy between pooled case-control and cohort studies.

One limitation of the prospective study design is the lag time between exposure assessment and outcome which may potentially obscure acute effects of coffee intake on the risk of heart disease. Examining the time interval between reported coffee consumption and the manifestation of coronary disease, LaCroix et al reported that the relative risk for at least 5 cups per day, compared with none, increased from 1.8 (95% CI 0.8 to 4.0) when intake was assessed ten or more years previously, to 2.5 (95% CI 1.1 to 5.8) when the intake within the last five years was used⁴. Thus, coffee consumption that was reported nearest in time to the first manifestation of coronary disease was associated with a significant elevation in risk. Other studies, however, have failed to corroborate these findings. The limitations of the Precursors Study have already been discussed and more recent studies with larger statistical power have 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^{8,9}.

In the Nurses Health Study, a more recent cohort study that was not included in earlier meta-analysis, participants were asked questions about coffee with caffeine, tea, cola beverages and chocolate intake⁹. Questions about decaffeinated coffee consumption were included but at a later date. The study reported a positive association between coffee consumption and relative risk of CHD [the relative risk for ≥ 6 cups.d⁻¹ compared with non-consumers was 1.43 (95% CI 1.10 to 1.86)]. However, controlling for cigarette smoking and age completely eliminated any suggestion of a positive association. Multivariate analysis also found no important positive association

between consumption of decaffeinated coffee and risk of CHD during the time period that this was recorded.

Intervention studies

Boiled versus filtered coffee

The substantial variability in findings from previous studies of coffee consumption and CHD risk has not always been explained, despite the controlling of identifiable confounding factors such as smoking and has led to some uncertainty^{10,11}. One plausible explanation has been the identification of a lipid-soluble fraction in unfiltered coffee that raises blood cholesterol¹². Thus, the positive associations in Norway and Greece, where unfiltered coffee has been used traditionally, might be accounted for by this factor.

Three RCT's using healthy habitual coffee drinkers have demonstrated that boiled coffee relative to filtered coffee consumption (more than 5 cups.d⁻¹) raises total blood cholesterol approximately 10% above baseline, primarily through an increase in blood LDL-C^{13,14,15}. The size of this effect is dependent on the number of cups consumed per day.

Few studies have been identified that examined the effects of these different brewing methods in hypercholesterolaemic patients. In one RCT Aro et al examined the effects of boiled coffee, filtered coffee and tea on blood lipoprotein lipids and apoproteins¹⁶. Forty-two, middle-aged, hypercholesterolaemic subjects (total blood cholesterol between 6.5 mmol.L⁻¹ and 10.0 mmol.L⁻¹), who were not on any prescribed hyperlipidaemic drug therapy, consumed the beverages, 8 cups.d⁻¹, in random order during four, successive, four-week periods. From the level recorded during habitual coffee intake, total blood cholesterol concentration showed a continuous increase throughout the four-week period with boiled coffee (7.92±0.14 mmol.L⁻¹ at baseline; 8.56±0.18 mmol.L⁻¹ at end of four-week intervention, $p<0.01$), while the concentration declined during abstinence of coffee. During the filtered coffee period, blood cholesterol levels followed closely the levels recorded during the consumption of tea. The HDL-C concentration remained unchanged during all study periods. Apoprotein B levels were significantly higher during boiled coffee than during the other two periods.

The RCT evidence for the cholesterol-raising effect of boiled coffee is supported by observational studies^{17,18,19}. In a population-based sample of 1,625 healthy, middle-aged subjects in Northern Sweden, 50% were consuming boiled coffee and 50% filtered coffee¹⁷. Consumers of boiled coffee had significantly higher blood cholesterol levels than consumers of filtered coffee. This relationship was again described as being dose-dependent where subjects who consumed at least 5 cups.d⁻¹ of boiled coffee had significantly ($p<0.01$) higher blood cholesterol levels than those who consumed 4 cups.d⁻¹ or less (6.51±0.07 vs. 6.26±0.06 mmol.L⁻¹).

The diterpenes, cafestol and kahweol, have been implicated as the components in boiled coffee responsible for its hypercholesterolaemic effects. High-performance, liquid chromatography has identified that Scandinavian-style boiled coffee and Turkish-style coffee contain the highest amounts, equivalent to 7.2 and 5.3 mg cafestol per cup and 7.2 and 5.4 mg kahweol per cup, respectively²⁰. In contrast, instant and drip-filtered coffee brews contain negligible amounts of these diterpenes, and espresso coffee contained intermediate amounts, about 1 mg cafestol and 1 mg kahweol per cup ([Table 1](#)).

Experimental data suggests that the cholesterol-raising effects of these diterpenes maybe mediated through their action on LDL-C receptor activity^{21,22}. Halvorsen et al recently illustrated that the coffee lipid, cafestol, significantly reduced the binding, uptake and degradation of LDL-C in human fibroblasts²¹. Furthermore, reduced amounts of LDL-C receptor protein and reductions in the synthesis of cholesterol, and an increase in cholesterol esterification, were confirmed. This suggests that the elevation of LDL-C after the intake of boiled coffee may be due to a down-regulation of the activity of the LDL-C receptors.

Table 1. Preparation techniques of various coffee brews and levels of cafestol and kahweol in coffee brews and predicted effects on total blood cholesterol levels with chronic consumption of 5 cups.d⁻¹²³. Estimates are based on the observation that for every 10 mg of cafestol plus a similar amount of kahweol raises blood cholesterol by 0.13 mmol.L⁻¹²⁴.

