

REVIEW

A systematic review and meta-analysis of elevated blood pressure and consumption of dairy foods

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Hypertension is a public health priority in developed countries and worldwide, and is strongly associated with increased risk and progression of cardiovascular and renal diseases. A systematic review and meta-analysis were conducted to examine the association between dairy food intake during adulthood and the development of elevated blood pressure (EBP), specifically comparing the association of EBP with consumption of low-fat dairy foods versus high-fat dairy foods, as well as cheese versus fluid dairy foods (milk or yogurt). Seven databases were searched and five cohort studies selected for inclusion, involving nearly 45 000 subjects and 11 500 cases of EBP. Meta-analysis of consumption of dairy foods and EBP in adults gave a relative risk (RR) of 0.87 (95% confidence interval (CI)

0.81–0.94). Separation of high- and low-fat dairy foods, however, indicated a significant association with low-fat dairy foods only (RR of 0.84 (95% CI 0.74–0.95)). Additional analyses showed no association between EBP and cheese, although fluid dairy foods were significantly associated with a reduced development in EBP (RR of 0.92 (95% CI 0.87–0.98)). Little heterogeneity was observed among the data presented. This meta-analysis supports the inverse association between low-fat dairy foods and fluid dairy foods and risk of EBP. Understanding these relationships can aid in the development of public health messages involving dairy foods, and supports current recommendations.

Journal of Human Hypertension (2012) 26, 3–13; doi:10.1038/jhh.2011.3; published online 10 February 2011

Keywords: blood pressure; cheese; dairy products; milk; yogurt

Introduction

With 29% of the world's adult population projected to develop hypertension by 2025, both prevention and management of hypertension has become a public health priority.¹ In the US, in 2003–2006, 32% of non-institutionalised adults (20 years and older) had hypertension,² whereas in Australia approximately one-third of those aged over 25 years in 1999–2000 had hypertension or were receiving anti-hypertensive medication.³ Hypertension is strongly associated with increased risk and progression of cardiovascular and renal diseases,^{4–6} including stroke, coronary heart disease, heart failure and kidney failure.^{4,6} As the mortality risk of cardiovascular disease amplifies across the range of blood pressure (BP), attempts to decrease BP to the normal range are well justified even among pre-hypertensive individuals.⁷

Hypertension can be attributed to genetic and environmental factors, as well as to interactions among these determinants.^{5–6} Diet is the strongest environmental factor influencing BP, with reduced salt intake, increased potassium intake and reduced alcohol intake having the largest impact.⁶ The Dietary Approaches to Stop Hypertension trial demonstrated that a dietary pattern abundant in fruits, vegetables and low-fat dairy products, in the context of a reduced intake of total and saturated fat, can considerably reduce BP in both normotensive and hypertensive individuals, without concomitant sodium reduction or weight loss.⁸ Notably, this diet, which includes dairy products, elicited a more pronounced BP-lowering effect than a diet rich in fruits and vegetables alone.⁸ This highlights the potential role of dairy products in prevention and/or treatment of hypertension.

Despite this, previous research examining associations between dairy consumption and BP has shown inconsistent relationships.^{9–18} A few cross-sectional studies first indicated that dairy intake might be inversely associated with the risk of hypertension,^{11,14,15} independent of calcium intake.^{11,14} Although supported by data emerging from some prospective studies,^{9,13,17,18} here it was unclear

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Received 20 August 2010; revised 6 December 2010; accepted 10 December 2010; published online 10 February 2011

whether the reported BP-lowering effect was because of consumption of the dairy food itself or because of nutrient components such as calcium that might readily be supplied from alternate food sources.¹⁵ Furthermore, several other studies have found no significant association between dairy intake and BP.^{10,12,16}

The purpose of this systematic review and meta-analysis was therefore to examine the association between dairy food intake during adulthood and the development of elevated blood pressure (EBP). In particular, comparisons are made between the effects of low-fat dairy foods versus high-fat dairy foods, as well as between solid dairy food (cheese) versus liquid foods (milk or yogurt). To our knowledge, this is the first systematic review and meta-analysis making these comparisons. Understanding these relationships can aid in the development of public health messages to the public, and provide an evidence base for those who provide dietary advice to members of the public. The American Heart Association and the Dietary Guidelines for Americans both recommend including 2–3 servings of non-fat or low-fat dairy products per day.^{19,20}

Methods

This systematic review to examine the relationship between dairy products and varied health outcomes was a part of the Australian Dietary Guidelines systematic literature review, which was commissioned by the Australian National Health and Medical Research Council. The Dietary Guidelines Working Committee of the Australian National Health and Medical Research Council approved the initial search criteria. Seven databases (Cinahl, Medline, PreMedline, PsycInfo, Cochrane/Database of Abstracts of Reviews of Effects, ScienceDirect and Educational Resources Information Center) were searched in April 2009, applying the following limits: published from January 2002 to April 2009, written in English and undertaken in human subjects. Although the original search included all keywords relating to the principal project, keywords limited to dairy and hypertension are listed in Table 1. As also shown in the table, an additional search of the PubMed database was conducted in November 2009 to recover studies published since 1980. No attempt was made to recover unpublished studies.

Abstracts recovered from searches undertaken in April and November 2009 were reviewed. The full article was retrieved for all studies investigating the effect of dairy food consumption on EBP or hypertension in adults. Studies on subjects with any acute or chronic medical condition and studies on elite athletes were excluded. Studies examining cow's, goat's or sheep's milk, skim, low-fat, or full-fat milk, yogurt, cheese and custard were included, whereas studies examining ice confections, ice creams, cream, sour cream, butter or eggs were excluded.

