

Systematic Review

The effect of dairy foods on CHD: a systematic review of prospective cohort studies

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There is interest in the degree to which fats in dairy foods contribute to CHD. We undertook a systematic review to investigate the effect of dairy consumption on CHD using prospective cohort studies. A systematic search of electronic databases identified studies relating dairy food intake in adulthood to episodes or death from CHD, IHD and myocardial infarction. Included studies were assessed for quality based on study methodology, validity of dietary assessment, success of follow-up, standardised assessment of CHD, IHD or myocardial infarction end points and appropriateness of statistical adjustment. Data from twelve cohorts involving >280 000 subjects were included. Most studies had follow-up of >80 %, adjusted statistically for three or more confounders and used standard criteria to determine end points. About half the studies used a validated FFQ, administered the FFQ more than once or had follow-up of >20 years. Fewer than half the studies involved subjects representative of the general population. Four of the twelve cohorts found no association between dairy intake and CHD. Eight studies reported varying relationships between different dairy foods and CHD or differential associations based on race, sex or over time. Although dairy foods contribute to the SFA composition of the diet, this systematic review could find no consistent evidence that dairy food consumption is associated with a higher risk of CHD. This could be due to the limited sensitivity of the dietary assessment methods to detect an effect of a single food in a mixed diet on complex clinical outcomes.

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Diets containing dairy fats are thought to contribute to CHD primarily by increasing saturated fat intake and as a result many learned bodies recommend avoiding high-fat dairy foods as part of a healthy diet^(1–3). The rationale for the association between dairy fat consumption and CHD is that saturated fats increase plasma cholesterol⁽⁴⁾, which in turn is associated with increased risk of CHD⁽⁵⁾. Surprisingly, there are conflicting data concerning the simple relationship between dairy consumption and blood lipids. While dairy fats are generally rich in SFA, they are unique in the food supply since they have a wide range of chain lengths from C2 to C20. Dairy fats are also high in MUFA, which lower plasma cholesterol levels⁽⁶⁾. Furthermore, dairy fats contain other biologically active lipids including conjugated linoleic acid and low levels of the *n*-3 long-chain PUFA that have the potential to attenuate risk factors for CHD⁽⁷⁾. In addition,

dairy foods are rich in Ca and two separate meta-analyses have reported an inverse relationship between higher Ca intake and reduced blood pressure^(8,9).

Comparisons of national food data with CHD incidence supports the association between dairy fat consumption and CHD⁽¹⁰⁾; however, this type of comparison does not account for the multiple dietary and lifestyle factors affecting the development of CHD or IHD⁽¹¹⁾. Case-control studies are also unable to account for the large number of factors that may influence consumption of dairy foods and development of CHD and may also be subject to recall bias. Moreover, high-quality evidence from randomised controlled trials is not available to examine the long-term effects of dairy food consumption on CHD. To date, randomised controlled trials have been limited to specific types of dairy foods (e.g. cheese), and measured short-term indicators of CHD

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risk, such as changes to cholesterol levels^(12–14). Hence, large cohort studies with prospectively collected baseline data on health, lifestyle and diet provide important information necessary to assess the effect of dietary exposure on CHD. Hence, we aimed to investigate the relationship between dairy food consumption and death from CHD/IHD using data from prospective cohort studies.

Experimental methods

Search strategy

The MEDLINE, CENTRAL, EMBASE, CINAHL, citation index (Web of Science) and Australian and International dissertation libraries were searched for relevant articles using the search string ‘dairy food*’ or ‘dairy product*’ or ‘dairy’ and ‘CHD’ or ‘heart disease’. No language restriction was applied. Reference lists of identified articles were searched for other potentially relevant studies. The last search was performed in December 2007.

Selection

Prospective cohort studies assessing intake of dairy foods and incidence of CHD, IHD or myocardial infarct were included in the systematic review. Other types of studies such as those that correlated national food data with coronary mortality, case-control studies or randomised controlled trials were not included. No restriction was placed on the duration of follow-up or dietary assessment method. Studies that reported ‘patterns’ of food consumption (such as a Mediterranean-style diet), or grouped dairy food consumption with other foods, or did not explicitly describe the intake of dairy foods were not included. Participants were adult men and women (>18 years of age) irrespective of BMI, ethnicity or risk factors for CHD.

Quality assessment of studies

Assessment of study quality was determined according to the reporting of the study design, method and statistical analysis. Quality assessments considered the success and duration of follow-up (>80% considered high), the validity and content of the dietary assessment method (where FFQ measured frequency and amount, and specifically asked questions on intake and type of two or more core dairy foods), the application of standardised criteria to measure CHD end points, whether the records were reviewed by an independent assessor and the number and appropriateness of adjustment for confounding factors.

Data abstraction

Titles and abstracts from the electronic and bibliographic searches were screened by two investigators (L. G. S., M. V.) for inclusion based on study design and primary outcome measures. The full text of the article was retrieved if it was unclear whether the study met inclusion criteria.

Data synthesis and analysis

Qualitative data from each study including design, participant characteristics, methodology, results and statistical analysis were extracted and tabulated for comparative analysis. No assessment of publication bias was undertaken owing to the small number of included studies, the difficulty in combining multiple publications from the same cohort and mixed associations between specific dairy foods and CHD reported within studies.

Results

An initial search of the MEDLINE electronic database identified 211 papers. Many papers were eliminated on examination of abstracts as they were not prospective cohort studies or did not assess CHD. Of the possible studies for inclusion, twenty-seven complete papers were retrieved for further assessment. The reference list of each paper was cross-checked and identified a further seven potentially relevant studies, resulting in a total of thirty-four articles assessed for consideration. No additional articles were identified by searches of other databases.