Type of Coffee	Preparation technique	Diterpenes per cup		Predicted rise in total blood cholesterol level with consumption of 5 cups.d ⁻¹ (mmol.L ⁻¹)
		Cafestol (mg)	Kahweol (mg)	
Filtered	Boiled water is poured over finely ground roasted coffee beans in a paper filter, either by hand or by using an electric coffee maker	0.1	0.1	< 0.01
Percolated	Coarsely ground roasted coffee beans are extracted by recirculating boiling water until the desired brew strength is reached	0.1	0.1	< 0.01
Instant	2-3 g of soluble coffee granules are dissolved in 150-190 ml of hot water	0.2	0.2	0.01
Espresso	Hot water is forced under high pressure through a bed of finely ground, usually dark - roasted, coffee beans	1.5	1.8	0.10
Mocha	Just overheated water is forced through a bed of finely ground, usually dark -roasted, coffee beans	1.1	1.4	0.07
Boiled	Coarse grounds are boiled with water for 10 minutes or more, or infused with hot water, and the liquid is decanted without the use of a filter	3.0	3.9	0.19
Plunger pot	Hot water is poured onto course grounds, and after two to five minutes the metal screen strainer is pushed down to separate the grounds from the fluid	3.5	4.4	0.23
Turkish	Very fine/powdery grounds are brought to a boil once or repeatedly, or incubated with hot water, and the liquid is decanted without the use of a filter	3.9	3.9	0.25

Two RCT's have identified that the cholesterol-raising factor in boiled coffee can be retained by filtering^{25,26}. Van Dusseldorp et al randomized 64 healthy volunteers to receive 6 cups.d⁻¹ either boiled coffee, boiled and filtered coffee, or no coffee for 17 days²⁵. total blood cholesterol rose by 0.42 mmol.L⁻¹ (95% CI 0.14 to 0.71), LDL-C by 0.41 mmol.L⁻¹ (95% CI 0.16 to 0.66), and apoprotein B levels by 0.22 mmol.L⁻¹ (95% CI 0.10 to 0.35) in those who consumed boiled coffee relative to those that consumed boiled and filtered coffee. Ahola et al corroborated these findings and reported that the filtering process could remove more than 80% of the lipid-soluble substance that was present in the boiled coffee²⁶.

Regular or decaffeinated coffee

Blood lipids

Five RCT's were found that examined the differences between caffeinated and decaffeinated coffee varieties on blood lipoproteins^{27,28,29,30,31}. In the largest and most recent of these, 181, healthy, free-living, non-smoking, male, coffee drinkers were randomly assigned to one of three groups²⁷. This included standard filtered caffeinated coffee consumption (control), decaffeinated coffee consumption, or no coffee consumption. After the initial run-in period, subjects underwent eight weeks of intervention. In comparison with the control group, a significant increase in blood LDL-C concentration (0.12±0.65 mmol.L⁻¹; *p*<0.025) was seen only in the group that changed to decaffeinated coffee suggesting that it is not the caffeine in coffee that is the agent responsible for reported LDL-C elevation. A significant increase was also observed in apo B concentration.

No significant differences were observed for changes in concentration of blood TG, total blood cholesterol, HDL-C subfractions (HDL-C and HDL₂-C), or for apo A-1 for the decaffeinated coffee versus control group.

The authors suggest that the aetiology of the cholesterol - raising effect may lie in the heterogeneity of coffee - processing methods and type of coffee bean, where the *robusta* beans, which have a higher phenolic content than *arabica* beans, were used for making decaffeinated coffee and *arabica* beans for caffeinated coffee.

Other RCT's have failed to find significant differences between caffeinated and decaffeinated coffee consumption and blood lipids, or differences among decaffeinated varieties made from different coffee bean types^{28,29,30,31}. In a small Dutch sub-group of 45 healthy volunteers with a habitual coffee intake of 4-6 cups.d⁻¹, differences between the effects of decaffeinated and regular coffee were essentially zero²⁸. The effect on total blood cholesterol was 0.01±0.36 mmol.L⁻¹, that on HDL-C was 0.01±0.11 mmol.L⁻¹, and that on TGs was 0.03±0.29 mmol.L⁻¹.

In examining the effect the different coffee beans in decaffeinated coffee may have on blood lipids, 119 healthy students were screened on the basis of consuming 3-6 cups.d⁻¹ of caffeinated, filtered coffee³¹. They were then randomized to one of three interventions where they continued drinking caffeinated coffee, or consumed two different types of decaffeinated coffee (one made of *arabica* and the other a blend of *arabica* and *robusta*). For both types of decaffeinated coffee, no effects on total blood cholesterol and LDL-C were observed. Thus, differences in the type of coffee bean in decaffeinated coffee did not seem to play a role in possible effects on blood lipids.

Blood pressure

The relationship between caffeine and blood pressure has been reported in six RCT's^{32,33,34,35,36,37}. Forty-five, normotensive, healthy, young, non-smoking adults were randomized to receive either five cups of filtered coffee or five cups of decaffeinated coffee per day for a period of six weeks³². Independent of treatment sequence, use of decaffeinated coffee led to a slightly but significantly lower mean systolic (-1.5±0.4 mm Hg; $p=0.002$) and diastolic (-1.0±0.4 mm Hg; $p=0.017$), ambulant, blood pressure, and to a somewhat higher heart rate (+1.3±0.6 beats/min; $p=0.031$).

Thus, in this population subgroup, a change from caffeinated to decaffeinated coffee may lead to a small but significant reduction in blood pressure. Supporting this effect of caffeine on blood pressure, Green and Suls have also reported maximum systolic and diastolic increases of 3.6 and 5.6 mm Hg respectively in subjects supplemented with 125 mg caffeine³⁵.

Goldstein et al found blood pressure increases, when compared with placebo, of 5.8/6.5 mm Hg in young male coffee drinkers supplemented with 150 mg caffeine and a further increase of 2.4/5.2 mm Hg with a second caffeine dose three hours after³⁷. Smaller increases can be observed with subsequent caffeine ingestion although the absolute response is smaller and related to the subjects' pre-coffee blood caffeine level. These persistent cardiovascular effects of caffeine have been supported by other less well-designed studies^{38,39}.

