Review

The Survival Advantage of Milk and Dairy Consumption: an Overview of Evidence from Cohort Studies of Vascular Diseases, Diabetes and Cancer

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Objectives: To conduct a detailed evaluation, with meta-analyses, of the published evidence on milk and dairy consumption and the incidence of vascular diseases and diabetes. Also to summarise the evidence on milk and dairy consumption and cancer reported by the World Cancer Research Fund and then to consider the relevance of milk and dairy consumption to survival in the UK, a typical Western community. Finally, published evidence on relationships with whole milk and fat-reduced milks was examined.

Methods: Prospective cohort studies of vascular disease and diabetes with baseline data on milk or dairy consumption and a relevant disease outcome were identified by searching MEDLINE, and reference lists in the relevant published reports. Meta-analyses of relationships in these reports were conducted. The likely effect of milk and dairy consumption on survival was then considered, taking into account the results of published overviews of relationships of these foods with cancer.

Results: From meta-analysis of 15 studies the relative risk of stroke and/or heart disease in subjects with high milk or dairy consumption was 0.84 (95% CI 0.76, 0.93) and 0.79 (0.75, 0.82) respectively, relative to the risk in those with low consumption. Four studies reported incident diabetes as an outcome, and the relative risk in the subjects with the highest intake of milk or diary foods was 0.92 (0.86, 0.97).

Conclusions: Set against the proportion of total deaths attributable to the life-threatening diseases in the UK, vascular disease, diabetes and cancer, the results of meta-analyses provide evidence of an overall survival advantage from the consumption of milk and dairy foods.

INTRODUCTION

Most mammals stop drinking milk soon after weaning. In mammals generally, and in some human races the gene for the enzyme lactase gets switched off in most individuals and the ability to digest lactose, the sugar in milk, is lost. In Northern Europeans, however, the gene remains active in most people and well over 90% can digest lactose throughout life and consequently consume relatively high quantities of milk [1].

As early as 1965 striking racial differences in the prevalence of lactose malabsorption were noted [2]. A "geographic hypothesis' was proposed, based on "random genetic drift. . . or some other process of selection independent of dairying, which led certain communities to take up dairying and the use of milk as food'. The "aberrant' persons'. . .would then enjoy a significant selective advantage' [3]. In addition to a survival advantage, it was suggested that lactose absorbers might have experienced a small breeding advantage.

Support for all this was recently obtained in an archaeological dig. DNA samples were obtained from 55 bone samples belonging to eight Neolithic subjects dated to around 5500 BC.

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The mutation in the lactase gene was found to be absent, suggesting that the ability to digest lactose and hence to consume virtually unlimited quantities of milk, probably developed within the past seven thousand years [4]. The high prevalence of the mutation within Northern European communities is consistent with it having conferred a considerable survival advantage. However, even if the mutation in the lactase gene did confer advantages to primitive man, modern man has such a different diet and different environment that it could well be that milk consumption no longer carries any survival or breeding advantage.

The possible health benefits of milk, if any, could best be tested in randomised controlled trials. No adequate trials have been reported nor are ever likely to be done, so the best evidence on the present day associations between milk and dairy consumption, and health and survival, comes from cohort studies. We report the results of a literature search for prospective cohort and case-control studies of milk and dairy consumption as predictors of vascular disease and diabetes and meta-analyses of the results in the papers identified. We then summarise the conclusions of the recent report by the World Cancer Research Fund and American Institute for Cancer Research [5], and finally we examine the evidence related to consumption of whole vs. reduced fat milks and consider the likely effect of milk and dairy consumption on survival.

MATERIALS AND METHODS

Data Used

Using Cochrane systematic review methods [6] the computerised database MEDLINE was searched up to June 2008. Each search was limited to human/adult. The key words Milk/milk protein/dairy/dairy calcium produced 11,102 hits. Heart disease/coronary artery disease/myocardial infarction/ischaemic heart disease produced 125,572 hits, and stroke produced 61,878 hits. Diabetes/metabolic syndrome gave 58,473 hits. Combined, these gave 180 papers on milk etc. and heart disease etc, 33 papers on milk and stroke and 111 on milk and diabetes. These were all examined and those, which were population based and prospective, and gave baseline data on milk or dairy consumption, together with a vascular disease outcome, or incident diabetes, were accepted for review. The references listed in each of these selected papers were also searched for other suitable reports. For heart diseases 11 papers were found to be relevant and to contain the data necessary for inclusion in a meta-analysis; for stroke seven and for diabetes four papers. Cross sectional case-control papers were also identified for the metabolic syndrome (four papers) and for myocardial infarction four.

Meta-analysis

Reported adjusted relative risks (RR) given in each paper were noted. We obtained pooled estimates of the RR by weighting the natural logs of the reported RR in each report by the inverse of the variance, as described by Gao et al. [7]. Where variance was not estimable from confidence intervals, the standard error from a study of similar size was used. However results are reported excluding studies with estimates. We present no original evidence on milk/dairy consumption and cancer, but we summarise the results given in a recent major international report [5]. In order to estimate the effect of milk/dairy consumption on survival, we relate the data on disease risks to data on mortality in a major part of the UK (England and Wales) from the various life-shortening diseases considered, i.e. vascular disease, diabetes and cancer. Finally, in the examination of papers, which we describe above, studies which give disease risks in relation to the type of milk, whole or fat-reduced, within the same cohort, were examined.