Of the thirty-four articles retrieved, nineteen were excluded and not assessed further. Reasons for exclusion included: no assessment of dairy food (the study design evaluated dietary patterns but not specifically dairy foods)^(15–20); results not reported as a full journal article and not able to be assessed⁽²¹⁾; study design involved a randomised trial⁽²²⁾; a case-control comparison^(23–25); review articles on a related topic^(26–30). Of the remaining articles, three reported stroke and not CHD or IHD^(31–33). A total of fifteen papers^(34–48) describing twelve well-known prospective cohort studies^(34–45) were reviewed (data from three cohorts were reported in additional papers^(46–48)).

Summary of included studies

The studies included in this systematic review are summarised and alphabetically listed in Table 1^(34–48). The duration of follow-up for the included studies ranged from 8 years⁽³⁵⁾ to more than 20 years^(36,40,41,43,45). Participant characteristics and the methods for assessing consumption and classification of dairy foods varied widely between studies. A description of the methodology and the outcomes for each study are included in Table 1.

Participant characteristics

The included studies involved more than 280 000 adults, with study sizes ranging between 2400⁽³⁶⁾ and >80 000⁽³⁸⁾. Most studies involved subjects with an age range between 40 and 60 years at baseline. Five studies involved men only^(34,36,40–42) and two involved women only^(35,38). Six included studies assessed populations possibly representative of the people living in the region^(36,37,41,42,44,45), whereas the other studies assessed health professionals^(34,38), post-menopausal women⁽³⁵⁾, a religious group⁽⁴³⁾, vegetarians⁽³⁹⁾ or cohorts from different countries with varying socioeconomic and background characteristics⁽⁴⁰⁾.

Table 1. Summary of included studies

Study name, dates and reference	Cohort details	Relationship with dairy examined	Dietary assessment	Primary outcome		General comment on quality of study
				Effect of dairy on death CVD, CHD, IHD or MI (95% CI)	Statistical methods*	
Health Professionals Follow-up Study, USA ⁽³⁴⁾ Set-up: 1986 Follow-up at: 12 years	Sex: M. Age: 40–75 years. <i>n</i> 39 800 USA health professionals. Excluded men with pre-existing CHD	Dairy Ca v. fatal IHD and non-fatal MI	Validated, SQ-FFQ at 4 years intervals. Assessed Ca in whole, skim or low-fat milk, yoghurt, ice cream, cheese and Ca supplements	No association†	Cox regression. Adjusted for eight confounding factors including lifestyle variables, medical history and dietary factors	94% Follow-up. Large sample size. Validated SQ-FFQ. Study sample not representative of population (health professionals only)
Iowa Women's Health Study of post-menopausal women, USA ^(35,46) Set-up: 1986 Follow-up at: 8 and 15 years	Sex: F. Age: 55–69 years. <i>n</i> 34 486 (1999 analysis). <i>n</i> 29 017 (2005 analysis). Post-menopausal, excluded women with pre-existing IHD	1999 Dairy foods v. fatal IHD. 2005 Dairy protein v. all-cause mortality and CHD mortality	Validated SQ-FFQ at regular intervals. Assessed milk, yoghurt, cream, ice cream and cheese. Butter not included	Mixed associations. 1999 No effect†. 2005 CHD mortality increased in mathematical isoenergetic substitution of dairy protein for carbohydrate. CHD mortality: RR = 1.41 (1.07, 1.87), <i>P</i> = 0.02	1999 Proportional hazards. Adjusted for twelve confounding factors including medical history, lifestyle and dietary factors. 2005 Adjusted for eight lifestyle factors, medical history and a further seventeen dietary factors	69–82% Follow-up. Large sample size. Validated SQ-FFQ. Sample not representative of population (women only). Excluded butter from dietary analysis
Caerphilly Cohort Study, UK ^(36,47) Set-up: 1979–83 Follow-up at: 20–24 years	Sex: M. Age: 44–59 years. <i>n</i> 2403 (FFQ analysis). <i>n</i> 665 (7 d WFR analysis). Participants with and without pre-existing CHD	Milk intake v. IHD	SQ-FFQ: only dairy food investigated was milk intake. SQ-FFQ was validated against 7 d WFR in sub-sample	No association in 2004 or 2005 analyses†	Cox proportional hazards. Adjusted for nine confounding factors including medical history, lifestyle and dietary factors	Follow-up 96% (2004). Study population possibly representative of males living in region. Milk only dairy food investigated. Modest sample size
National Health and Nutrition Examination Study I, USA ⁽³⁷⁾ Set-up: 1971–75 Follow-up at: 16 years	Sex: M and F. Age: 40–74 years. <i>n</i> 5811. Participants excluded if dietary habits changed due to CHD	Cheese v. CHD mortality and hospitalisation	FFQ	Mixed associations. Cheese inversely associated with CHD† RR = 0.88 (approximately 0.8–1.0), <i>P</i> = 0.002. Butter intake associated with increased CHD in specific ethnic groups (<i>P</i> = 0.015–0.026)	Logistic regression. Adjusted for thirteen lifestyle factors and medical history, as well as multiple dietary factors	28% Follow-up. Study possibly representative of population. Sampling strategy not accounted for
Nurses' Health Study, USA ⁽³⁸⁾ Set-up: 1976 Follow-up at: 14 years	Sex: F. Age: 34–59 years. <i>n</i> 80 082. Excluded women with pre-existing CHD, high serum cholesterol or diabetes	Dairy food v. non-fatal MI and CHD mortality	Validated FFQ. Assessed high-fat dairy (butter, ice cream, whole milk, hard or cream cheese) and low-fat dairy (skim or low-fat milk, yoghurt and cottage cheese)	Mixed associations. Positive effects: whole milk RR = 1.67 (1.14, 1.90), <i>P</i> < 0.0001‡. Ratio of high-fat to low-fat dairy RR = 1.27 (CI not reported), <i>P</i> = 0.0004‡. No effects: high-fat dairy†,‡, low-fat dairy†,‡, skim milk‡	Pooled logistic regression. Data adjusted for nine lifestyle factors and medical history. Adjusting for seven additional dietary factors resulted in non-significant effect in 12:0–18:0 group	Approximately 66% follow-up (unclear as study losses added to those excluded). Large sample size. Sample not representative of population (women health professionals only)
The Oxford Vegetarian Study, UK ^(39,48) Set-up: 1980–84 Follow-up at: 12–16 years	Sex: M and F. Age: 16–79 years. <i>n</i> 10 802 Vegetarians compared with control (friends or relatives)	Milk and cheese v. IHD and all-cause mortality	SQ-FFQ at baseline, 4 d diet diary in 1985–86. Assessed milk intake (pints/dl) and cheese (servings/week) excluding cottage cheese	Mixed associations. No effects: milk and IHD or all-cause mortality‡, cheese and all-cause mortality. Positive effect: cheese and IHD mortality‡ DRR = 2.47 (0.97–6.26), <i>P</i> < 0.01	Logistic regression. Adjusted for sex, three lifestyle and medical history factors. The contribution of dairy fats to total animal fat or saturated animal fat not reported	97% Follow-up. Sample included vegetarians v. their friends and relatives