In the largest RCT with normotensive subjects, 150 middle-aged males were randomized to standard caffeinated coffee, standard decaffeinated coffee, or discontinued coffee consumption³³. These authors reported no change in resting blood pressure after randomisation to no coffee or decaffeinated coffee. However, significant decreases were seen in systolic and diastolic, ambulatory, blood pressure in both of these groups. The authors suggested that: (i) tolerance to resting blood pressure changes may not extend to ambulatory blood pressure; and (ii) if caffeinated coffee consumption is associated with cardiovascular risk, a portion of this risk may be mediated by changes in daylong blood pressure, which are not apparent with resting blood pressure.

These findings are not supported by the few studies within mildly hypertensive individuals. Fifty-two patients with untreated borderline or mild hypertension (DBP 90-105 mm Hg), who typically drank three cups of coffee per day, were randomized to four different dietary regimens; normal diet, caffeine-free diet alone, caffeine-free diet with decaffeinated, instant coffee, caffeine-free

diet with caffeinated, instant coffee (instant coffee phases conducted double blind)³⁴. The authors reported that mean, ambulatory, blood pressure over 24-hours was not different between regimens. There was no difference in blood pressure variability between regimens. During the caffeine-free diet alone, morning ambulatory diastolic blood pressure was higher (2.8 mm Hg) than during the caffeine-free diet with caffeinated, instant coffee. While statistically significant ($p<0.01$), this may not be clinically significant. There was no significant correlation between blood caffeine concentration and blood pressure. While these results cannot be extrapolated to patients with more severe hypertension or to drinkers of percolated, filtered or brewed coffee, it does suggest that caffeine restriction or a change to decaffeinated coffee is not of clinical value in reducing blood pressure in the non-pharmacological management of patients with borderline hypertension. Eggertsen et al corroborate these findings where, in 23 mild to moderately hypertensive individuals, no effect was found on mean 24-hour, day or evening ambulatory blood pressure following a caffeine-restricted diet³⁶.

Caffeine and arrhythmias

Just four RCT's could be identified that examined the effect of caffeine on cardiac arrhythmias^{40,41,42,43}. Two of these studies could not find a significant, causal effect between caffeine ingestion and the severity of ventricular arrhythmias post MI. In the largest RCT, 300 mg caffeine* was administered to 70 patients approximately one week after the onset of acute MI⁴⁰. Continuous Holter electrocardiographic recording for four hours showed no significant differences in the proportion of patients who had ventricular ectopic activity or the total number and complexity of ventricular premature complexes after caffeine versus placebo. At a higher dose of 450 mg caffeine[†] still no increase was observed in the frequency or complexity of ventricular ectopy with 19 of 35 patients experiencing ventricular arrhythmias as monitored by holter electrocardiographic recording for eight hours⁴¹. In a prospective study, 22 patients (age range 39-72 years) with a history of symptomatic non-sustained, ventricular tachycardia, ventricular tachycardia, or ventricular fibrillation underwent electrophysiological testing before, and one hour after, ingestion of 275 mg caffeine[‡]. Rhythm severity was unchanged in 17 patients, more severe in two and less severe in three. The authors reported that in those patients with clinical, ventricular arrhythmias, caffeine did not significantly alter inducibility or severity of arrhythmias, suggesting little effect on the substrate supporting ventricular arrhythmias.

Findings from subjects with no history of heart disease are more conflicting. In 13 patients with symptomatic frequent, idiopathic, ventricular, premature beats, caffeine exposure of at least 3 cups.d⁻¹ produced no significant changes in palpitation scores or ventricular premature - beat frequencies⁴². However, in another RCT the ingestion of 5 mg.kg⁻¹ body weight caffeine produced a moderate but statistically significant prolongation of QRS complexes ($p<0.02$)⁴³.

While the few trials are suggestive that caffeine intake post MI will have little effect on ventricular arrhythmias, a greater number of trials are needed before a definitive recommendation can be made. It also remains to be determined whether excessive caffeine intake may be a factor in the genesis of arrhythmias prior to any cardiac event and again further appropriately controlled trials are needed. Until these trials are conducted, a conservative approach would be to limit the number of caffeine-containing beverages where arrhythmias exist.

Side effects of caffeine withdrawal

The symptoms of caffeine withdrawal include, headache, fatigue (reported as depression, weakness, lethargy, apathy and drowsiness) and anxiety (reported as nervousness, muscle tension, restlessness and insomnia). The withdrawal syndrome has an onset of 12 to 24 hours after caffeine withdrawal, peaks at 20 to 48 hours and may last for approximately one week⁴⁵.

* Approximately 5 cups instant coffee (Based on a 140 ml cup serving size)

† Approximately 7 cups instant coffee (Based on a 140 ml cup serving size)

‡ Approximately 4 cups instant coffee (Based on a 140 ml cup serving size)

Headache is one of the most frequently encountered symptoms resulting from caffeine withdrawal. While this phenomenon has received most attention in the context of high-intake levels (greater than 600 mg.d⁻¹)^{§46}, withdrawal from low to moderate (mean 235 mg.d⁻¹)^{**47}, and even low intake levels (100 mg.d⁻¹)^{††48} can produce caffeine-withdrawal headaches. Such headaches are relieved by caffeine ingestion ([Table 2](#))⁴⁵. An increased extracranial blood flow due to an enhanced sensitivity to adenosine in the vascular system has been implicated in the aetiology of caffeine-withdrawal headaches^{49,50}.

conclusion

In summary, inconsistent associations identified by observational studies between high coffee consumption and CHD need to be clarified by large-scale, RCT's. To expand on current evidence, further clinical trials are needed examining different brewing methods, and the effect of caffeinated and decaffeinated coffee consumption on CVD risk factors in healthy and high-risk populations.