RESULTS

Vascular Disease

Cardiovascular Risk Factors. Much has been written on the associations between consumption of milk and dairy products and individual vascular risk factors. Many studies have given evidence of a rise in total, or low-density lipoprotein cholesterol level following the consumption of milk or dairy foods [8,9]. There is however less evidence to judge the extent to which this is balanced by the concomitant increase in the concentration of high density lipoprotein cholesterol [10,11] together with a lower blood pressure, which is associated with milk consumption [12,13]. Furthermore, milk is a complex food containing numerous nutrients, many of which are likely to be relevant to biological mechanisms involved in vascular and other diseases, and it is unreasonable to base conclusions about health and disease from effects on a single mechanism.

On the other hand, a number of published studies have examined milk or dairy consumption and the so-called metabolic syndrome, which is the occurrence together of raised levels of blood glucose or plasma insulin, serum lipids, body mass index and blood pressure [14]. These risk factors, however they are combined in the metabolic syndrome, are together very strongly predictive of Type 2 diabetes and of ischaemic heart disease [15]. Table 1 summarises data from four large population based studies of milk and dairy consumption and the metabolic syndrome [16–19] together with a meta-analysis. This last indicates a reduction in the metabolic syndrome in the subjects with the highest milk consumption (RR and 95% confidence limits: 0.74; 0.64, 0.84).

Unfortunately the report of the Bogalusa study [20] does not give adequate data for this study to be included in our meta-analysis. In this study, 142 of 1,181 young subjects in a

Table 1. Case Control Studies of Milk Drinking and the Metabolic Syndrome

Study	Total number of subjects	Dietary item	Groups compared	Number with the syndrome	Adjustments for possible confounding	Adjusted RR[1] in high milk subgroups
Mennen et al. [16]	2,439 Males	Dairy	Four or more portions/day vs less than one/day	660	Age, energy, waist-hip ratio.	0.63 (0.40–0.99)[2]
	2,537 Females			941		0.76 (0.47–2.66)[3]
Azadbakht et al. [17]	827 Subjects	Dairy	Top and bottom quartile	97	Age, sex, activity, smoking, BMI, waist/hip ratio, energy, various foods, antihypertensive and oestrogen therapy	0.75 (0.63–0.96)
Liu et al. [18]	10,066 Females	Milk Dairy	Top and bottom quintile	1,731	Age, smoking, exercise, alcohol multivitamins parental MI	0.85 (0.71–1.02)[4] 0.66 (0.55–0.80)[5]
Elwood et al. [19]	2,251 Males	Milk	One pint/day vs. under a third/day	342	Age, smoking, social class, IHD, BMI, energy, alcohol, fasting total cholesterol HDL cholesterol and triglycerides	0.38 (0.18–0.78)
SUMMARY ESTIMATE: Relative risk of the metabolic syndrome in the high milk group 0.74 (95% CI 0.64–0.84)						

[1] Relative risk (95% Confidence Interval).
[2] Males.
[3] Females.
[4] Milk.
[5] Dairy.

population sample were judged to have the syndrome, and the dairy foods consumption of these (0.52 ± 0.10 servings) was significantly less than that of 468 subjects with no evidence of the syndrome (0.73 ± 0.05).

The studies in Table 1 are cross-sectional. The results are however consistent with findings in the prospective CARDIA study [21] in which 3,157 young people were followed for ten years. Among 923 individuals judged to be overweight at base-line (body mass index ≥25 kg/m^2), the odds of developing the metabolic syndrome within ten years was 0.28 (0.14, 0.58) in those with the highest dairy intake relative to those with the lowest intakes. There was no distinction between black and white races or between males and females. Each daily helping of dairy foods was estimated to be associated with a 21% lower odds of developing the syndrome. Using a different approach, Ma et al. [22], examined insulin sensitivity directly in a prospective study based on 1,036 US adults. They found a higher insulin sensitivity with increased dairy intake, though significance was lost after adjustment for demographic factors.

In contrast to the above is the finding on the metabolic syndrome reported from the British Women's Heart and Health Study [23] amongst whom 111 women (only 2.8% of the total cohort) reported that they never drank milk. These had a low odds ratio for the metabolic syndrome (0.55; 0.33–0.94), relative to 3,913 women who drank milk. The three percent of women who drink no milk were however unusual, and are unlikely to be representative of any meaningful group within the general population.

Overall, the data on the metabolic syndrome suggest a reduced incidence from milk and dairy consumption. Yet again, however, data on associations, whether based on a single, or a group of risk factors such as the metabolic syndrome, is a most uncertain basis for conclusions about health or disease risk in the general community, especially with a complex food such as milk.

Ischaemic Heart Disease. Evaluation in terms of disease outcomes has enormous advantages over the use of risk factors as predictors of disease. There are a number of research strategies and we present data from case-control comparisons, and from prospective cohort studies.

In case-control studies patients who have experienced an acute vascular event were asked about their prior consumption of milk and/or dairy foods, and their answers were compared with answers from "control' subjects who have had no vascular event.