Dairy foods and CHD

Table 1. Continued

Study name, dates and reference	Cohort details	Relationship with dairy examined	Dietary assessment	Primary outcome		General comment on quality of study
				Effect of dairy on death CVD, CHD, IHD or MI (95% CI)	Statistical methods*	
Seven Countries Study ⁽⁴⁰⁾ Set-up: 1958–64 Follow-up at: 25 years	Sex: M. Age: 40–59 years. <i>n</i> 12 707. Included sixteen cohorts from seven countries (Finland, Greece, Italy, Japan, USA, The Netherlands and former Yugoslavia)	Butter, milk and cheese v. CHD mortality	Food intake from a 'random subsample of the sixteen cohorts' between 1959 – 1960. 7 d WFR used in fourteen cohorts, 4 d WFR in Japan and 1 d WFR in USA. Included butter, milk and cheese	Mixed associations. Positive effects: milk and butter with CHD mortality in simple correlations: butter: 0.89 (0.68–0.96), milk: 0.6 (0.13–0.84). No effect: cheese and CHD mortality in simple correlation	Linear regression of simple food groups and coronary mortality. No adjustment for confounding factors	Follow-up reported as 99.5% although the number enrolled in original cohorts is unclear. No adjustment for any confounding factors. Male-only cohorts drawn from a wide range of backgrounds (including rural and coastal areas, market town rail-road workers and university professors)
The Collaborative Study, UK ⁽⁴¹⁾ Set-up: 1970–73 years Follow-up at: 25 years	Sex: M. Age: 35–64 years. <i>n</i> 5765 Scottish working class men	Milk intake v. CHD, CVD and all-cause mortality	SQ-FFQ at baseline and repeated in half cohort in 1977. Reliability of FFQ assessed by comparing baseline and follow-up assessments. Assessed milk intake (pints/dl)	Mixed association‡. No effect: milk and CHD mortality. Negative effects: milk and CVD mortality RR = 0.64 (0.40–1.00), <i>P</i> = 0.05. Milk and all-cause mortality RR = 0.81 (0.61–1.09), <i>P</i> = 0.005	Proportional hazards. Adjusted for sixteen lifestyle factors and medical history. No adjustment for other dietary factors	% Follow-up not clear. Study population may be possibly representative of males living in region. Milk was only dairy food measured and no analysis of background diet
British Regional Heart Study, UK ⁽⁴²⁾ Set-up: 1975 Follow-up at: 9.5 years	Sex: M. Age: 40–59 years. <i>n</i> 7735. Recruited from general practitioners clinics in twenty-four towns in UK	Milk and butter v. IHD	Simple questions on use of milk as a drink, on cereals or in tea/coffee and use of butter or margarine as a spread	No association after adjustment for confounders‡	Multiple regression. Adjusted for eight lifestyle factors and medical history. No adjustment for dietary factors	% Follow-up not clear. Reported as a short letter. Dietary information gathered by simple questions. Only milk and butter assessed
Seventh-Day Adventists, CA, USA ⁽⁴³⁾ Set-up: 1960 Follow-up at: 21 years	Sex: M and F. Age: 30–84 years. <i>n</i> 25 153. US cohort of same religious beliefs, included participants with pre-existing heart disease	Cheese and milk v. IHD mortality	Questionnaire on frequency of consumption (but not amounts) of particular foods. Data for milk (two glasses/d v. none) and cheese (daily v. none) reported	Mixed associations‡. No effect: cheese and IHD mortality: milk and IHD mortality in women. Negative effect: borderline effect of milk on IHD mortality in men RR = 0.94 (CI NR), <i>P</i> < 0.05	Cox regression model adjusted for four lifestyle factors and medical history, as well as meat, eggs, coffee and either cheese or milk consumption	% Follow-up not reported. Study focused on meat consumption, dairy products assessed as a confounding factor. Study sample not representative of general population
Japan Collaborative Cohort Study, Japan ⁽⁴⁴⁾ Set-up: 1988 Follow-up at: approximately 9.6 years	Sex: M and F. Age: 40–79 years. <i>n</i> 53 387. Participants from forty-five communities across Japan, excluded those with pre-existing CHD, stroke or cancer	Dairy Ca v. CHD mortality and total CVD mortality	Validated SQ-FFQ. Measured Ca in milk, yoghurt and cheese, as well as non-dairy sources using Japanese food tables	Mixed associations‡ No effect: dairy Ca and CHD mortality. Negative effects: weak negative effect of dairy Ca on total CVD mortality in men (RR = 0.73 (0.55–0.95), <i>P</i> = 0.06) and women (RR = 0.77 (0.58–1.03), <i>P</i> = 0.01)	Cox proportional hazards. Separate analyses for men and women. Adjusted for eight confounding factors including medical history, lifestyle and dietary variables	56% Follow-up. Large study focused on Ca intake from dairy and non-dairy foods. Total stroke reduced in men and women. Study sample likely to be representative of population