Table 2. Comparison of caffeine content of typically consumed beverages.

Beverage	mg per 100 ml	Serving Size	mg per serving
Soft Drinks			
Coca Cola	13.0	355 ml can	46.2
Diet Coke	12.8	355 ml can	45.4
Diet Pepsi	10.4	355 ml can	37.0
Pepsi Max	12.4	355 ml can	44.0
Pepsi	10.7	355 ml can	38.0
Mountain Dew	15.2	355 ml can	54.0
Energy Drinks			
Lift Plus	14.4	250 ml can	36.0
Proton	19.0	330 ml bottle	62.7
Red Eye	32.0	330 ml bottle	106.0
Black Stallion	32.0	250 ml can	80.0
Red Bull	32.0	250 ml can	80.0
Top Secret	32.0	355 ml can	113.0
V	32.0	350 ml bottle	112.0
Bagged Tea			
Black, 5 min brew	33.0	140 ml cup	46.0
Black, 1 min brew	20.0	140 ml cup	28.0
Loose Tea			
Black, 5 min brew	29.0	140 ml cup	40.0
Green, 5 min brew	25.0	140 ml cup	35.0
Green, Japan, 5 min brew	15.0	140 ml cup	20.0
Coffee			
Instant	44.0	140 ml cup	66.0
Percolated	73.0	140 ml cup	10.0
Dripolated	97.0	140 ml cup	146.0
Cocoa Powder	226.7	3 g (1 tsp)	6.8
Drinking Chocolate	50.0	3 g (1 tsp)	1.5
Horlicks	0.0	8 g (1 Tbsp)	0.0
Milo Powder	36.7	6 g (2 tsp)	2.2
Ovaltine	16.7	6 g (2 tsp)	1.0
Milk Chocolate	21.4	50 g bar	10.7
Baking Chocolate	125.0	50 g	62.5

Adapted from Pearce J. Nutritional analysis of fluid replacement beverages. *Aust J Nutr Diet* 1996; 53(4 Suppl): S35-S42⁵¹.

§ Approximately 9 cups instant coffee (Based on a 140 ml cup serving size)

** Approximately 4 cups instant coffee (Based on a 140 ml cup serving size)

†† Approximately 2 cups instant coffee (Based on a 140 ml cup serving size)

evidence tables

Evidence Table 3: Coffee drinking & CHD

Key Words: Coffee, CHD, meta-analysis

Reference: Kawachi I, Colditz GA and Stone CB. Does coffee - drinking increase the risk of coronary heart disease? Results from a meta-analysis. Br Heart J 1994; 72: 269-757.

Study Type/Grade	Meta-analysis Grade depends on primary studies used																								
Outcomes	Primary: Coronary heart disease and coffee consumption.																								
Design	<p>Focused on a discrete clinical question?: Yes.</p> <p>Explicit description of literature search?: No, identified by a computer aided literature search, as well as by bibliographical searches of review articles and previous meta-analysis.</p> <p>State methodological standards used to select studies for inclusion in meta-analysis: Early case - control studies were excluded as these reports included insufficient information to permit calculations of relative risks and SEMs. Two studies were excluded on the basis that they examined prevalence of heart disease only. Whenever more than one published report was generated with the same cohort or case control study, the most up-dated were included in the meta-analysis.</p> <p>Demographics of study population: Not specified.</p>																								
Validity	<p>Is the study type appropriate for the question(s) being asked? Yes.</p> <p>Data tested for homogeneity? Yes.</p> <p>Evidence of publication bias? Yes, excluded studies where relative risk or SEMs could not be determined.</p> <p>Summary: Studies subject to confounding typical of observational studies. Evidence of publication bias.</p>																								
Results	<p>Quantified results:</p> <p>Pooled odds ratios (OR) and relative risks (RR) (for the effects of drinking 5 cups.d⁻¹ vs. none).</p> <table border="1"> <thead> <tr> <th>Study</th> <th>Number</th> <th>OR or RR (95% CI)</th> <th>X² for heterogeneity</th> </tr> </thead> <tbody> <tr> <td>Case control</td> <td>8</td> <td>OR 1.63 (1.50 to 1.78)</td> <td>10.3</td> </tr> <tr> <td>Cohort</td> <td>15</td> <td>RR 1.05 (0.99 to 1.12)</td> <td>85.4</td> </tr> </tbody> </table> <p>Pooled OR's and RR's (for the effects of drinking 5 cups per day versus none), restricted to non-smokers.</p> <table border="1"> <thead> <tr> <th>Study</th> <th>Number</th> <th>OR or RR (95% CI)</th> <th>X² for heterogeneity</th> </tr> </thead> <tbody> <tr> <td>Case control</td> <td>3</td> <td>1.85 (1.42 to 2.42)</td> <td>7.2</td> </tr> <tr> <td>Cohort</td> <td>6</td> <td>1.04 (0.71 to 1.52)</td> <td>11.2</td> </tr> </tbody> </table>	Study	Number	OR or RR (95% CI)	X ² for heterogeneity	Case control	8	OR 1.63 (1.50 to 1.78)	10.3	Cohort	15	RR 1.05 (0.99 to 1.12)	85.4	Study	Number	OR or RR (95% CI)	X 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
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Cohort	6	1.04 (0.71 to 1.52)	11.2																						
Authors' 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 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 coronary heart disease".																								
Reviewers' Conclusions	Evidence of publication bias, control selection or recall bias and potential confounding weaken authors' conclusion. Agree that more studies are needed that control for caffeine content and brewing method.																								