Table 1 Databases and search terms used for this systematic review on the effects of dairy food consumption on protection against elevated blood pressure

| Database | Search terms |
|---|--|
| <i>Initial search in April 2009, searched from 2002</i> | |
| Cinahl | Hypertension and milk, cheese or custard |
| Medline | Hypertension and milk, goat's milk, sheep's milk, cheese, yogurt, low-fat milk, skim milk, full-fat milk or custard |
| Premedline | Hypertension and goat's milk, sheep's milk, yogurt, cheese, custard, full-fat milk, skim milk, reduced-fat milk, full-cream milk or low-fat milk |
| Psycinfo | Hypertension and cheese, yogurt, custard, skim milk, reduced-fat milk, low-fat milk, full-cream milk, full-fat milk, sheep's milk, cow's milk or goat's milk |
| Cochrane/Database of Abstracts of Reviews of Effects (DARE) | Cow's milk, goat's milk, sheep's milk, skim milk, full-fat milk, full-cream milk, milk, reduced-fat milk, low-fat milk, yogurt, cheese or custard |
| Sciencedirect | Hypertension and milk, skim milk, cow's milk, goat's milk, sheep's milk, full-cream milk, reduced-fat milk, low-fat milk, yogurt, cheese or custard |
| Educational Resources Information Center (ERIC) | Hypertension and cow's milk, sheep's milk, goat's milk, skim milk, low-fat milk, reduced-fat milk, full-cream milk, cheese, yogurt or custard |
| <i>Additional search in November 2009, searched from 1980</i> | |
| Pubmed | Hypertension and milk, goat's milk, sheep's milk, cheese, yogurt, low-fat milk, skim milk, full-fat milk or custard |

Studies examining specific casein proteins (A1 and A2 milks), or milks with added supplements (such as conjugated linoleic acid) were also excluded. Only studies providing level I or II evidence were considered for inclusion. Level I evidence was defined as a systematic review of level II evidence, whereas level II evidence consisted of well-designed, randomised controlled trials or prospective cohort studies.²¹ Only prospective cohort studies with numbers greater than 1000 subjects and with a follow-up period of at least 1 year were considered. All editorials, abstracts, commentaries, case series, cross-sectional studies, case-control studies and retrospective cohort studies were excluded.²¹ Codes were used to record study inclusion or exclusion and the reason for exclusion (that is, not a study, not a relevant population, not a relevant outcome or low level of evidence).

Retrieved studies considered suitable for inclusion were read carefully by two investigators (RR and JL). Extracted data included: author affiliation

Table 2 Questions used to assess the quality of cohort studies²²*Questions^a*

1. Was the research question clearly stated?
2. Was the selection of study subjects/patients free from bias?
3. Were dependent and independent variables and comparison(s) described in detail? Were intervening factors described?
4. Were outcomes clearly defined and the measurements valid and reliable?
5. Were subjects lost to follow-up considered and described?
6. Was the statistical analysis appropriate for the study design and type of outcome indicators? Were models adjusted for appropriate confounding factors?
7. Were conclusions supported by results with biases and limitations taken into consideration?
8. Is bias due to study's funding or sponsorship unlikely?

^aA positive rating was given if yes was answered to questions 2, 3 and 4, and to at least two of questions 1, 5, 6 and 7. A neutral rating was given if yes was answered to only two of questions 2, 3 and 4, and to at least two of questions 1, 5, 6 and 7. A negative rating was given if yes was answered to only three of the questions.

and financial support, study design and setting, type of study intervention, sample size and number of incident cases, characteristics of the study population, dairy food type and amount, outcomes measured and length of follow-up. Internal validity was assessed by examining treatment or measurement bias and the proportion of participants retained during follow-up. The quality of each study was assessed as negative, neutral, or positive using the questions listed in Table 2. The initial quality criteria were extracted from the American Dietetic Association Evidence Analysis Manual.²² Control of potential confounders (age, sex, smoking status, socioeconomic status, physical activity, body mass index, energy intake and other diet components, alcohol consumption, ethnicity and nutritional supplement use) was also noted,²³ but control of these potential confounders was not a requirement for inclusion in the meta-analysis.

Reference lists of Level I and II studies retrieved from our search criteria were also examined to further identify studies not retrieved by our searches. Individual cohort studies recovered in this manner were included in the current review if they met the above inclusion criteria. A list of all located citations can be obtained upon request from the authors.

Statistical methods

The association between EBP and intake of total dairy, low- and high-fat dairy, cheese (hard cheese, soft cheese and cheese spreads) and fluid dairy food (milk and yogurt) was examined using meta-analysis. Studies were not included if they examined only calcium or vitamin D intake rather than dairy food intake, and were not included if they reported only BP and not incidence of EBP or hypertension. EBP was defined as systolic BP (SBP)

≥ 130 mm Hg and/or diastolic BP (DBP) ≥ 85 mm Hg, or use of medications prescribed by a physician to lower BP.^{24,25} In contrast, hypertension is defined as SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg or use of medications prescribed by a physician to lower BP.²⁵