Table 1. Continued

Study name, dates and reference	Cohort details	Relationship with dairy examined	Dietary assessment	Effect of dairy on death CVD, CHD, IHD or MI (95% CI)	Primary outcome	Statistical methods*	General comment on quality of study
Middle-aged Dutch civil servants, The Netherlands ⁽⁴⁵⁾ Set-up: 1953–54 Follow-up at: 15 and 28 years	Sex: M and F. Age: 40–65 years. n 2605 Dutch civil servants, included those with pre-existing CHD	Dietary Ca v. CVD and CHD mortality	1-Week food frequency recall at 3 months into study. Total dietary Ca estimated from food tables Included spread, cheese, milk, yoghurt and non-dairy products	No associations	84% Follow-up. Study population representative of those living in region. The contribution of dairy foods to Ca intake is not reported	Logistic regression models. Men and women analysed separately. Adjusted for eight confounding factors including lifestyle variables and medical history. No assessment of background diet or low-fat compared with high-fat dairy foods	

MI, myocardial infarct; M, male; SO-FFQ, semi-quantitative FFQ; F, female; RR, risk ratio; WFR, weighed food record; DRR, death rate ratio; NR, not reported.

* Lifestyle factors included one or more of: age, smoking, physical activity, education, marital status, race, ethnicity, car user, social class, poverty or deprivation category, urban class, paternal social class, siblings, geographical region. Medical history variables included one or more of: pre-existing vascular disease; diabetes; hypercholesterolaemia; hypertension; angina; family history of MI or cancer; BMI; aspirin intake; waist:hip ratio; hormone use (e.g. post-menopausal oestrogen use); serum cholesterol; electrocardiogram ischaemia; bronchitis; forced expiratory volume; percentage of desirable weight. Dietary factors included one or more of: total energy intake; alcohol consumption; vitamin E intake; intake of saturated fat; polyunsaturated fat; monounsaturated fat; trans fat; fibre; K; cholesterol; methionine; meat; eggs; cheese milk or coffee; servings of fruit and vegetables; multivitamins use.

† RR calculated from the highest compared with the lowest category of dietary intake.

‡ RR calculated from the highest compared with the lowest category of servings per day.

\$ OR calculated from the lowest compared with the highest category of Ca intake.

|| 1 pint = 568 ml.

Four of the twelve studies excluded people with pre-existing heart disease^(34,35,38,44), whereas six studies included participants regardless of CVD history and adjusted for this in the statistical analysis^(36,39,41–43,45). The presence of pre-existing heart disease at entry was not reported in one study⁽⁴⁰⁾ and another excluded subjects with pre-existing heart disease only if they had changed their eating habits as a result of their disease⁽³⁷⁾.

Assessment of dairy food intake

Intake of dairy food (diet assessment) was measured with a validated FFQ in seven studies^(34–36,38,39,41,44), a weighed food record in one study⁽⁴⁰⁾ and a 1-week food-frequency recall in another⁽⁴⁵⁾. The tool for assessing diet was poorly defined in two studies^(42,43) and was not described in one study⁽³⁷⁾.

Of the twelve included studies, two measured dairy foods as a group v. cardiovascular outcomes⁽³⁵⁾, two measured milk intake^(36,41) and three measured Ca in dairy^(34,44,45). The remaining six studies reported various combinations of dairy foods against CHD end points including: butter, milk and cheese⁽⁴⁰⁾; milk and cheese^(39,43); milk and butter⁽⁴²⁾; butter and cheese⁽³⁷⁾ or whole milk, skim milk, high- and low-fat dairy⁽³⁸⁾. Three studies presented information about the fat content of dairy foods^(34,35,38), two of which reported data on fat intake from dairy foods^(35,38), and one reported the ratio of high- to low-fat dairy products⁽³⁸⁾.

The majority of studies separated subjects into tertiles, quartiles or quintiles based on dairy serves, or frequency of dairy or Ca (mg/d)^(34–39,41,44,45). Two studies divided participants into frequency of dairy consumption based on the assessment questions (for example, no milk, milk in tea/coffee, milk as a drink)^(42,43). The analysis in the remaining study simply assessed the correlation between death from CHD and individual dairy foods (butter, milk and cheese).

Assessment of outcome measures

All of the included studies identified heart disease cases using standard criteria from the International Classification for Disease index^(35–37,39–41,43–45) or the WHO diagnostic criteria^(34,38) (for the British Regional Heart study⁽⁴²⁾ the method for classifying IHD was described in a separate publication⁽⁴⁹⁾).

Statistical analysis and adjustment for confounders

Nearly all studies used statistical analysis methods including logistic regression using Cox-regression analysis or a proportional hazard models to adjust for confounders^(34–39,41–47). The number and type of potential confounders used for statistical adjustment varied between studies, with most including age, smoking, social class and sex (when both sexes were included). One study used a simple analysis of linear correlation, which does not adjust for confounders⁽⁴⁰⁾.

Six studies adjusted for dietary intake of total energy^(34–36,38,44,45) and four of these studies also adjusted for dietary fats^(34–36,38). One study adjusted only for meat,

eggs and coffee consumption in background diet⁽⁴³⁾ and four studies did not adjust for any background dietary factors^(39–42). Although some foods or dietary variables were tested as confounding factors in one study, the specific details were not clearly reported⁽³⁷⁾. No studies specifically examined the contribution of dairy food to dietary intake of cholesterol, although three studies reported dietary cholesterol data, one of which describe the relationship between dietary cholesterol and IHD⁽³⁹⁾, while the other two studies adjusted for dietary cholesterol in their analyses^(38,46).