Evidence Table 4: Caffeinated coffee & blood lipids

Key Words: Coffee, lipoproteins, cholesterol, lipoprotein lipase, apolipoprotein B

Reference: Superko HR, Bortz W, Williams PT et al. Caffeinated and decaffeinated coffee effects on plasma lipoprotein cholesterol, apolipoproteins, and lipase activity: A controlled, randomized trial. Am J Clin Nutr 1991; 54: 599-60527.

Study Type/Grade	Randomized Controlled Trial Grade A																																	
Outcomes	Primary: Changes in blood lipoproteins and apolipoproteins. Secondary: Resting heart rate and blood pressure.																																	
Design	N= 186. Relevant risk factors: None present. Inclusion and exclusion criteria: Non-smoking male coffee drinkers were recruited on the basis of a history of consuming 3-6 cups of caffeinated coffee per day. Subjects were excluded if they smoked cigarettes, if a major medical problem existed, if lipid-lowering medications were being used, if average resting blood pressure was >160/95 mm Hg, if abnormalities existed in a baseline 12 lead ECG, if fasting blood TG concentrations were >5.6 mmol.L ⁻¹ , if fasting total blood cholesterol was >7.8 mmol.L ⁻¹ , or if body weight was >140% ideal body weight. Power: Not specified. Method of randomisation: Subjects assigned to a standard caffeinated coffee, and two months later, baseline tests were performed. Subjects then randomized to one of three groups: continued standard caffeinated coffee consumption, decaffeinated coffee consumption, or no coffee consumption. Intervention: Subjects assigned to coffee dose that reflected their pre-study intake. Blinding: Double blind. Length of follow -up: 8 weeks. Completeness of follow -up: 97% follow -up.																																	
Validity	Is the study type appropriate for the question being asked? Yes. Was the study population typical of patients with this disease? No, much healthier. Were the treatment/control groups comparable at baseline? Yes. Was the intervention compared to placebo and/or best - accepted intervention? Yes, standard caffeinated coffee consumption used as the control or comparison. Was there compliance with the intervention? One subject could not complete the randomized phase owing to an inability to tolerate caffeinated coffee withdrawal symptoms. Was there equal intensity of observation of study and control subjects? Yes. Was the process of observation likely to effect the outcome? In decaffeinated group withdrawal symptoms may affect outcomes. One subject could not complete randomized phase because of this. Intention to treat analysis? Yes. Did conclusions about safety take into account the limited size of the study? No. Is effectiveness proven? Yes. Summary: Typically a much healthier population than those requiring lowering of blood lipids.																																	
Results	Quantified results: In comparison with the caffeinated coffee group; <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th></th> <th>Decaffeinated Coffee (n = 61)</th> <th>No Coffee (n = 58)</th> </tr> </thead> <tbody> <tr> <td>TG (mmol.L⁻¹)</td> <td>0.03 ± 0.045</td> <td>-0.01 ± 0.44</td> </tr> <tr> <td>Total cholesterol (mmol.L⁻¹)</td> <td>0.01 ± 0.70</td> <td>-0.11 ± 0.54</td> </tr> <tr> <td>LDL-C (mmol.L⁻¹)</td> <td>0.12 ± 0.65⁺</td> <td>-0.11 ± 0.52</td> </tr> <tr> <td>HDL-C (mmol.L⁻¹)</td> <td>0.01 ± 0.16</td> <td>-0.02 ± 0.18</td> </tr> <tr> <td>Apo A-I (g.L⁻¹)</td> <td>0.02 ± 0.15</td> <td>0.00 ± 0.12</td> </tr> <tr> <td>Apo B (by NIA) (g.L⁻¹)</td> <td>0.06 ± 0.12[☆]</td> <td>0.01 ± 0.08</td> </tr> <tr> <td>Apo B (by RIA)</td> <td>0.06 ± 0.24⁺</td> <td>-0.02 ± 0.16</td> </tr> <tr> <td>Heart rate (bpm)</td> <td>0.90 ± 8.2</td> <td>-0.50 ± 5.8</td> </tr> <tr> <td>SBP (mm Hg)</td> <td>-2.50 ± 8.8</td> <td>-1.10 ± 7.7</td> </tr> <tr> <td>DBP (mm Hg)</td> <td>-0.60 ± 6.1</td> <td>-1.50 ± 6.3</td> </tr> </tbody> </table> <p>⁺ p < 0.025 [☆] p < 0.0004</p>		Decaffeinated Coffee (n = 61)	No Coffee (n = 58)	TG (mmol.L ⁻¹)	0.03 ± 0.045	-0.01 ± 0.44	Total cholesterol (mmol.L ⁻¹)	0.01 ± 0.70	-0.11 ± 0.54	LDL-C (mmol.L ⁻¹)	0.12 ± 0.65 ⁺	-0.11 ± 0.52	HDL-C (mmol.L ⁻¹)	0.01 ± 0.16	-0.02 ± 0.18	Apo A-I (g.L ⁻¹)	0.02 ± 0.15	0.00 ± 0.12	Apo B (by NIA) (g.L ⁻¹)	0.06 ± 0.12 [☆]	0.01 ± 0.08	Apo B (by RIA)	0.06 ± 0.24 ⁺	-0.02 ± 0.16	Heart rate (bpm)	0.90 ± 8.2	-0.50 ± 5.8	SBP (mm Hg)	-2.50 ± 8.8	-1.10 ± 7.7	DBP (mm Hg)	-0.60 ± 6.1	-1.50 ± 6.3
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Authors' Conclusions	"This finding suggests that a coffee component other than caffeine is responsible for the LDL-C, apolipoprotein B, and lipase activity changes reported in this investigation".																																	
Reviewers' Conclusions	Agree with authors' conclusions, valid within this population.																																	

Evidence Table 5: Effects of caffeine consumption on blood pressure

Key Words: Coffee, caffeine, blood pressure, normotensive

Reference: Superko HR, Myll J, DiRicco C et al. Effects of cessation of caffeinated-coffee consumption on ambulatory and resting blood pressure in men. *Am J Cardiol* 1994; 73: 780-8433.