The statistical measure for risk of developing EBP was recorded for each individual study, comparing the highest versus the lowest category of dairy food intake. Five separate meta-analyses were conducted for the association of total dairy foods, low- and high-fat dairy foods, cheese and fluid dairy foods, with development of EBP. Allocation of foods into the low- and high-fat categories was completed by the original study authors and varied among studies. Only two studies^{12,26} defined low- and high-fat dairy foods in relation to total fat content; low-fat dairy: milk and milk products with <2.0 g fat per 100g, cheese products with <20 g fat per 100g; high-fat dairy: milk and milk products with >3.5 g fat per 100g, cheese products with >20 g fat per 100g. Another two studies^{9,18} merely outlined foods within the categories; low-fat dairy comprising skim or low-fat milk, yogurt, or cheese; high-fat dairy comprising full-fat milk, yogurt or cheese. Foods included in low- and high-fat dairy are unique from each other, as are foods in the cheese and fluid dairy categories. Two studies included risk statistics separately for milk and yogurt,^{16,18} in each case, both these values were included in the meta-analysis. Analysis of total dairy foods is not a sum of subcategories, but is an analysis of total dairy foods, as reported by the original study authors.

Summary statistics for overall RRs were generated with Review Manager Version 5.0.24 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark), using the generic inverse variance method and the random effects model. In meta-analysis, the weight of an individual study is based on the inverse variance of the effect estimate, meaning a study with a smaller confidence interval (CI) has a larger weight in the calculation of the summary statistic. This is observed in studies with a larger sample size.²⁷ If an individual study reported a CI that was asymmetrical around the mean, the widest CI was used to calculate the summary statistic. Three studies reported hazard ratios, one study reported relative risk (RR), and one study reported odds ratio (OR). As hazard ratios assess change in risk over time, they can be reported as RRs.²⁸ ORs and RRs also approximate when the OR is within 20% of 1.0 (in which 1.0 indicates no effect).²⁹ As the largest OR used here was 1.19; ORs and RRs have been treated as equivalent in our meta-analyses. RRs with 95% CI and corresponding *P*-values are reported. Heterogeneity between studies within subgroups was examined first qualitatively, then quantitatively by using the *I*² statistic, chosen because it does not depend upon the number of studies in the analysis.^{30,31} Low, moderate and high heterogeneity was defined by an *I*² value of <25, <50 and <75%, respectively.³¹

Results

Figure 1 illustrates the progression of study selection for the meta-analysis. From the initial search of seven databases in April 2009, seven studies were retrieved on the topic of EBP. Five studies provided only low-level evidence, whereas two met the criteria for inclusion in the present review. An additional search of PubMed in November 2009 resulted in 138 citations: two had already been retrieved by the earlier search, 111 met exclusion criteria (described above) and 25 appeared relevant. Of these 25, 9 provided only low-level evidence. Of the remaining 16, 6 were randomised controlled trials, 4 were systematic reviews and 6 were cohort studies. Upon further examination of all retrieved studies, all randomised controlled trials and three cohort studies were excluded. An appraisal of studies reported within the four systematic reviews revealed one additional cohort study that met inclusion criteria. This additional study used the same cohort as one of the studies identified in the April 2009 search, but reported data on the complete cohort rather than only on the overweight participants; thus the study reporting on the overweight participants only was excluded. Overall, we identified a total of five cohorts to be included in our final meta-analysis.

A summary of the five studies included in the meta-analysis is shown in Tables 3 and 4. These studies include nearly 45 000 subjects (15% men, 85% women) from the United States, Spain and the Netherlands, with over 11 500 cases of EBP. Length of follow-up ranged from 2 to 15 years. Intakes in the highest intake category ranged from 691 to 757 g and 3.4–3.7 servings of total dairy per day, 507–615 g of low-fat dairy per day, 166–272 g of high-fat dairy per day, 0.5–2.7 servings of fluid dairy per day and 0.7–2.1 servings of cheese per day. Standard serving sizes vary among countries; to assist data interpretation, Table 5 compares standard serving sizes for the United States, Canada, Australia and for the United Kingdom.

The results of meta-analysis of the published data examining total dairy, low- and high-fat dairy, cheese and fluid dairy (milk and yogurt) are shown in Figure 2. Consumption of total dairy foods for the highest compared with the lowest intake category was associated with a significantly reduced risk of EBP: meta-analysis of five studies^{9,12,16,18,26} resulted in a RR of 0.87 (95% CI 0.81–0.94). Examination of the four studies^{9,12,18,26} that reported consumption of high- and low-fat dairy food showed a significant association for low-fat dairy only. Meta-analysis resulted in an overall RR of 0.84 (95% CI 0.74–0.95) in subjects consuming high amounts of low-fat dairy foods. Overall the RR in subjects consuming high amounts of high-fat dairy foods was 1.00 (95% CI 0.89–1.11).

Four studies examined specific categories of dairy foods.^{12,16,18,26} Between cheese and fluid dairy food, only fluid dairy food was significantly associated with a reduction in the development of EBP. Meta-analysis of these four studies resulted in an overall RR of 0.92 (95% CI 0.87–0.98) in subjects consuming high amounts of fluid dairy foods. Of the two studies that reported two risk estimates for fluid dairy foods (milk and yogurt), the meta-analysis results were similar when only the risk estimates for milk were used. Conversely, the overall RR was 1.00 (95% CI 0.89–1.12) in subjects with a high consumption of cheese. Little heterogeneity was observed among the data presented, indicating that meta-analysis was acceptable (Figure 2). Heterogeneity using the I^2 statistic was calculated as 0% for total dairy and fluid dairy and as 11% for cheese (levels accepted as 'low'), but calculated as 38% for low-fat dairy and 27% for high-fat dairy, indicating 'moderate' heterogeneity for these two analyses.³¹