Studies reporting no association between dairy intake and CHD or IHD

Four of the twelve included studies found no association between dairy intake and CHD^(34,36,42,45), representing over 50 000 people of similar age, predominantly men, with and without pre-existing CHD (Table 1). Of these studies, one assessed milk intake only⁽³⁶⁾ and another assessed milk and butter⁽⁴²⁾. Two studies measured the association between dietary Ca and CHD end points^(34,45), which is not a direct measure of dairy food consumption as dietary Ca may have come from foods other than dairy. Of these two studies^(34,45), one included the contribution of cheese, milk and yoghurt intake to dietary Ca⁽⁴⁵⁾, but did not report the overall contribution of dairy food to total dietary Ca. The largest study to report no association between dairy intake and CHD reported both total dietary Ca as well as Ca from dairy foods (which included whole and low-fat milk, yoghurt, ice cream and cheese) against CHD end points⁽³⁴⁾. Three of the four studies investigated cohorts that may be representative of their general population^(36,42,45); however, two had relatively small sample sizes $n \leq 2600$ ^(36,45). Other limitations of these studies include a study population that may not be representative of the general population⁽³⁴⁾ and poor specificity or detail of questions asked in the FFQ used to assess participants' dairy intake⁽⁴²⁾.

Studies reporting an association between dairy intake and CHD or IHD

The majority of studies assessing the relationship between dairy food intake and CHD reported mixed findings. Three of the twelve included studies reported a negative relationship between dairy foods and CHD end points (including milk and CVD or all-cause mortality⁽⁴¹⁾, milk and IHD in men⁽⁴³⁾ and dairy Ca with CVD⁽⁴⁴⁾), but also no association between milk⁽⁴¹⁾, cheese⁽⁴³⁾ or Ca from dairy food⁽⁴⁴⁾ and CHD. Together, these studies involved over 80 000 men and women of similar ages followed for between 9 and 25 years, most of which did not have pre-existing CHD at enrolment. Two of these three studies reported sex-based differences in CHD outcomes including a negative effect of milk on IHD mortality in men but not women⁽⁴³⁾ and a negative effect of dairy Ca on total CVD mortality in women, which was driven by the effect of dietary Ca on stroke and not CHD⁽⁴⁴⁾.

Four of the twelve studies reported positive associations between intake of dairy protein⁽⁴⁶⁾ or specific dairy foods (including milk⁽³⁸⁾, cheese⁽³⁹⁾ or milk and butter⁽⁴⁰⁾) and CHD. However, these same cohorts also reported no effect of skim milk⁽³⁸⁾, milk (type not classified)⁽³⁹⁾, cheese⁽⁴⁰⁾ or

dairy food⁽³⁵⁾ intake on CHD. Together, these studies involved over 138 000 participants predominantly women without a history of CHD at study entry. The majority of participants were followed up between 8 and 16 years, with a small proportion of men followed to 25 years⁽⁴⁰⁾. In addition to the relationships with specific dairy foods, two included trials reported positive associations between saturated animal fat or total dietary saturated fat intake and increased CHD; however, these findings included foods other than dairy^(38,39). The majority of mixed relationships relate to different dairy foods; however, one cohort reported disparate relationships over time^(35,46). The primary publication from the Iowa Women's Health Study reported no association between dairy food consumption and CHD at 8 years after enrolment⁽³⁵⁾. However, dietary modelling of data collected after 15 years showed that dairy protein was associated with an increased risk of CHD mortality when dairy protein was isoenergetically substituted for carbohydrate, while holding total energy and fat constant, and adjusting for multiple dietary (e.g. cholesterol intake) and lifestyle confounders (e.g. smoking). One study was compromised by the statistical analyses and should be interpreted with caution as the analyses involved a cross-cultural comparison of CHD data from seven countries but did not incorporate individual dietary data nor account for the effect of multiple lifestyle characteristics that differ across populations groups⁽⁴⁰⁾.

Only one of the twelve included studies reported both positive and negative associations between dairy foods and CHD; a positive association was found between butter intake and CHD in specific ethnic groups (African-American, American-Indian, Hispanics and Asians) as well as a negative association between cheese intake and CHD⁽³⁷⁾. These observations need to be interpreted with caution because the analyses could not account for the stratification and clustering of the sampling strategy even though there was extensive adjustment of potential confounders⁽³⁷⁾ and the modest sample size (n 5811).

Discussion

This systematic review shows no consistent findings to support the concept that dairy food consumption is associated with a higher risk of CHD. While there is no doubt that dairy foods contribute to the intake of saturated fats⁽³⁸⁾, and saturated fat intake has previously been associated with higher incidence of CHD⁽⁵⁰⁾, the evidence extracted from these twelve prospective cohort studies does not consistently demonstrate a direct relationship between the intake of dairy foods and the risk of CHD.

The present recommendations by health authorities and governments to eat low-fat dairy in preference to high-fat dairy foods was supported by the data published in 1999 from the Nurses' Health Study⁽³⁸⁾, as this was the only study included in the review to examine high- v. low-fat dairy foods. In this large study, the ratio of high- to low-fat dairy food consumption was positively associated with an increased risk of CHD⁽³⁸⁾, even though separate analyses of high- or low-fat dairy food intake was not significantly associated with CHD. The most prominent relationship was between the intake of SFA and risk of CHD, particularly for 16:0 and 18:0. Because dairy foods contributed to the

intake of 15 % of the total dietary SFA and only 10 % to 16 : 0 and 18 : 0, it was not possible to determine whether the association with CHD was driven by specific chain length of SFA or because longer chain saturates were more abundant in the diet. Even beef consumption accounted for only 23 % of the total saturated fat intake, highlighting the difficulty in ascribing a causal outcome to a single food group.

Overall, the data from the larger observational studies with good follow-up, using validated questionnaires examining multiple dairy foods and appropriate statistical analyses offer important insight into the association between dairy foods and CHD^(34,35,38,39,44,45). However, the disparate findings from this review suggests that the association between saturated fat intake from dairy foods and CHD may be weaker than expected by examining the relationship between national food consumption data and CHD mortality rates^(10,51). This is not surprising as studies investigating national food data are unable to adequately address the confounding influences of lifestyle variables.