Study Type/Grade	Randomized Controlled Trial Grade A																											
Outcomes	Primary: Changes in resting and ambulatory blood pressure. Secondary: Changes in resting heart rate.																											
Design	N= 186. Relevant risk factors: None present. Inclusion and exclusion criteria: Non-smoking, male, coffee drinkers were recruited on the basis of a history of consuming 3-6 cups of caffeinated coffee per day. Subjects were excluded if they smoked cigarettes, if a major medical problem existed, if lipid-lowering medications were being used, if average resting blood pressure was >160/95 mm Hg, if abnormalities existed in a baseline 12 lead ECG, if fasting blood TG concentrations were >5.6 mmol.L ⁻¹ , if fasting total blood cholesterol was >7.8 mmol.L ⁻¹ , or if body weight was >140% ideal body weight. Power: Not specified. Method of randomisation: Subjects assigned to a standard caffeinated coffee, and two months later, baseline tests were performed. Subjects then randomized to one of three groups: continued standard caffeinated coffee consumption, decaffeinated coffee consumption, or no coffee consumption. Intervention: Subjects assigned to coffee dose that reflected their pre-study intake. Blinding: Double blind. Length of follow -up: 8 weeks. Completeness of follow -up: 81% follow -up.																											
Validity	Is the study type appropriate for the question being asked? Yes. Was the study population typical of patients with this disease? No, much healthier. Were the treatment/control groups comparable at baseline? Yes. Was the intervention compared to placebo and/or best - accepted intervention? Yes, standard caffeinated coffee consumption used as the control or comparison. Was there compliance with the intervention? One subject could not complete the randomized phase owing to an inability to tolerate caffeinated coffee withdrawal symptoms. Was there equal intensity of observation of study and control subjects? Yes. Was the process of observation likely to effect the outcome? In decaffeinated group withdrawal symptoms may affect outcomes. One subject could not complete randomized phase because of this. Intention to treat analysis? Yes. Did conclusions about safety take into account the limited size of the study? No. Is effectiveness proven? Yes. Summary: 19% lost to follow -up which may affect study outcome. Typically a much healthier population than those requiring blood pressure reduction.																											
Results	Quantified results: In comparison with the caffeinated coffee group <table border="1" style="margin-left: 40px;"> <thead> <tr> <th></th> <th>Decaffeinated Coffee (n = 51)</th> <th>No Coffee (n = 47)</th> </tr> </thead> <tbody> <tr> <td>SBP resting</td> <td>NS</td> <td>NS</td> </tr> <tr> <td>SBP (0900-1200)</td> <td>-4.0 ± 11; p = 0.014</td> <td>-4.1 ± 9; p = 0.007</td> </tr> <tr> <td>SBP (1200-1500)</td> <td>-5.3 ± 10; p = 0.001</td> <td>-3.3 ± 10; p = 0.023</td> </tr> <tr> <td>SBP (1500-1800)</td> <td>-3.2 ± 10; p = 0.003</td> <td>-2.2 ± 11; p = 0.015</td> </tr> <tr> <td>DBP resting</td> <td>NS</td> <td>NS</td> </tr> <tr> <td>DBP (0900-1200)</td> <td>NS</td> <td>NS</td> </tr> <tr> <td>DBP (1200-1500)</td> <td>-1.8 ± 10; p = 0.063</td> <td>-2.6 ± 6; p = 0.006</td> </tr> <tr> <td>DBP (1500-1800)</td> <td>-1.8 ± 10; p = 0.059</td> <td>-2.1 ± 6; p = 0.016</td> </tr> </tbody> </table> No significant changes were reported in resting or ambulatory heart rate		Decaffeinated Coffee (n = 51)	No Coffee (n = 47)	SBP resting	NS	NS	SBP (0900-1200)	-4.0 ± 11; p = 0.014	-4.1 ± 9; p = 0.007	SBP (1200-1500)	-5.3 ± 10; p = 0.001	-3.3 ± 10; p = 0.023	SBP (1500-1800)	-3.2 ± 10; p = 0.003	-2.2 ± 11; p = 0.015	DBP resting	NS	NS	DBP (0900-1200)	NS	NS	DBP (1200-1500)	-1.8 ± 10; p = 0.063	-2.6 ± 6; p = 0.006	DBP (1500-1800)	-1.8 ± 10; p = 0.059	-2.1 ± 6; p = 0.016
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Authors' Conclusions	"Cessation of caffeinated coffee consumption results in significant reductions in ambulatory systolic and diastolic blood pressure in normotensive men, which is not apparent from resting blood pressure measurements".																											
Reviewers' Conclusions	Agree with authors' conclusion, although this was a very healthy population. No extrapolation could be made to those with elevated blood pressure.																											

abbreviations

AHA	American Heart Association
ATBC	Alpha Tocopherol, Beta Carotene Cancer Prevention Study
BMI	Body Mass Index
CARE	Cholesterol and Recurrent Events Trial
CARET	Beta Carotene and Retinol Efficacy Trial
CCPT	Chicago Coronary Prevention Trial
CHAOS	Cambridge Heart Antioxidant Study
CHO	Carbohydrate
CHD	Coronary Heart Disease
CI	Confidence Interval
CVD	Cardiovascular Disease
DART	Diet and Reinfarction Trial
DASH	Dietary Approaches to Stop Hypertension
DBP	Diastolic Blood Pressure
DHA	Docosahexenoic Acid
DNSBA	Dietary and Nutrition Survey of British Adults
EPA	Eicosapentenoic Acid
EURAMIC	European Antioxidant Myocardial Infarction and Breast Cancer
GI	Glycaemic Index
HDL-C	High Density Lipoprotein Cholesterol
INTERSALT	International Study of SALT
LED	Low Energy Diet
LDL-C	Low Density Lipoprotein Cholesterol
LNA	Alpha Linolenic Acid
Lp (a)	Lipoprotein (a)
LRC-CPPT	Lipid Research Clinic Coronary Primary Prevention Trial
MEDLINE	Medical Literature Analysis and Retrieval System Online
MeSH	Medical Subject Heading
MI	Myocardial Infarction
MONICA	Monitoring of Trends and Determinants in Cardiovascular Disease
MRFIT	Multiple Risk Factor Intervention Trial
MUFA	Monounsaturated Fat
NAS	Normative Aging Study
NCEP	National Cholesterol Education Program