Gramenzi et al. [24] questioned 287 women admitted to hospital during 1983–9 with acute myocardial infarction (MI) and 649 control women admitted with other acute disorders, about the frequency and amount of various foods consumed prior to the onset of symptoms of infarction. Tavani et al. [25] based a similar study on 507 patients with acute MI, Lockheart et al. [26] studied 106 patients and Biong et al [27] reported on 111 patients. Results from these studies are summarised in Table 2 and a meta-analysis gives an overall risk of MI associated with milk consumption of 0.83 (0.66–0.99). This estimate of risk is however of limited value as the case-control strategy is open to a number of possible biases, not least differences in the recall of patients and controls.

In prospective cohort studies a dietary or other possible

Table 2. Summary of Case-Control Studies of Milk and Myocardial Infarction (MI)

Study	Dietary item	No. of cases	No. of controls	RR[1]
Gramenzi et al. [24]	Milk intake	287	649	0.90
Tavani et al. [25]	Milk intake	507	478	0.78 (0.54–1.12)
Lockheart et al. [26]	Dairy intake	106	105	0.82 (0.58–1.16)
Biong et al. [27]	Dairy fat intake	111	107	0.67 (0.24–1.83)
SUMMARY ESTIMATES: RR of MI in the high milk group 0.83 (95% CI 0.66–0.99)				
(Excluding Gramenzi et al. [24] with estimated variance 0.79 (0.59–0.99)				

[1] Relative risk (95% Confidence Interval).

determinant, such as milk and/or dairy consumption, is recorded at base-line for a large cohort and the subjects are then followed forward in time and new, incident disease events are noted. The risk of an event can then be compared in sub-groups of subjects defined by levels of the predictive factor of interest.

Table 3 gives a summary of data relevant to milk/dairy consumption and vascular disease in the papers identified in the literature search we described above [28–42]. Together these studies included over six hundred thousand subjects (over eight million man-years of observation) of whom over seventeen thousand had an incident ischaemic heart disease or stroke event during follow-up.

Table 4 summarises the results of meta-analyses of these studies. Overall there was a reduction of about 10 to 15% in the incidence of heart disease in the subjects who had reported drinking the most milk, relative to those drinking the least milk.

There is a difficulty with the data from Hu et al [34]. While the relative risk estimate given for low-fat milk (0.78; 0.63–0.96) is consistent with all the other risk estimates, that for whole milk (1.67; 1.14–1.90) is significantly heterogeneous with most of the other estimates of association shown in the table. Furthermore, as we indicate in a footnote to Table 4, the inclusion of the estimate of Hu et al. [34] for whole milk in the meta-analysis introduces marked heterogeneity, and the meta-analysis strictly becomes unacceptable. The best estimate of the overall association between milk/dairy and ischaemic heart disease is therefore 0.84 (0.76–0.93) obtained by including the estimate by Hu et al. [34] for low-fat milk but omitting their estimate for whole milk.

Stroke. In seven studies, stroke was the outcome, and 5,787 strokes occurred during the follow-up periods. The meta-analysis indicates about a 20% reduction in stoke events in the subjects who had reported drinking the most milk, relative to those drinking the least milk within each cohort. Two studies give separate evidence on haemorrhagic and ischaemic strokes. Kinjo et al. [33] estimate the relative risk in the high milk drinking group to be 0.74 (0.68–0,80) for haemorrhage and 0.85 (0.77–0.92) for ischaemic stroke, both significant, and Umesawa et al. [42] estimated the risks in the top quintile of dairy calcium intake to be 0.46 (0.23–0.91) and 0.53 (0.29–0.99) respectively, again both significant.

All the cohort studies included in Table 4 were based either on answers about milk/dairy consumption in a food frequency questionnaires, or details included in a 24-hour diet recall interview and in some of the studies these data had been obtained from postal returns [34,41]. However, in one of the studies [36] a sub-group of 665 men completed 7-day weighed dietary intake records and these were checked by interview at baseline [43]. This enabled the estimation of total milk intake from milk drunk, milk used in cooking and powdered milk included in recipes. The follow-up results from this cohort are consistent with the above showing a RR for ischaemic heart disease of 0.88 (0.56, 1.40), and for stroke, 0.82 (0.76, 0.88).

The cohort strategy is powerful, but is still open to uncertainties and possible biases from a number of sources, in particular confounding by dietary and other factors apart from milk and dairy consumption. While the relative risk estimates reported for the various studies had all been internally adjusted for confounding (see Table 3), residual confounding is still possible. It does however seem most unlikely that a true harmful effect of milk on vascular disease could have been missed simply because of some important, but as yet unknown, confounding factor(s).

Fatty Acid 15:0. Another approach to the evaluation of dairy products is based on the case-control difference, or the predictive power for heart disease of plasma or tissue levels of the fatty acid 15:0. This fatty acid occurs only in the fat of ruminant mammals and can therefore be used as a marker for dairy fat consumption [44,45]. In 1987 Thomas et al. [46] took adipose tissue from the abdominal wall of 59 men within a major cohort who had experienced a "silent' MI (EKG evidence of infarction with no relevant symptoms). The concentrations of C15:0 in these differed by only 0.01 (SE 0.02) from the levels in adipose tissue taken from 61 matched control men [46]. In another case-control study, the odds for MI were between 0.79 and 0.72 for one SD increase in serum C15.0, though significance was lost on adjustment for clinical factors including blood pressure [47]. In another case-control study [48] the odds ratio for MI were significantly reduced (0.36; 0.13, 0.99) in subjects within the top quartile of adipose tissue C15.0 levels.