Discussion

This analysis showed that consumption of total dairy foods was associated with a 13% reduction in

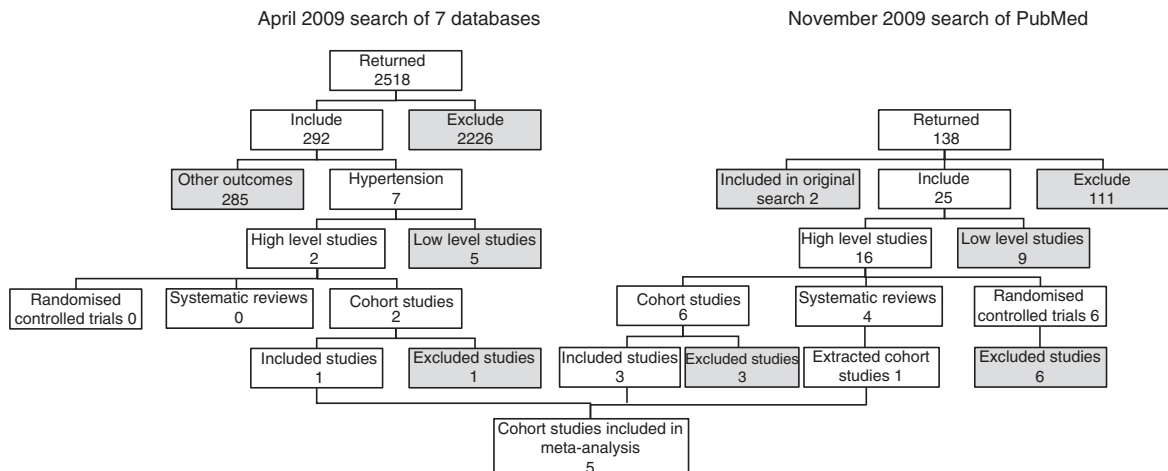


Figure 1 Flow diagram depicting selection of studies to be included in final review.

Table 3 Characteristics of cohort studies included in meta-analysis examining total dairy food, low-fat dairy foods and high-fat dairy foods

| Published study | Study cohort and characteristics (age in years) | Length of follow-up (years) | Intake | Size of cohort | Number of cases | Outcome | Measure of effect size (95% CI) | P _{trend} | Quality |
|----------------------------------|---|-----------------------------|----------------------------------|----------------|-----------------|------------------------------------|---------------------------------|--------------------|---------|
| <i>Total dairy foods</i> | | | | | | | | | |
| Alonso 2005 ^{9, a} | Spain: SUN, 39% male, age 20–90 | 2 | Quintile 5 vs 1 | 5880 | 180 | HR for hypertension | 0.75 (0.45–1.27) | 0.12 | 0 |
| Engberink 2009a ^{26, b} | The Netherlands: MORGEN, 45% male, age 20–65 | 5 | 757 g vs 206 g per day | 3454 | 713 | OR for hypertension | 1.11 (0.85–1.44) | 0.60 | P |
| Engberink 2009b ^{12, c} | The Netherlands: Rotterdam Study, 43% male, age > 55 | 6 | 691 g vs 164 g per day | 2245 | 984 | HR for hypertension | 0.84 (0.70–1.01) | 0.09 | P |
| Steffen 2005 ^{16, d} | US: CARDIA, 43% male, 49% African American, age 18–30 | 15 | > 3.4 vs < 1.1 servings per day | 4304 | 997 | HR for elevated blood pressure | 0.82 (0.59–1.14) | 0.14 | P |
| Wang 2008 ^{18, e} | US: Women's Health Study, 100% female, age > 45 | 10 | > 2.99 vs < 0.9 servings per day | 28 886 | 8710 | HR presented as RR of hypertension | 0.86 (0.79–0.94) | 0.003 | 0 |
| <i>Low-fat dairy foods</i> | | | | | | | | | |
| Alonso 2005 ^{9, a} | Spain: SUN, 39% male, age 20–90 | 2 | 614.7 vs 2.5 g per day | 5880 | 180 | HR for hypertension | 0.46 (0.26–0.84) | 0.02 | 0 |
| Engberink 2009a ^{26, b} | The Netherlands: MORGEN, 45% male, age 20–65 | 5 | 507 vs 59 g per day | 3454 | 1022 | OR for hypertension | 0.82 (0.64–1.06) | 0.24 | P |
| Engberink 2009b ^{12, c} | The Netherlands: Rotterdam Study, 43% male, age > 55 | 6 | 561 vs 21 g per day | 2245 | 984 | HR for hypertension | 0.84 (0.70–1.01) | 0.07 | P |
| Wang 2008 ^{18, e} | US: Women's Health Study, 100% female, age > 45 | 10 | > 2 vs < 0.3 servings per day | 28 886 | 8710 | HR presented as RR of hypertension | 0.89 (0.81–0.98) | 0.01 | 0 |
| <i>High-fat dairy foods</i> | | | | | | | | | |
| Alonso 2005 ^{9, a} | Spain: SUN, 39% male, age 20–90 | 2 | Quintile 5 vs 1 | 5880 | 180 | HR for hypertension | 1.37 (0.77–2.42) | 0.44 | 0 |
| Engberink 2009a ^{26, b} | The Netherlands: MORGEN, 45% male, age 20–65 | 5 | 166 vs 43 g per day | 3454 | 392 | OR for hypertension | 1.19 (0.92–1.54) | 0.11 | P |
| Engberink 2009b ^{12, c} | The Netherlands: Rotterdam Study, 43% male, age > 55 | 6 | 272 vs 28 g per day | 2245 | 984 | HR for hypertension | 0.93 (0.76–1.13) | 0.66 | P |
| Wang 2008 ^{18, e} | US: Women's Health Study, 100% female, age > 45 | 10 | > 1.1 vs < 0.2 servings per day | 28 886 | 8710 | HR presented as RR of hypertension | 0.96 (0.89–1.03) | 0.13 | 0 |

Abbreviations: CARDIA, Coronary Artery Risk Development in Young Adults; HR, hazard ratio; MORGEN, Monitoring Project on Risk Factors for Chronic Diseases; OR, odds ratio; P, positive; RR, relative risk; SUN, University of Navarra Follow-Up Study; 0, neutral.