Adjusting study data for the many known confounding factors of heart disease is a limiting factor in some of the observational studies included in this review. Dairy food consumption differs by lifestyle and cultural factors between countries, as well as within a country according to socio-economic and educational factors^(52–54). Hence, statistical adjustment for socio-economic variables is imperative and findings from studies that have not adjusted for these factors may be subject to bias. In addition, some of the smaller studies included in the review may lack the statistical power to detect an effect of dairy food consumption on CHD, even if it existed^(36,37,41,45,47). Another issue affecting the generalisability of the findings is that most of the included studies were unable to address the changing pattern of dairy food consumption over time. Regular assessment of dietary fat intake in the Nurses' Health Study demonstrated a reduction in the total fat intake and the proportion of saturated fat over a 20-year period⁽¹⁷⁾. Of the twelve studies included in our systematic review, eight were set-up during or before the 1970s when whole milk was the only type of milk available. Skim and low-fat milk were introduced in the 1980s. Hence the results of early studies may relate to the consumption of high-fat dairy products as low-fat alternatives only became available in the latter part of these studies. Most included studies did not distinguish high- from low-fat dairy consumption, which may be related to changes in consumption patterns or insensitivity of the dietary collection methods. Both the failure to fully adjust for baseline lifestyle and socio-economic factors, as well as changes in food consumption patterns over time, may have contributed to the disparity in findings between studies and added complexity to the results of our systematic review.

The varying nutrient composition of specific dairy foods examined by each study may also contribute to the heterogeneous effects of dairy intake on CHD. There is some preliminary evidence that particular dairy foods may have differential effects on risk factors for CHD. For example, in a controlled setting cheese may have a milder effect on blood cholesterol levels than a similar quantity of dairy fats from butter^(12,14,55). However, the quantity of dairy fats tested have been relatively high when compared with diets of free-living subjects^(52,56). Furthermore, the relationship

between cholesterol and cheese does not appear to extend to the relationship with CHD in observational cohorts, as the studies included in this systematic review have reported no effect⁽⁴³⁾, positive⁽³⁹⁾ and negative⁽³⁷⁾ relationships between cheese and CHD risk. Although fermented dairy foods have been associated with a mild reduction in cholesterol⁽⁵⁷⁾, no studies included in this systematic review specifically evaluated the relationship between fermented dairy foods and CHD.

It has been suggested that nutrients other than saturated fat present in dairy foods such as Ca, conjugated linoleic acid, MUFA or PUFA and protein may modify risk factors for CHD. Dairy foods are rich in Ca and two meta-analyses of randomised controlled trials have demonstrated that increased Ca intake appears to reduce high blood pressure^(8,9). However, a direct relationship between Ca from dairy foods and a reduction in risk of CHD was not reported by the four trials included in our systematic review^(34,35,44,45), and this may be related to the fact that dietary Ca may have come from foods other than dairy. Although these findings might suggest that observational studies may be inadequate for assessing the effect of dairy Ca on CHD, the large sample size, the cultural and dietary diversity of the populations studied and the consistency between these observational studies indicate that other factors may exert a stronger effect on CHD than Ca from dairy foods in the community setting. Although in human studies conjugated linoleic acid has been associated with modest weight loss⁽⁷⁾, the relationship between conjugated linoleic acid intake from dairy foods and CHD could not be evaluated in this systematic review as no data were reported in the included studies. Up to half of the fat in dairy foods may comprise MUFA, which tend to have a lowering effect on cholesterol levels compared with saturated fats⁽⁶⁾. Dairy foods also contain low levels of PUFA, which may influence CHD mortality through modifying risk factors such as reducing LDL-cholesterol, cardiac arrhythmia, anti-thrombotic effects and enhancing endothelial function⁽¹¹⁾. Although one study showed that a higher ratio of PUFA to saturated fats was associated with a reduction in risk of CHD⁽³⁸⁾, contribution of dairy foods to the PUFA:SFA ratio was not described. Finally, dairy proteins have been identified as a possible factor involved in ameliorating hypertension^(58,59). However, a reduction in risk of CHD by dairy proteins was not supported by the complex statistical analyses of Kelemen *et al.*⁽⁴⁶⁾, where the effect of substituting dairy protein in place of carbohydrate showed a 41 % increase in risk of CHD between the highest compared with the lowest quintiles (representing 2.74 and 0.6 serves of dairy food per 4184 kJ (1000 kcal), respectively). Using analysis of dietary patterns, it is possible to draw links between dairy food intake and risk factors for CHD such as improved insulin sensitivity⁽⁶⁰⁾. However, further research is necessary to determine the full effects of consuming specific types of dairy foods on CHD risk factors.

This systematic review has highlighted inconsistencies in the results from studies investigating dairy food consumption and risk of CHD. A key issue for future studies is to fully assess the contribution of saturated fats from dairy foods on the risk of CHD and to determine the relative merits of a diet containing low-fat dairy foods recommended by

numerous medical organisations. Patterns of food consumption have changed dramatically from more traditional diets over the last few decades, therefore the evidence in relation to dairy food intake and CHD needs to be re-evaluated in the context of the contemporary diet.

Conclusion

Although dairy foods contribute to the SFA composition of the diet, this systematic review of prospective cohort studies has highlighted that the studies available for examining the effect of dairy food consumption on CHD are too varied in design, quality and dietary assessment methodology to evaluate the nature of the relationship. Furthermore, research involving large cohorts in which regular and comprehensive assessments of dairy food intakes are collected is needed.