These results give no evidence of harm attributable to the fat in milk and dairy foods but in contrast Qi Sun et al. [49] made estimations of C15:0 on samples of plasma taken at base-line from 166 women within the Nurses' Health Study cohort who later experienced an ischaemic heart disease event, and from

Table 3. Prospective Cohort Studies on Milk/Dairy Consumption and Incident Vascular Disease Events

Study	No. of subjects	Duration of follow-up	No. of events	Groups compared	Adjustments for possible confounding
Milk and Dairy Foods					
Snowdon et al. [28]	24,172 Subjects	20 years	758 male IHD deaths 841 female IHD deaths	Two glasses of milk/ day vs none	Age, smoking and other food items, weight, marital status
Shaper et al. [29]	7,735 Males	9.5 years	608 IHD events	Milk drunk and taken on cereals vs none	Age, social class, smoking, cholesterol, blood pressure and diabetes.
Abbott et al. [30]	3150 Males	22 years	229 strokes	16oz/day milk drunk vs. non-drinkers	Age, dietary K and Na, alcohol, smoking, activity, cholesterol and glucose, uric acid and haematocrit
Mann et al. [31]	10,802 Vegetarian subjects	13 years	63 IHD deaths	More than 1/2 pint milk per day vs less than 1/2 pt	Age, sex, smoking, social class
Bostick et al. [32]	34,486 Females	8 years	387 IHD deaths	Top and bottom quartile	Age, energy, BMI, waist-hip ratio, diabetes, smoking, Vit. E, saturated fat,
Kinjo [33]	223,170 Subjects	15 years	11,030 strokes	Milk four or more times/week vs less than once/week	Sex, age, area, smoking, alcohol, occupation
Hu et al. [34]	80,082 Females	14 years	939 vascular events	More than two glasses of milk/day vs less than one glass per week	Time period, BMI, smoking, menopause, parental history, vit E, alcohol, hypertension, aspirin use, exercise
Ness et al. [35]	5,765 Males	25 years	892 IHD deaths 198 stroke deaths	More than one pint/day vs less than one third/day	Social class, health behaviour and health status.
Elwood et al. [36]	2,512 Males	20 years	493 IHD events	One or more pint/day vs one third of a pint or less/day	Age, smoking, social class, IHD, BMI, energy, alcohol, fasting cholesterol, HDL cholesterol and triglycerides
Sauvaget et al. [38]	40,349 Subjects	16 years	185 strokes 1,462 stroke deaths	Milk almost daily	Smoking, alcohol, BMI, education, diabetes, hypertension, area
Lamarche [37]	2,000 Males	13 year	217 IHD events	Dairy almost daily Above and below average intake of dairy products	Age, smoking, BMI, diabetes
Dairy or Total Dietary Calcium Intake					
Vijvjer et al. [39]	2,606 Subjects	28 years	366 male IHD deaths 178 female IHD deaths	Top and bottom quintile	Age, smoking, BMI, systolic BP, cholesterol, energy, alcohol
Iso et al. [40]	85,764 Females	14 years	690 strokes	Top and bottom quintile	Age, smoking, time interval, BMI, alcohol, menopause, hormone use, exercise, multivitamins, fatty acid intake, history of hypertension, diabetes and cholesterol
Al-Delaimy et al. [41]	39,800 Males	12 years	1,458 IHD events	Top and bottom quintile	Age, duration, energy, diabetes, hyperchol., family history, smoking, aspirin, BMI, alcohol, activity, vit E, various nutrients
Umesawa et al. [42]	21,068 Males 32,319 Females	10 years	234 IHD deaths 566 stroke deaths	Top and bottom quintile of dairy calcium intake	Age, BMI, hypertension, diabetes, smoking, alcohol, potassium, energy

Table 4. Meta-analysis of Prospective Studies of Milk and Dairy Consumption, Ischaemic Heart Disease and Stroke