^aAdjusted for age, sex, BMI, physical activity, alcohol consumption, sodium intake, total energy intake, smoking, hypercholesterolemia, quintiles of fruit, vegetable, fibre, caffeine, magnesium, potassium, MUFA and SFA intakes.

^bAdjusted for age, sex, total energy intake, socioeconomic status, BMI, smoking, daily intake of alcohol, fruit, vegetables, fish, meat, bread, coffee and tea.

^cAdjusted for age, sex, BMI, smoking, educational level, total energy intake, alcohol consumption, intake of vegetables, fruit, meat, bread, coffee and tea.

^dAdjusted for baseline age, sex, race, Center, energy intake, education, physical activity, alcohol intake, smoking and vitamin supplement use.

^eAdjusted for age, race, energy, treatment, smoking, alcohol use, exercise, postmenopausal, multivitamin use, BMI, history of diabetes and hypercholesterolemia, and intake of fruit and vegetable, whole grain, red meat and vitamin D.

the risk of EBP. This association is likely because of consumption of low-fat dairy foods, which were associated with a 16% reduction in risk, whereas high-fat dairy foods showed no association. Investigation of specific categories of dairy foods showed that consumption of fluid dairy foods (including low-fat and full-fat milk and yogurt) was associated with an 8% reduction in risk, whereas cheese consumption did not produce significant results. Although only four studies were included in the meta-analyses for cheese and fluid dairy foods, the statistical power was sufficient to produce a significant result, although the individual studies were

too small to achieve this. It is important to note that the amount reported in the highest categories of dairy consumption (usually > 2 servings per day) is consistent with current recommendations for 2–3 servings of non-fat or low-fat dairy products per day (Table 5).^{19,20} These are also consistent with American Heart Association recommendations for saturated fat intake of < 7% of total energy intake.⁵

Although findings from the Dietary Approaches to Stop Hypertension have pointed to the benefits of low-fat dairy foods combined with a diet high in fruits and vegetables,⁸ to our knowledge this is the first systematic review and meta-analysis to make

Table 4 Characteristics of cohort studies included in meta-analysis examining cheese and fluid dairy foods

| Published study | Study cohort and characteristics (age in years) | Length of follow-up (years) | Type of food | Intake | Size of cohort | Number of cases | Outcome | Measure of effect size (95% CI) | P_{trend} | Quality |
|----------------------------------|---|-----------------------------|-------------------------------------|--|----------------|-----------------|------------------------------------|---------------------------------|-------------|---------|
| <i>Cheese</i> | | | | | | | | | | |
| Engberink 2009a ^{26, a} | The Netherlands: MORGEN, 45% male, age 20–65 | 5 | Cheese and cheese products | 62 vs 12 g per day | 3454 | 169 | OR for hypertension | 1.17 (0.90–1.52) | 0.77 | P |
| Engberink 2009b ^{12, b} | The Netherlands: Rotterdam Study, 43% male, age > 55 | 6 | Cheese and cheese products | 58 vs 15 g per day | 2245 | 984 | HR for hypertension | 0.98 (0.81–1.18) | 0.76 | P |
| Steffen 2005 ^{16, c} | US: CARDIA, 43% male, 49% African American, age 18–30 | 15 | Cheese | > 1.2 vs < 0.3 servings per day | 4304 | 997 | HR for elevated blood pressure | 1.07 (0.85–1.33) | 0.57 | P |
| Wang 2008 ^{18, d} | US: Women's Health Study, 100% female, age > 45 | 10 | Cottage cheese | ≥ 5 servings per week vs < 1 serving per month | 28 886 | 8589 | HR presented as RR of hypertension | 0.87 (0.70–1.06) | 0.33 | 0 |
| <i>Fluid dairy foods</i> | | | | | | | | | | |
| Engberink 2009a ^{26, a} | The Netherlands: MORGEN, 45% male, age 20–65 | 5 | Milk and milk products ^e | 719 vs 169 g per day | 3454 | 180 | OR for hypertension | 1.09 (0.84–1.42) | 0.63 | P |
| Engberink 2009b ^{12, b} | The Netherlands: Rotterdam, 43% male, age > 55 | 6 | Milk and milk products ^e | 651 vs 127 g per day | 2245 | 984 | HR for hypertension | 0.83 (0.69–1.01) | 0.07 | P |
| Steffen 2005 ^{16, c} | US: CARDIA, 43% male, 49% African American, age 18–30 | 15 | Milk | > 2.1 vs < 0.3 servings per day | 4304 | 997 | HR for elevated blood pressure | 0.87 (0.70–1.08) | 0.03 | P |
| Wang 2008 ^{18, d} | US: Women's Health Study, 100% female, age > 45 | 10 | Yogurt | > 0.5 vs < 0.1 serving per day | 4304 | 997 | HR for elevated blood pressure | 0.88 (0.75–1.04) | 0.14 | |
| | | | Skim milk | ≥ 2 servings per day vs < 1 serving per month | 28 886 | 8634 | RR of hypertension | 0.93 (0.86–1.01) | 0.002 | 0 |
| | | | Yogurt | ≥ 1 serving per day vs < 1 serving per month | 28 886 | 8531 | HR presented as RR of hypertension | 0.97 (0.85–1.11) | 0.36 | |

Abbreviations: CARDIA, Coronary Artery Risk Development in Young Adults; HR, hazard ratio; MORGEN, Monitoring Project on Risk Factors for Chronic Diseases; OR, odds ratio; P, positive; RR, relative risk; 0, neutral.