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References

- Lichtenstein AH, Appel LJ, Brands M, *et al.* (2006) Diet and lifestyle recommendations revision 2006: a scientific statement from the American heart association nutrition committee. *Circulation* **114**, 82–96.
- British Nutrition Foundation (2004) Heart Disease and Stroke (Cardiovascular Disease). <http://www.nutrition.org.uk/home.asp?siteId=43§ionId=404&subSectionId=321&parentSection=299&which=1> (accessed January 2007).
- National Health and Medical Research Council of Australia (2003) *Dietary Guidelines for Australians: A Guide to Healthy Eating*. Canberra: Commonwealth of Australia.
- Mensink RP & Katan MB (1992) Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. *Arterioscler Thromb* **12**, 911–919.
- Gordon T (1988) The diet-heart idea. Outline of a history. *Am J Epidemiol* **127**, 220–225.
- Yu S, Derr J, Etherton TD, *et al.* (1995) Plasma cholesterol-predictive equations demonstrate that stearic acid is neutral and monounsaturated fatty acids are hypocholesterolemic. *Am J Clin Nutr* **61**, 1129–1139.
- Whigham LD, Watrus AC & Schoeller DA (2007) Efficacy of conjugated linoleic acid for reducing fat mass: a meta-analysis in humans. *Am J Clin Nutr* **85**, 1203–1211.
- Bucher HC, Cook RJ, Guyatt GH, *et al.* (1996) Effects of dietary calcium supplementation on blood pressure. A meta-analysis of randomized controlled trials. *JAMA* **275**, 1016–1022.
- Allender PS, Cutler JA, Follmann D, *et al.* (1996) Dietary calcium and blood pressure: a meta-analysis of randomized clinical trials. *Ann Intern Med* **124**, 825–833.
- Segall JJ (1977) Is milk a coronary health hazard? *Br J Prev Soc Med* **31**, 81–85.
- Hu FB & Willett WC (2002) Optimal diets for prevention of coronary heart disease. *JAMA* **288**, 2569–2578.
- Nestel PJ, Chronopoulos A & Cehun M (2005) Dairy fat in cheese raises LDL cholesterol less than that in butter in mildly hypercholesterolaemic subjects. *Eur J Clin Nutr* **59**, 1059–1063.
- Fonollá J, López-Huertas E, Machado FJ, *et al.* (2008) Milk enriched with 'healthy fatty acids' improves cardiovascular risk markers and nutritional status in human volunteers. *Nutrition* **25**, 408–414.
- Biong AS, Muller H, Seljeflot I, *et al.* (2004) A comparison of the effects of cheese and butter on serum lipids, haemostatic variables and homocysteine. *Br J Nutr* **92**, 791–797.
- Fehily AM, Yarnell JWG, Sweetnam PM, *et al.* (1993) Diet and incident ischaemic heart disease: The Caerphilly Study. *Br J Nutr* **69**, 303–314.
- Hu F, Rimm E, Stampfer M, *et al.* (2000) Prospective study of major dietary patterns and risk of heart disease in men. *Am J Clin Nutr* **72**, 912–921.
- Oh K, Hu FB, Manson JE, *et al.* (2005) Dietary fat intake and risk of coronary heart disease in women: 20 years of follow-up of the Nurses' Health Study. *Am J Epidemiol* **161**, 672–679.
- Shimazu T, Kuriyama S, Hozawa A, *et al.* (2007) Dietary patterns and cardiovascular disease mortality in Japan: a prospective cohort study. *Int J Epidemiol* **36**, 600–609.
- Tanasescu M, Cho E, Manson JE, *et al.* (2004) Dietary fat and cholesterol and the risk of cardiovascular disease among women with type 2 diabetes. *Am J Clin Nutr* **79**, 999–1005.
- Waijers PM, Ocke MC, van Rossum CT, *et al.* (2006) Dietary patterns and survival in older Dutch women. *Am J Clin Nutr* **83**, 1170–1176.
- Brown L, Rosner B, Willett W, *et al.* (1999) Red meat, eggs, and dairy food consumption in relation to risk of coronary heart disease in pravastatin-treated patients with myocardial infarction. *Am J Epidemiol* **149**, 11 Suppl., S32.
- Hsia J, Heiss G, Ren H, *et al.* (2007) Calcium/vitamin D supplementation and cardiovascular events. *Circulation* **115**, 846–854.
- Gramenzi A, Gentile A, Fasoli M, *et al.* (1990) Association between certain foods and risk of acute myocardial infarction in women. *Br Med J* **300**, 771–773.
- Rastogi T, Reddy KS, Vaz M, *et al.* (2004) Diet and risk of ischemic heart disease in India. *Am J Clin Nutr* **79**, 582–592.
- Sun Q, Ma J, Campos H, *et al.* (2007) Plasma and erythrocyte biomarkers of dairy fat intake and risk of ischemic heart disease. *Am J Clin Nutr* **86**, 929–937.
- Elwood PC, Pickering JE, Hughes J, *et al.* (2004) Milk drinking, ischaemic heart disease and ischaemic stroke II. Evidence from cohort studies. *Eur J Clin Nutr* **58**, 718–724.
- Hu FB & Willett WC (2002) Optimal diets for prevention of coronary heart disease. *JAMA* **288**, 2569–2578.
- Iestra JA, Kromhout D, van der Schouw YT, *et al.* (2005) Effect size estimates of lifestyle and dietary changes on all-cause mortality in coronary artery disease patients: a systematic review. *Circulation* **112**, 924–934.
- Tholstrup T (2006) Dairy products and cardiovascular disease. *Curr Opin Lipidol* **17**, 1–10.
- Tucker KL (2004) Dietary intake and coronary heart disease: a variety of nutrients and phytochemicals are important. *Curr Treat Options Cardiovasc Med* **6**, 291–302.
- Abbott RD, Curb JD, Rodriguez BL, *et al.* (1996) Effect of dietary calcium and milk consumption on risk of thromboembolic stroke in older middle-aged men: The Honolulu Heart Program. *Stroke* **27**, 813–818.