Study	Number of subjects	Number of events	Predictive factor	Adjusted RR (95% CI)
Ischaemic heart disease				
Snowdon et al. [28] (males)	8,724	758	Milk	0.94
(females)	15,448	841		1.11
Shaper et al. [29]	7,735	608	Milk	0.88 (0.55–1.40)
Mann et al. [31]	10,802	63	Milk	1.50 (0.81–2.78)
Bostick et al. [32]	34,486	387	Milk	0.94 (0.66–1.35)
Hu et al. [34]	80,082	939	Whole milk	1.67 (1.14–1.90)
			Low-fat milk	0.78 (0.63–0.96)
			High-fat dairy	1.04 (0.96–1.12)
			Low-fat dairy	0.93 (0.85–1.02)
Ness et al. [35]	5,765	892 deaths	Milk	0.68 (0.40–1.13)
Elwood et al. [36]	2,512	493	Milk	0.71 (0.40–1.26)
Al Delaimy et al. [41]	39,800	1,458	Dairy calcium	1.03 (0.86–1.26)
Van Vijjver et al. [39]			Dietary	
(males)	1,340	366	calcium	0.77 (0.53–1.11)
(females)	1,265	178		0.91 (0.55–1.50)
Lamarche [37]	2,000	217	Dairy intake	0.73 (0.56–0.93)
Umesawa [42]	53,387	234 deaths	Dairy calcium	0.80 (0.45–1.44)
Stroke				
Kinjo et al. [33]	223,170	11,030	Milk	0.79 (0.75–0.83)
Ness et al. [35]	5,765	196 deaths	Milk	0.84 (0.31–2.30)
Sauvaget et al. [38]	40,349	1,462	Milk	0.94 (0.79–1.12)
			Dairy products	0.73 (0.57–0.94)
Elwood et al. [36]	2,512	185	Milk	0.66 (0.24–1.81)
Abbott et al. [30]	3,150	229	Dairy calcium	0.67 (0.45–1.00)
Iso et al. [40]	85,764	690	Dairy calcium	0.83 (0.66–1.04)
Umesawa [42]	53,387	566 deaths	Dairy calcium	0.53 (0.34–0.81)
SUMMARY ESTIMATES:				
RR of IHD in the high milk group, including Hu et al. [34] whole milk: 0.91 (95% CI 0.82–1.00), see note 1 below (Excluding Snowdon et al. [28] with estimated variance: 0.90 (0.80–0.99))				
RR if IHD in the high milk group, including Hu et al low fat milk: 0.84 (95% CI 0.76–0.93) see note 2 and 3 (Excluding Snowdon et al. [28] with estimated variance: 0.83 (0.74–0.91))				
RR of stroke in the high milk group: 0.79 (95% CI 0.75–0.82)				

1. When the estimates of Hu et al. [34] of 1.67 for whole milk is included there is considerable heterogeneity: (I^2 = 54.1%).
2. There is homogeneity when their estimate of 0.78 for low fat milk is used in the meta-analysis.
3. The estimates by Hu et al. [34] for dairy foods were not included in the meta-analyses.

327 control women. The adjusted risk for heart disease in the third of women with the highest plasma C15:0 levels, relative to that in the third of women with the lowest levels, was 2.36 (1.16, 3.89). This result is remarkable, implying a very high vascular risk from dairy consumption in one third of women. It has however been challenged [50].

Diabetes

Four prospective cohort studies have reported the incidence of Type 2 diabetes in relation to milk and dairy consumption [19,51–53] (Table 5). Together these show that the relative risk for Type 2 diabetes is almost 10% lower in people who had had a high milk intake (0.92; 0.86–0.97). The authors of the two larger studies [51,52] estimated that each daily serving of dairy foods was associated with an annual reduction in diabetes incidence of 9% and 4% respectively.

Cancer

The literature on milk/dairy consumption and cancer is extensive. However, unlike vascular disease, the majority of the evidence comes from case-control comparisons, and only a few studies have been prospective. Furthermore, few reports give sufficient information for inclusion in meta-analyses. A detailed examination of this evidence is beyond the scope of this review, and we therefore summarise in Table 6 the relevant findings in the recent report of the World Cancer Research Fund [5].

An increased consumption of milk or dairy foods is associated with a significant reduction in colon cancer, the relative risk attributable to milk being between about 0.78 and 0.94 per serving per day in pooled cohort studies. On the other hand, there is a significantly increased risk of prostate cancer, the risk associated with milk and dairy consumption in pooled cohort studies being 1.06 (1.01, 1.11) per serving per day. Case-control studies suggest

Table 5. Prospective Studies of Milk/Dairy Consumption and Incident Diabetes

Study	Number of subjects	Duration of follow-up	Groups compared	Number who developed diabetes	Adjustments for possible confounding	Adjusted RR[1]
Choi et al. [51]	41,254 Males	12 years	Top and bottom quintiles of total dairy	1,243	Age, total energy, follow-up time, family history, smoking, BMI, hypercholest., hypertension, activity, alcohol, certain nutritional factors	0.91 (0.85–0.97)
Liu et al. [52]	37,183 Females	10 years	Two or more servings of dairy foods per week vs less than one serving per month	1,603	Age, total energy, diabetes in family, smoking, BMI, hypercholesterolaemia, hypertension, hormone therapy, activity, total fat, glycaemic load, diet Ca, vit D, Mg	1.04 (0.84–1.30)[2] 0.92 (0.78–1.09)[3]
Van Damm et al. [53]	41,186 Females	8 years	Quintiles of dietary calcium intake	1,964	Age, total energy, BMI, smoking, physical activity, alcohol, parental diabetes, education, coffee and soft drinks, processed and red meat.	0.93 (0.75–1.15)
Elwood et al. [19]	640 Males	20 years	Highest quartile of milk intake vs. lowest quantile	41	Age, smoking, BMI, social class	0.57 (0.20–1.63)
SUMMARY ESTIMATES: Relative risk of incident diabetes in the high milk group 0.92 (0.86–0.97) (using the estimate by Liu et al. [52] for low-fat milk 0.91 (0.86–0.96)						

[1] Relative risk (95% Confidence Interval).

[2] Whole milk.

[3] Skimmed milk.