^aIncludes milk, yogurt, coffee creamer, curd, pudding, porridge, custard and whipped cream.

^bAdjusted for age, sex, BMI, physical activity, alcohol consumption, sodium intake, total energy intake, smoking, hypercholesterolemia, quintiles of fruit, vegetables, fibre, caffeine, magnesium, potassium, MUFA and SFA intakes.

^cAdjusted for age, sex, BMI, smoking, educational level, total energy intake, alcohol consumption, intake of vegetables, fruit, meat, bread, coffee and tea.

^dAdjusted for baseline age, sex, race, center location, energy intake, education, physical activity, alcohol intake, smoking and vitamin supplement use.

^eAdjusted for age, race, energy, treatment, smoking, alcohol use, exercise, postmenopausal, multivitamin use, BMI, history of diabetes and hypercholesterolemia, and intake of fruit and vegetable, whole grain, red meat and vitamin D.

^fIncludes milk, yogurt, coffee creamer, curd, pudding, porridge, custard, and whipped cream.

Table 5 Daily amount of cheese, milk, and yogurt recommended by the US, Canada, Australia, and the UK, and amount of calcium provided

| | USA ²⁰ | Canada ⁴⁶ | Australia ⁴⁵ | UK ⁴⁷ |
|--|-------------------|----------------------|-------------------------|------------------|
| Suggested servings per day ^a | 3 | 2 | 2 | 3 |
| <i>Cheese</i> | | | | |
| Serving size (g) | 42.5 | 50 | 40 | 30 |
| Ca ²⁺ (mg) per serving ^b | 215–408 | 253–480 | 202–384 | 152–288 |
| Total (g) per day | 127.5 | 100 | 80 | 90 |
| Ca ²⁺ (mg) per day | 645 | 506 | 404 | 456 |
| <i>Milk</i> | | | | |
| Serving size (g (ml)) | 244 (240) | 258 (250) | 258 (250) | 203 (200) |
| Ca ²⁺ (mg) per serving ^b | 276–299 | 291–315 | 291–315 | 230–249 |
| Total (g (ml)) per day | 732 (720) | 516 (508) | 516 (508) | 609 (509) |
| Ca ²⁺ (mg) per day | 828 | 582 | 582 | 690 |
| <i>Yogurt</i> | | | | |
| Serving size (g (ml)) | 245 (240) | 175 (171) | 200 (196) | 150 (147) |
| Ca ²⁺ (mg) per serving ^b | 223–345 | 159–246 | 182–282 | 137–211 |
| Total (g (ml)) per day | 735 (720) | 350 (343) | 400 (392) | 450 (441) |
| Ca ²⁺ (mg) per day | 669 | 318 | 364 | 411 |

^aOn the basis of a typical adult consuming 1600+kcal per day (US) or aged 19–50 years (Canada, Australia and UK).

^bDetermined using the United States Department of Agriculture National Nutrient Database for Standard Reference.⁴¹

comparisons between low- versus high-fat dairy foods and cheese versus fluid dairy foods. There are many beneficial components of low-fat dairy foods that may contribute to their protective effects, including minerals such as calcium,^{32–34} magnesium³⁵ and potassium,³⁶ vitamin D in fortified dairy foods³⁷ and bioactive milk peptides.^{38,39} Calcium is well understood to have a role in the protective effects of low-fat dairy foods; two independent meta-analyses of randomised controlled trials,^{33,34} as well as a follow-up analysis³² showed that calcium supplementation resulted in small, significant reductions in SBP, but had no effect on DBP.^{33,34} Because the association between BP and dairy foods is much stronger than the association between BP and calcium intake, it has been suggested that components in dairy foods other than calcium must also have an important role.^{9,33} This is supported by findings that dietary calcium, but not calcium supplementation, was associated with reduced risk of hypertension in the Women's Health Study.¹⁸ For example, components raising recent interest are the lactotripeptides, bioactive peptides released from dairy foods after fermentation during food processing or digestion in the small intestine. These peptides are thought to inhibit the action of angiotensin I-converting enzyme, thereby preventing blood vessel constriction.^{38–39}

There are many reasons why an association was found between EBP and low-fat but not high-fat dairy foods. It is possible that when consumed with fat, the bivalent cations of calcium and magnesium bind to fatty acids in the small bowel, forming insoluble soaps that are not absorbed by enterocytes.^{9,40} Alternatively, the high-saturated fat content of high-fat dairy foods might counteract the

beneficial effect of the other components of dairy foods,⁶ negating the association. In addition, subjects with a higher consumption of low-fat dairy foods tend to have a healthier lifestyle. Two of the included studies found direct correlations between high consumption of low-fat dairy foods and fruit, vegetable, and whole-grain consumption, potassium, calcium, vitamin D, and fibre intake, and physical activity, and inverse correlations with tobacco smoking and alcohol, saturated fat, and cholesterol intake.^{9,18} Although these studies attempted to control for such confounders, it is possible that residual confounders may still interfere.