NHANES	National Health and Nutrition Examination Survey
NHLBI	National Heart, Lung and Blood Institute
NSP	Non-Starch Polysaccharide
NZ	New Zealand
NZDA	New Zealand Dietetic Association
OPPT	Oslo Primary Prevention Trial
PTCA	Percutaneous Transluminal Coronary Angioplasty
PUFA	Polyunsaturated Fat
RDA	Recommended Daily Allowance
RCT	Randomized Controlled Trial
4S	Scandinavian Simvastatin Survival Study
SBP	Systolic Blood Pressure
SFA	Saturated Fat
STARS	St Thomas' Atherosclerosis Regression Study
TG	Triglyceride
tHcy	Total Homocysteine
TOHP	Trials of Hypertension Prevention
TONE	Trial of Nonpharmacologic Interventions in the Elderly
USDA	United States Department of Agriculture
UK	United Kingdom
US	United States of America
VLED	Very Low Energy Diet
VLDL-C	Very Low Density Lipoprotein Cholesterol
WC	Waist Circumference
WHO	World Health Organisation
WHR	Waist to Hip Ratio
WOSCOPS	West of Scotland Coronary Prevention Study

references

1. Thelle DS, Arnesen E and Forde OH. The Tromso heart study: Does coffee raise serum cholesterol? *N Engl J Med* 1983; 308: 1454-57.
2. Kark JD, Friedlander Y, Kaufman NA et al. Coffee, tea and plasma cholesterol: The Jerusalem lipid research clinic prevalence study. *BMJ* 1985; 291: 699-703.
3. Curb JD, Reed DM, Kautz JA et al. Coffee, caffeine and serum cholesterol in Japanese men in Hawaii. *Am J Epidemiol* 1986; 123: 648-55.
4. LaCroix AZ, Mead LA, Liang K et al. Coffee consumption and the incidence of coronary heart disease. *N Engl J Med* 1986; 315 (16): 977-82.
5. Tverdal A, Stensvold I, Solvoll K, Foss OP et al. Coffee consumption and death from coronary heart disease in middle-aged Norwegian men and women. *BMJ* 1990; 300: 566-69.
6. Haffner SM, Knapp JA, Stern MP et al. Coffee consumption, diet and lipids. *Am J Epidemiol* 1985; 122: 1-12.
7. Kawachi I, Colditz GA and Stone CB. Does coffee-drinking increase the risk of coronary heart disease? Results from a meta-analysis. *Br Heart J* 1994; 72: 269-71.
8. Grobbee DE, Rimm EB, Giovannucci et al. Coffee, caffeine and cardiovascular disease in men. *N Engl J Med* 1990; 323: 1026-32.
9. Willet WC, Stampfer MJ, Manson JE et al. Coffee consumption and coronary heart disease in women. A ten-year follow-up. *JAMA* 1996; 275(6): 458-62.
10. Greenland S. A meta-analysis of coffee, myocardial infarction, and coronary death. *Epidemiology* 1993; 4: 366-74.
11. Hennekens CH, Drolette MJ, Jesse MJ et al. Coffee-drinking and death due to coronary heart disease. *N Engl J Med* 1976; 294: 633-36.
12. Zock PL, Katan MB, Merkus MP et al. Effect of a lipid-rich fraction from boiled coffee on serum cholesterol. *Lancet* 1990; 335: 1235-37.
13. Bak AA and Grobbee DE. The effect on serum cholesterol levels of coffee brewed by filtering or boiling. *N Engl J Med* 1989; 321: 1432-37.
14. Aro A, Teirila J and Gref CG. Dose-dependent effect on serum cholesterol and apoprotein B concentrations by consumption of boiled, non-filtered coffee. *Atherosclerosis* 1990; 83: 257-61.
15. Urgert R, Meyboom S, Kuilman M et al. Comparison of effect of cafetiere and filtered coffee on serum concentrations of liver aminotransferases and lipids: six-month, randomized, controlled trial. *BMJ* 1996; 313: 1362-66.
16. Aro A, Tuomilehto J, Kostianen E et al. Boiled coffee increase serum low-density lipoprotein concentration. *Metabolism* 1987; 36(11): 1027-30.
17. Lindahl B, Johansson I, Huhtasaari F et al. Coffee-drinking and blood-cholesterol-effects of brewing method, food intake and lifestyle. *J Intern Med* 1991; 230: 299-305.
18. Pietinen P, Aro A, Tuomilehto J et al. Consumption of boiled coffee is correlated with serum cholesterol in Finland. *Int J Epidemiology* 1990; 19(3): 586-90.
19. Bonna K, Arnesen E, Steinar D et al. Coffee and cholesterol: Is it all in the brewing? The Tromso study. *BMJ* 1988; 297: 1103-04.
20. Gross G, Jaccaud E and Huggett AC. Analysis of the content of the diterpenes cafestol and kahweol in coffee brews. *Food Chem Toxicol* 1997; 35(6): 547-54.