Table 6. Summary of Relationships between Milk/Dairy Consumption and Cancer Taken From the Report of the World Cancer Research Fund [5]

Cancer	Predictor	No. of studies	Pooled relative risk[1]	Heterogeneity
Colorectal	Milk	4 cohorts	0.94 (0.85–1.03)	'low'
	Milk	10 cohorts	0.78 (0.69–0.88)	Not state
Prostate	Milk	8 cohorts	1.05 (0.98–1.14)	'low'
	Milk	6 case-control	1.08 (0.98–1.19)	'moderate'
	Milk and dairy	8 cohorts	1.06 (1.01–1.11)	'moderate'
	Milk and dairy	5 case-control	1.03 (0.99–1.07)	'low'
Bladder	Milk	4 cohorts	0.82 (0.67–0.99)	'moderate'
	Milk	3 case control	1.00 (0.87–1.14)	'high'

[1] ñ

that these foods may also be associated with an increased risk of bladder cancer, though the estimate of risk from pooled cohort studies is 0.82 (0.67, 0.99) per serving per day. No relationship of importance was reported for any other cancer.

Whole and Fat-Reduced Milks

A number of studies give results for whole milk and for fat-reduced milks. Details from those, which were noted during the literature searches described above [18,25,26, 34,51–60] are listed in Table 7. In each of these studies the pairs of data indicating the disease risks associated with the two types of milk are derived from the same cohort, and have been adjusted within each study for a number of confounding factors.

Nevertheless, persons who choose to drink fat-reduced milks will almost certainly have adopted other "healthy' behaviours, and these will undoubtedly be responsible for further confounding. These other factors cannot all be known, but they will be responsible for biases, which cannot possibly be estimated or allowed for. No reasonable conclusions can therefore

Table 7. Relationships with Whole Milk and Fat Reduced Milks Compared

Study	Total number in the study	Type of study	Outcome disease	RR in highest 1/4 or 1/5	
				Whole milk (1) High fat dairy (3)	Fat reduced (2) Low fat dairy (4)
Hu et al. [34]	80,082 Females	Prospective	Ischaemic heart disease	1.67 (1.14–1.90)[1]	0.78 (0.63–0.96)[2]
				1.08 (0.96–1.12)[3]	0.82 (0.85–1.02)[4]
Tavani et al. [25]	985 Subjects	Case-control	Fatal MI	0.89 (0.57–1.38)[1]	0.83 (0.59–1.16)[2]
Lockheart et al. [26]	211 Subjects	Case/control	Myocardial infarction	0.48 (0.20–1.14)[3]	0.96 (0.42–2.23)[4]
Lui et al. [18]	10,066 Females	Cross sectional	Metabolic syndrome	0.71 (0.58–0.87)[3]	0.78 (0.64–0.95)[4]
Choi et al. [51]	41,254 Males	12 years prospective	Diabetes	1.19 (1.00–1.43)[1]	0.95 (0.80–1.13)[2]
Liu et al. [52]	37,183 Females	10 years prospective	Diabetes	1.00 (0.96–1.05)[3]	0.92 (0.84–1.01)[4]
Van Dam et al. [53]	41,186 Females	8 years prospective	Diabetes	1.03 (0.88–1.20)[3]	0.87 (0.76–1.00)[4]
Mettlin et al. [54]	2,561 Subjects	Case control	Colon cancer	1.8; 1.3–2.4[1]	1.0 (0.7–1.4)[2]
			Rectal cancer	2.0; 1.4–2.8[1]	0.8 (0.5–1.3)[2]
			Prostate cancer	1.5; 1.0–2.2[1]	1.2 (0.7–2.1)[2]
			Bladder cancer	2.0; 1.3–3.1[1]	0.6 (0.3–1.2)[2]
Veierod et al. [55]	25,708 Males	9–15 years prospective	Prostate cancer	Set at 1.0[1]	2.2 (1.3–3.7)[2]
Sing & Frazer [56]	32,051 Subjects	6 years prospective	Colon cancer	1.04 (0.69–1.59)[1]	0.97 (0.66–1.42)[2]
Michaud et al. [57]	51,529 Males	10 year Prospective	Prostate cancer	1.12 (0.70–1.8)[1]	1.37 (0.90–1.5)[2]
Kampman et al. [58]	16,945 Subjects	Case control	Colon cancer	1.1 (0.8–1.5)[3,5]	0.8 (0.6–1.0)[4,5]
				0.9 (0.6–1.2)[3,6]	0.7 (0.5–1.0)[4,6]
Tseng et al. [59]	3,612 Males	Prospective	Prostate cancer	0.8 (0.5–1.3)[1]	1.5 (1.1–2.2)[2]
Gallus et al. [60]	3,247 Subjects	Case control	Colon cancer	0.99 (0.86–1.13)[1]	0.84 (0.73–0.97)[2]
			Rectum cancer	1.22 (1.03–1.44)[1]	0.76 (0.64–0.91)[2]
			Prostate cancer	1.06 (0.90–1.25)[1]	1.11 (0.94–1.31)[2]

[1] Whole milk.
[2] Low-fat milk.
[3] High fat dairy.
[4] Low-fat dairy.
[5] Males.
[6] Females.

be based on these data and we refrain from conducting any kind of meta-analysis or summary statistics.