The average serving size of 240 g of milk and 40 g of cheese provide similar amounts of energy, but very different amounts of saturated fat and minerals. This may in part explain why a significant association was observed between EBP and consumption of fluid milk but not of cheese. Compared with full-fat cheddar cheese, one serving of full-fat milk and one serving of low-fat milk (<2% fat) provide approximately half and one-third as much saturated fat, respectively,⁴¹ possibly negating the beneficial effect of cheese as a dairy food. In addition, the higher potassium and lower sodium content of milk and other fluid dairy foods compared with cheese could in part explain the lack of association observed between BP and cheese consumption. Dietary potassium has been reported as inversely related to hypertension in population studies, and an adequate potassium intake can reduce the increase in BP associated with sodium sensitivity.³⁶

Most studies included in the systematic review reported that an intake of ≥ 488 g of dairy foods per day, provided at least 550 mg calcium (assuming milk is the primary dairy food consumed). Examining

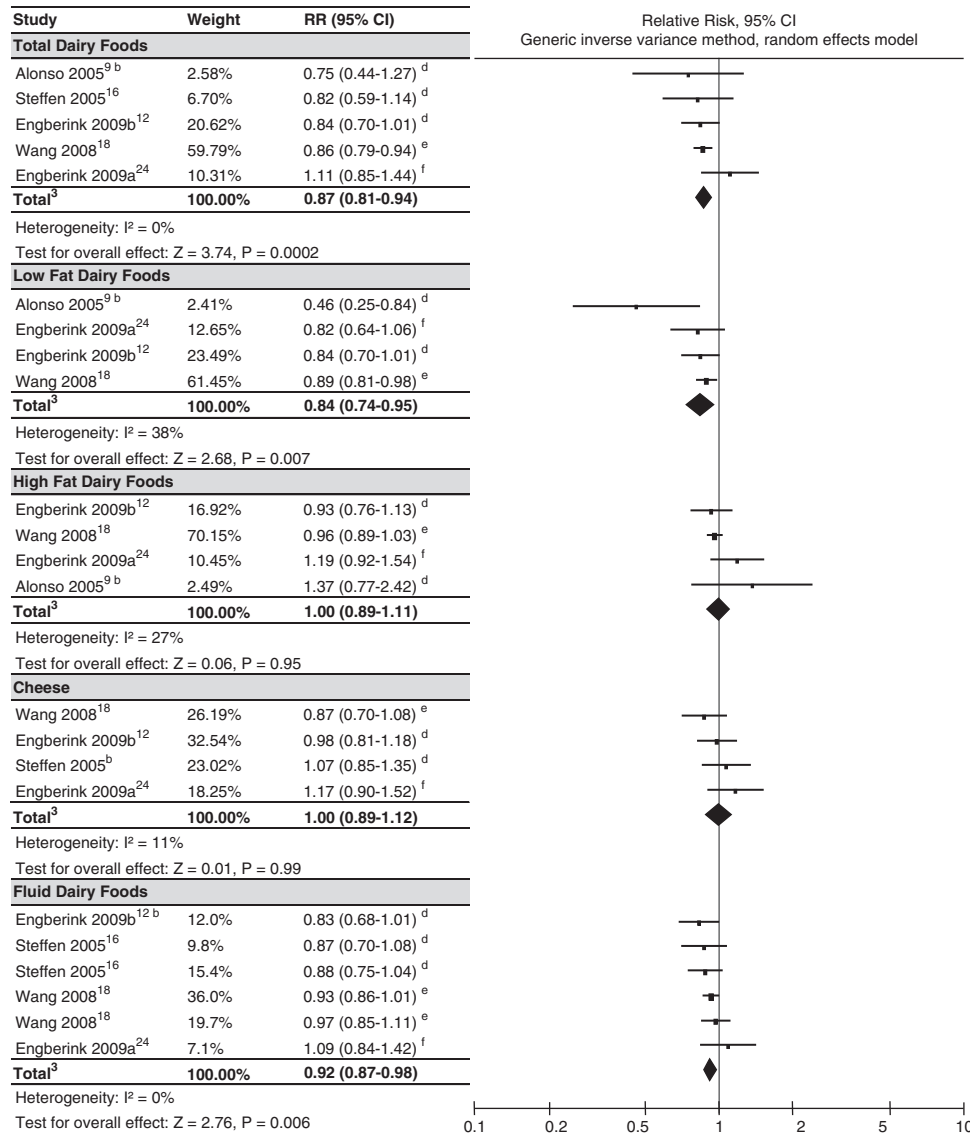


Figure 2 Forest plot of prospective studies examining the association between total dairy, low-fat dairy, high-fat dairy, cheese and fluid dairy foods and risk of elevated blood pressure (EBP). Abbreviations: RR, relative risk; CI, confidence interval. ^aEBP was defined as systolic blood pressure ≥ 130 mm Hg, diastolic blood pressure ≥ 85 mm Hg or use of medications prescribed by a physician to lower blood pressure. ^bStudy reported a CI that was asymmetrical around the mean; therefore, the widest CI was used to calculate the summary statistic. ^cSummary statistics for overall RRs were generated with Review Manager Version 5.0.24 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark), using the generic inverse variance method and the random effects model. ^dStudy reported hazard ratio (HR). HRs are generally equivalent to RRs but are used when risk changes over time;²⁸ therefore the HR is reported here as RR. ^eStudy's outcome measure was HR, but study reported RR. ^fStudy reported odds ratio (OR). ORs and RRs are approximately the same when the OR is within 20% of 1 (with 1 indicating no effect).²⁹ The largest OR used in the analysis was 1.19; therefore the OR is reported here as RR.