32. He K, Merchant A, Rimm EB, *et al.* (2003) Dietary fat intake and risk of stroke in male US healthcare professionals: 14-year prospective cohort study. *Br Med J* **327**, 777–782.
33. Iso H, Hennekens CH, Stampfer MJ, *et al.* (1999) Prospective study of aspirin use and risk of stroke in women. *Stroke* **30**, 1764–1771.
34. Al-Delaimy WK, Rimm E, Willett WC, *et al.* (2003) A prospective study of calcium intake from diet and supplements and risk of ischaemic heart disease among men. *Am J Clin Nutr* **77**, 814–818.
35. Bostick RM, Kushi LH, Wu Y, *et al.* (1999) Relation of calcium, vitamin D and dairy food intake to ischaemic heart disease mortality among postmenopausal women. *Am J Epidemiol* **149**, 151–161.
36. Elwood PC, Pickering JE, Fehily AM, *et al.* (2004) Milk drinking, ischaemic heart disease and ischaemic stroke I. Evidence from Caerphilly cohort. *Eur J Clin Nutr* **58**, 711–717.
37. Gartside PS, Wang P & Glueck CJ (1998) Prospective assessment of coronary heart disease risk factors: the NHANES I epidemiologic follow-up study (MHEFS) 16-year follow-up. *J Am Coll Nutr* **17**, 263–269.
38. Hu FB, Stampfer MJ, Manson JE, *et al.* (1999) Dietary saturated fats and their food sources in relation to the risk of coronary heart disease in women. *Am J Clin Nutr* **70**, 1001–1008.
39. Mann JI, Appleby PN, Key TJ, *et al.* (1997) Dietary determinants of ischaemic heart disease in health conscious individuals. *Heart* **78**, 450–455.
40. Menotti A, Kromhout D, Blackburn H, *et al.* (1999) Food intake patterns and 25-year mortality from coronary heart disease: cross cultural correlations in the Seven Countries Study. *Eur J Epidemiol* **15**, 507–515.
41. Ness AR, Davey Smith G & Hart C (2001) Milk, coronary heart disease and mortality. *J Epidemiol Community Health* **55**, 379–382.
42. Shaper AG, Wannamethee G & Walker M (1991) Milk, butter and heart disease. *Br Med J* **302**, 785–786.
43. Snowdon DA, Phillips RL & Fraser GE (1984) Meat consumption and fatal ischemic heart disease. *Prev Med* **13**, 490–500.
44. Umesawa M, Iso H, Date C, *et al.* (2006) Dietary intake of calcium in relation to mortality from cardiovascular disease: The JACC Study. *Stroke* **37**, 20–26.
45. Van der Vijver LPL, van der Waal MAE, Weterings KGC, *et al.* (1992) Calcium intake and 28-year cardiovascular and coronary heart disease mortality in Dutch civil servants. *Int J Epidemiol* **21**, 36–39.
46. Kelemen LE, Kushi LH, Jacobs DR Jr, *et al.* (2005) Associations of dietary protein with disease and mortality in a prospective study of postmenopausal women. *Am J Epidemiol* **161**, 239–249.
47. Elwood PC, Strain JJ, Robson PJ, *et al.* (2005) Milk consumption, stroke, and heart attack risk: evidence from the Caerphilly cohort of older men. *J Epidemiol Community Health* **59**, 502–505.
48. Appleby PN, Thorogood M, Mann JI, *et al.* (1999) The Oxford Vegetarian Study: an overview. *Am J Clin Nutr* **70**, Suppl. 3, 525S–531S.
49. Walker M, Whincup PH & Shaper AG (2004) The British Regional Heart Study 1975–2004. *Int J Epidemiol* **33**, 1185–1192.
50. McGee DL, Reed DM, Yano K, *et al.* (1984) Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Relationship to nutrient intake. *Am J Epidemiol* **119**, 667–676.
51. Moss M & Freed D (2003) The cow and the coronary: epidemiology, biochemistry and immunology. *Int J Cardiol* **87**, 203–216.
52. Sanchez-Villegas A, Martinez JA, Prattala RS, *et al.* (2003) A systematic review of socioeconomic differences in food habits in Europe: consumption of cheese and milk. *Eur J Clin Nutr* **57**, 917–929.
53. Lopez-Azpiazu I, Sanchez-Villegas A, Johansson L, *et al.* (2003) Disparities in food habits in Europe: systematic review of educational and occupational differences in the intake of fat. *J Hum Nutr Diet* **16**, 349–364.
54. Prattala RS, Groth MV, Oltersdorf US, *et al.* (2003) Use of butter and cheese in 10 European countries: a case of contrasting educational differences. *Eur J Public Health* **13**, 124–132.
55. Tholstrup T, Hoy C-E, Andersen LN, *et al.* (2004) Does fat in milk, butter and cheese affect blood lipids and cholesterol differently? *J Am Coll Nutr* **23**, 169–176.
56. Sun Q, Ma J, Campos H, *et al.* (2007) Plasma and erythrocyte biomarkers of dairy fat intake and risk of ischemic heart disease. *Am J Clin Nutr* **86**, 929–937.
57. Agerholm-Larsen L, Bell ML, Grunwald GK, *et al.* (2000) The effect of a probiotic milk product on plasma cholesterol: a meta-analysis of short-term intervention studies. *Eur J Clin Nutr* **54**, 856–860.
58. Jauhiainen T & Korpela R (2007) Milk peptides and blood pressure. *J Nutr* **137**, 3 Suppl. 2, 825S–829S.
59. Groziak SM & Miller GD (2000) Natural bioactive substances in milk and colostrum: effects on the arterial blood pressure system. *Br J Nutr* **84**, Suppl. 1, S119–S125.
60. Liu E, McKeown NM, Newby PK, *et al.* (2009) Cross-sectional association of dietary patterns with insulin-resistant phenotypes among adults without diabetes in the Framingham Offspring Study. *Br J Nutr* (Epublication ahead of print version 16 February 2009).