21. Halvorsen B, Ranheim T, Nenseter MS et al. Effect of a coffee lipid on cholesterol metabolism in human skin fibroblasts. *J Lipid Res* 1998; 39: 901-12.
22. Post SM, de Wit EC and Princen HM. Cafestol, the cholesterol-raising factor in boiled coffee, suppresses bile acid synthesis by downregulation of cholesterol 7 alpha-hydroxylase and sterol 27-hydroxylase in rat hepatocytes. *Arterioscler Thromb Vasc Biol* 1997; 17(11): 3064-70.
23. Urgert R, Van der Weg G, Kosmeijer-Schuil et al. Levels of the cholesterol-elevating diterpenes cafestol and kahweol in various coffee brews. *J Agric Food Chem* 1995; 43: 2167-72.
24. Weusten-van der Wouw MPME, Katan MB, Viani R et al. Identity of the cholesterol-raising factor from boiled coffee and its effects on the liver function enzymes. *J Lipid Res* 1994; 35: 721-33.
25. van Dusseldorp M, Katan MB, van Vliet T et al. Cholesterol-raising factor from boiled coffee does not pass a paper filter. *Arterioscler and Thromb* 1991; 11(3): 586-93.
26. Ahola I, Jauhiainen M and Aro A. The hypercholesterolaemic factor in boiled coffee is retained by a paper filter. *J Intern Med* 1991; 230(4): 293-97.
27. Superko HR, Bortz W, Williams PT et al. Caffeinated and decaffeinated coffee effects on plasma lipoprotein cholesterol, apolipoproteins, and lipase activity: A controlled, randomized trial. *Am J Clin Nutr* 1991; 54(3): 599-605.
28. van Dusseldorp M, Katan MB and Demacker PN. Effect of decaffeinated versus regular coffee on serum lipoproteins. A 12-week, double-blind trial. *Am J Epidemiol* 1990; 132(1): 33-40.
29. Burr ML, Gallacher JE, Butland BK et al. Coffee, blood pressure and plasma lipids: A randomized, controlled trial. *Eur J Clin Nutr* 1989; 43(7): 477-83.
30. Bak AA and Grobbee DE. Caffeine, blood pressure and serum lipids. *Am J Clin Nutr* 1991; 53(4): 971-75.
31. Wahrburg U, Martin H, Walek T et al. Effects of two kinds of decaffeinated coffee on serum lipid profiles in healthy young adults. *Eur J Clin Nutr* 1994; 48: 172-79.
32. van Dusseldorp M, Smits P, Thien T et al. Effect of decaffeinated versus regular coffee on blood pressure. A twelve-week, double blind trial. *Hypertension* 1989; 14: 563-69.
33. Superko R, Myll J, Di Ricco et al. Effects of cessation of caffeinated, coffee consumption on ambulatory and resting blood pressure in men. *Am J Cardiol* 1994; 73: 780-84.
34. MacDonald TM, Sharpe K, Fowler G et al. Caffeine restriction: effect on mild hypertension. *BMJ* 1991; 303: 1235-38.
35. Green PJ and Suls J. The effects of caffeine on ambulatory blood pressure, heart rate, and mood in coffee drinkers. *J Behav Med* 1996; 19(2): 111-28.
36. Eggertsen R, Andreasson A, Hendner T et al. Effect of coffee on ambulatory blood pressure in patients with hypertension. *J Intern Med* 1993; 233(4): 351-55.
37. Goldstein IB, Shapiro D, Hui KK et al. Blood pressure response to the 'second cup of coffee'. *Psychosom Med* 1990; 52(3): 337-45.
38. Lane JD and Manus DC. Persistent cardiovascular effects with repeated caffeine administration. *Psychosom Med* 1989; 51: 373-80.
39. Smits P, Thien T and van't Laar A. Circulatory effects of coffee in relation to the pharmacokinetics of caffeine. *Am J Cardiol* 1985; 56: 958-63.
40. Myers MG, Harris L, Leenen FH et al. Caffeine as a possible cause of ventricular arrhythmias during the healing phase of acute myocardial infarction. *Am J Cardiol* 1987; 59(12): 1024-28.
41. Myers MG and Harris L. High-dose caffeine and ventricular arrhythmias. *Can J Cardiol* 1990; 6(3): 95-98.

42. Newby DE, Neilson JMM, Jarvie DR et al. Caffeine restriction has no role in the management of patients with symptomatic, idiopathic, ventricular, premature beats. *Heart* 1996; 76: 355-57.
43. Donnerstein RL, Zhu D, Samson R, et al. Acute effects of caffeine ingestion on signal-averaged electrocardiograms. *Am Heart J* 1998; 136(4 Pt 1): 643-46.
44. Chelsky LB, Cutler JE, Griffith K et al. Caffeine and ventricular arrhythmias: An electrophysiological approach. *JAMA* 1990; 264(17): 2236-40.
45. Griffiths RR and Woodson PP. Caffeine physical dependence: A review of human and laboratory studies. *Psychopharmacology* 1988; 94: 437-51.
46. Greden JF, Victor BS, Fontaine P et al. Caffeine-withdrawal headache: A clinical profile. *Psychomatics* 1980; 21: 411-18.
47. Silverman K, Evans SM, Strain EC et al. Withdrawal syndrome after the double-blind cessation of caffeine consumption. *N Engl J Med* 1992; 327: 1109-14.
48. Griffiths RR, Evans SM, Heishmann SJ et al. Low-dose caffeine physical dependence in humans. *J Pharmacol Exp Ther* 1990; 255: 1123-32.
49. von Borstel RW, Wurtman RJ, Conlay LA. Chronic caffeine consumption potentiates the hypotensive action of circulating adenosine. *Life Sci* 1983; 32: 1151-58.
50. Mathew RJ, Wilson WH. Caffeine-induced changes in cerebral circulation. *Stroke* 1985; 16: 814-17.
51. Pearce J. Nutritional analysis of fluid-replacement beverages. *Aust J Nutr Diet* 1996; 53(4 Suppl): S35-S42.