country-specific recommendations for dairy food intake (Table 5), all milk recommendations provide at least this level of calcium. For yogurt and cheese however, intakes with > 550 mg calcium are provided only by the US recommendations. Owing to the small recommended serving size for yogurt in Canada, Australia and in the UK, if yogurt is the only source of dairy and these recommendations are adhered to, then only 350–450 g yogurt will be consumed per day providing only 318–411 mg

calcium. Similarly, the recommended serving size of cheese in Canada, Australia and in the UK provides for a calcium intake of < 550 mg per day.

The positive quality of the included studies (that is, meeting most/all quality criteria (Table 2) is a strength of this systematic review. Although three studies were of positive quality and two studies were of neutral quality, the only factor that lowered the quality of the two neutral studies was recruitment of study participants. One recruited only

health professionals¹⁸ and the other recruited only nurses and university graduates,⁹ resulting in educated cohorts of higher socioeconomic status and with greater health interest. All included studies adjusted for the following confounding factors: age, gender, body mass index, smoking status, alcohol consumption, total energy intake and consumption of the major food groups. However, two studies did not adjust for physical activity^{12,26} and three studies did not adjust for socioeconomic status^{9,16,18} ethnicity or nutritional supplement use.^{9,12,26}

All high-quality systematic reviews have the capability to reduce bias through their methodical process.⁴² In addition, the statistical power of cohort studies might be increased through use of meta-analysis. The search strategy used in this review was approved by the Australian National Health and Medical Research Council Dietary Guidelines Working Committee and was very comprehensive, including seven different databases. The methods of study selection were unbiased, and inclusion criteria were predetermined. Only moderate-to-large cohort studies were included in the meta-analysis, minimising the introduction of small-study bias. A set of predetermined questions was used to assess quality, additionally minimising bias.⁴³ The quality assessment, data extraction and analysis methods were appropriate and can be reproduced.

This review also has limitations. It includes only studies published in English, and made no investigation to recover unpublished studies.⁴⁴ Restriction to studies in English might overestimate the effect only by around 2%.⁴⁴ As in each individual study, the highest category of dairy food intake was compared only with the lowest category of intake, it has not been possible to determine the lowest intake of fluid dairy or low-fat dairy foods that provide protection against EBP. Diversity of study populations, study design and biases in the original publication are concerns in all meta-analyses of prospective studies. However, heterogeneity was assessed both qualitatively and quantitatively, with the I^2 statistic showing only low-to-moderate heterogeneity for included studies. One example of heterogeneity is the outcome measure—one study¹⁶ defined EBP as SBP >130 or DBP >85 mm Hg, whereas the other four studies defined hypertension as SBP >140 or DBP >90 mm Hg. Therefore, we report only EBP and not hypertension. In addition, one study cohort¹⁸ included in this meta-analysis was much larger than the other studies, resulting in a larger weight in the calculation of the summary statistic. Therefore, any biases or inaccuracies in this study are carried through to the summary statistic. Although few studies have been analysed, it can be noted that the World Cancer Research Fund advises use of meta-analysis from as few as two cohort studies.²³ Nevertheless, the limitations raised should be considered when interpreting the summary statistic.

In conclusion, this meta-analysis of nearly 45 000 subjects supports an inverse association between low-fat dairy foods and fluid dairy foods and increased risk of EBP. These findings can be used as an evidence base for dietary guidance, and support the current recommendations in the United States, Canada, Australia, and in the United Kingdom that adults should consume 2–3 servings of low-fat dairy products per day.^{19,20,45} Considering calcium content and risk of EBP, some recommended serving sizes might need to be reconsidered.

What is known about the topic

- Diet is the strongest environmental factor influencing blood pressure, and cross-sectional and longitudinal studies suggest that dairy foods in particular may be effective in lowering blood pressure.

What this study adds

- In this meta-analysis, consumption of total dairy foods, low-fat dairy foods and milk was associated with reduced risk of elevated blood pressure.
 - These findings support the current recommendations in the United States, Canada, Australia and in the United Kingdom that adults should consume 2–3 servings of low-fat dairy products per day.
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Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We acknowledge the National Health and Medical Research Council, Australia (<http://www.nhmrc.gov.au/>) for funding this project and the Dietitians Association of Australia for overseeing the project and administering the contract. *Source of support:* this work was undertaken as part of a systematic literature review to update the Dietary Guidelines for Australians by the Dietitians Association of Australia under contract to the National Health and Medical Research Council, Australia. *Authorship:* RR conducted the November 2009 search, determined studies for exclusion and inclusion, extracted data from retrieved studies, performed the meta-analysis, and drafted the manuscript excepting the introduction. JL recovered the publications, determined studies for exclusion and inclusion, extracted data from retrieved studies and drafted the introduction. HT oversaw and advised the entire study, contributed ideas throughout the review and helped with manuscript revision. CP determined studies for exclusion and inclusion, extracted data from included studies and contributed to manuscript revision. KW oversaw and advised the entire study, designed the review process, chose studies to be retrieved and contributed to manuscript preparation and revision. All authors approved the final manuscript.

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