Survival Advantage of Milk/Dairy Consumption

Fig. 1 shows the relative disease risks in relation to milk and dairy consumption together with an indication of the numbers of deaths in England and Wales in 2005 [61].

We have not attempted to estimate an overall quantitative survival advantage as this would require a number of major assumptions as to the nature of the various relationships and their independence. Clearly however, once the numbers of deaths from the various causes are taken into account, there is evidence which is highly suggestive of an overall reduction in the number of deaths and hence an increase in survival attributable to the consumption of milk and dairy foods.

DISCUSSION

Vascular disease, diabetes and cancer are the major causes of death, and they represent the main limitations to survival. The overviews, which we have presented for these diseases give fairly convincing evidence of a beneficial effect of milk and dairy consumption on health and survival. More conclusive evidence would of course come from randomised controlled intervention trials, but no such studies have been reported and none is ever likely to be attempted because of the numbers of subjects required and the compliance necessary for a randomised trial of adequate power. Results from cohort studies therefore represent the best evidence available at present and likely to be available for the foreseeable future.

We have chosen to consider reports on relationships with milk together with reports on dairy foods, dietary calcium, and in one paper, total dietary calcium. We accept that it would be more informative to consider individual dairy foods separately, and we accept that the combining of data on foods together with data on calcium, may have introduced some uncertainties. We have however checked for heterogeneity between different markers of milk intake by sensitivity analyses, commencing with studies of milk alone and then adding data from studies of dairy foods, dietary calcium and total dietary calcium. No heterogeneity was attributable to different measures of milk

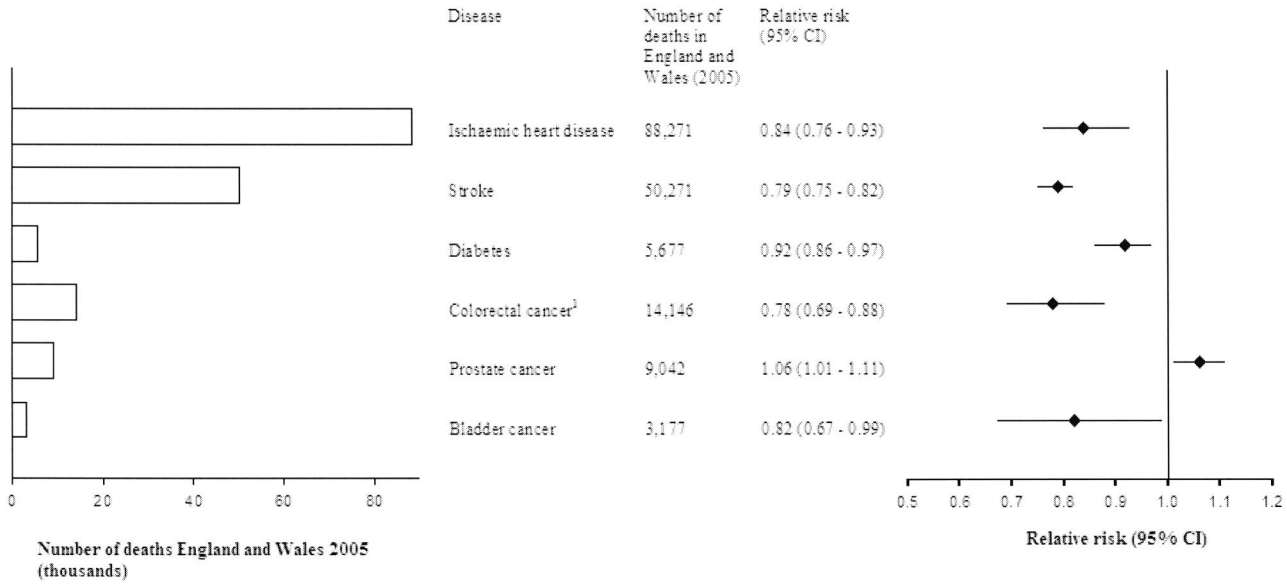

Fig. 1. The numbers of deaths in England and Wales in 2005 from various causes, and the risks for these causes in the subjects with the highest milk/dairy consumption, relative to the risk in the subjects with the lowest milk/diary consumption. RR estimates used for all cancers are those in Table 6, which are statistically significant.

intake and relative risks were very similar if only studies reporting amount of milk drunk were included in analyses.

Unfortunately it is not possible to estimate quantitative relationships for milk and for dairy consumption with any confidence. Within the studies, the quantity of milk defined as high varied. Most studies used quartiles or quintiles of the distribution of intakes, while others defined in terms of "glasses' drunk and others simply accepted the number of occasions on which milk or dairy foods were consumed. Nevertheless, some guidance can be taken from definitions in several of the studies. Thus several studies defined a "high' intake as the consumption of one pint (568 ml) or more per day [30,35,36], others two or more "glasses' per day [28,51], while in the study based on weighed dietary intakes [43], the mean daily consumption of milk in the subjects who showed a reduction in vascular disease and diabetes was over one third of a pint (189 ml).

We present no new evidence on milk/dairy and cancer but in Table 6 we have summarised the relevant findings in the report of the World Cancer Research Fund [5]. The summary statement in that report on colorectal cancer is: "The evidence on milk from cohort studies is reasonably consistent, supported by stronger evidence from dietary calcium as a dietary marker. There is evidence for plausible mechanisms. Milk probably protects against colorectal cancer.' The corresponding statement on prostate cancer is: "The evidence is inconsistent from both cohort and case-control studies. There is limited evidence suggesting that milk and dairy products are a cause of prostate cancer.' Bladder is the only other cancer which the report considers in relation to milk or dairy consumption, and their conclusion is: 'The evidence is inconsistent and comes mainly from evidence on dietary calcium. There is limited evidence suggesting that milk protects against bladder cancer.'

Whatever his intake of milk, primitive man probably had a high intake of salicylates from fruit and vegetables. For modern man a report which, looked for possible synergism between calcium and aspirin is therefore of special interest [62]. This report summarises two randomised trials. In one, subjects who had been randomly assigned to a calcium supplement and declared that they frequently took aspirin or another non-steroidal anti-inflammatory drug (RR 0.35; 95% CI 0.13, 0.96) while in the second, subjects who had been randomised to aspirin and were also taking calcium supplements, had an 80% risk reduction (RR 0.20; 95% CI 0.05, 0.81).

In Fig. 1 we indicate the numbers of deaths in England and Wales from the diseases to which milk and dairy consumption is relevant. Taking the data together, there is evidence clearly suggestive of a reduction in overall mortality, and hence an increase in survival. The impact of milk and dairy consumption on morbidity and hence on health care costs are however likely to be considerable. The economic consequences, which might follow the promotion of milk and dairy foods should there be investigated. There is certainly no evidence that milk consumption might increase deaths from any condition - other than prostate cancer. The relationship with prostate disease is worrying. A number of mechanisms have been suggested and these have been summarised elsewhere [63]. Much has been written on biological mechanisms, which might lead to harm from the consumption of milk [64], but clearly, research should now focus on reasons why milk is beneficial and to identify mechanisms in the metabolism of milk and other dairy products, which are relevant to disease processes.

Questions remain regarding fat-reduced milk. Despite the widespread belief that whole milk is "fattening' and that it increases the risk of vascular disease, the appropriate question to ask is whether or not fat-reduced milks provide any advantage further to the benefits conferred by the consumption of whole milk. Low fat milks were not widely used in the USA until about 1989 and about 2000 in the UK, and a large part of the follow-up periods of most of the cohort studies which we have included in the meta-analyses relate therefore to times when the milk drunk was almost entirely whole milk. The data on vascular disease and diabetes (Tables 3 and 5), and probably that on cancer (Table 6) relate therefore for the most part to whole, full-fat milk. Given the large increase in consumption of fat-reduced milks in recent times, this is an area requiring critical study.

At the same time, the issue of residual confounding by unknown dietary and other 'healthy' behaviours on the part of many or most of those who consume fat-reduced milks makes the evidence from observational studies, such as those listed in Table 7 impossible to interpret with any confidence. In the absence of evidence from large randomised trials the statement of German and Dillard [65] is therefore most apposite: "Such hypotheses (about fat-reduced milks) are the basis of sound scientific debate; however they are not the basis of sound public health policy'.

CONCLUSIONS

The suggestion that milk consumption by primitive man was of relevance to the survival and perhaps the reproductive success of early man [1,2] carries limited direct weight for modern man. Most people in Western communities now have a totally different diet to primitive man and live in a totally different environment. In primitive man the nutritional benefits and advantages of milk consumption and its effects on growth and bone health are likely to have been of considerable importance, while effects on chronic diseases later in life will have had limited relevance to reproduction and survival. Today however, while growth and bone health are of great importance to health and function, it is the effects of milk and dairy consumption on chronic disease incidence that are of the greatest relevance to survival. The analyses we have presented gives fairly clear evidence of a reduction in vascular disease and Type 2 diabetes by milk and dairy consumption. Taken together with the probable reduction in colon cancer and allowing for some increase in prostate cancer there is fairly convincing overall evidence that milk and dairy consumption is associated with an increase in survival in Western communities.

Apart from their effects on plasma lipids and on blood pressure, very little is known about the biological mechanisms likely to be involved in the relationships of milk and dairy foods with human diseases or indeed whether milk can be modified to provide further health advantages. Clearly more work should be done.

There is evidence that milk consumption has fallen greatly over the past 20–25 years in many countries [66–69]. Within the UK the fall has been around one third during the past 25 years. Milk is the main source of calcium and within the UK it has been estimated that 20% of adolescent girls and 10% of boys have less than the recommended intakes of calcium [70]. Furthermore, there is evidence of a marked socio-economic gradient in the decline, the average consumption in households in social classes IV and V being 10–20% lower than that those within households in classes I and II [68]. This gradient in intakes may therefore contribute to health inequalities.

Due to a focus on the small rise in blood cholesterol with milk drinking, the debate on milk has never achieved a reasonable balance in the evaluation of risks and benefits. We believe that the debate about the health risks and benefits of milk and dairy consumption in Western communities should focus on evidence of direct relevance to health and survival, such as we have presented, and this would benefit greatly if it were supported by a concerted and targeted research effort to understand the underlying mechanisms.

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