Introduction

Introduction to the Proceedings of the Symposium "Scientific Update on Dairy Fats and Cardiovascular Diseases"

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The symposium "Scientific Update on Dairy Fats and Cardiovascular Diseases" was held on 25 June 2008 in Reading (UK). The event was hosted by the University of Reading (UK) and organized and facilitated by the International Dairy Federation's Standing Committee on Nutrition and Health. The objectives of this symposium were to provide a reappraisal of the impact of dairy foods and milk fat on cardiovascular diseases (CVD) and to place dairy fat into the context of overall human health.

An adequate supply of good quality food is essential for human health and well-being. It is unsurprising then that ruminant milk and dairy products have been recognised as important human food sources from as early as 4000 B.C. as evidenced by the depiction of dairying in rock drawings from the Sahara and from cheese remains being found in Egyptian tombs dating back to 2300 B.C. [1]. The dairy sector has made continuous advancement over the years and today there is a wide variety of milks and dairy products readily available to the consumer. In response to considerable scientific research on the nutritional value of milk, dietary guidelines around the world have recommended daily consumption of dairy products for the overall health of the population [2]. The important contributions of these products in meeting human dietary requirements for energy, high quality protein and several key minerals and vitamins are well documented [3,4], although the nutritional importance of dairy fats is often less well understood. With the projected growth in world population and the increased demand for animal-derived food products as living standards improve, dairy products will undoubtedly continue to be an important dietary source of nutrients.

Food provides essential nutrients, but there is also growing consumer recognition of the link between diet and health; this awareness impacts food choices. For over half a century, the concept of eating healthy has become synonymous with avoiding dietary fat and cholesterol, especially saturated fat, and on a population basis, a diet low in saturated fat remains at the heart of nutritional advice in many countries for lowering plasma cholesterol and reducing CVD risk. In the case of dairy products, there has been a general perception that a food containing saturated fat is unlikely to be beneficial to health. Yet, over the last decade, evidence has been accumulated that the composition and quantities of dietary fat is very important in determining the relative risk to diseases such as CVD and cancer, and that milk-derived fat may offer significant health benefits compared to some common sources of dietary fats [5–7].

On average bovine milk contains about 33 g total lipid (fat) per litre. Triacylglycerols, which account for about 97% of the lipid fraction, are composed of fatty acids of different carbon chain length (4 to 24 atoms), degree of saturation and positional specificity on the glycerol backbone. Other milk lipids are diacylglycerol (about 2% of the lipid fraction), cholesterol (less than 0.5%), phospholipids (about 1%) and free fatty acids (less than 0.5% of total milk lipids). Milk fat is present as complex globules with structural properties distinct from other biological sources of fats. It is one of the most complex naturally-occurring fats with more then 400 different fatty acids reported, however, only about 20 of these make up approximately 95% of the total [8]. It is important to recognize that a large diversity of dairy foods of widely differing composition is manufactured from this unique raw material.

Research continues to unravel the complexities associated

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with individual fatty acids and fats from different sources and it is becoming increasingly apparent that not all fatty acids, or saturated fatty acids, have the same biological effects. It is important to understand that the saturated fatty acids in milk vary in their structure and many have no effect on plasma cholesterol. This was highlighted by The Nutrition Committee of the American Heart Association whom emphasised the diversity in the biological effects of individual fatty acids and the need to evaluate specific fatty acids with respect to a range of variables related to the risk of coronary heart disease (CHD) [9]. About 60% of the fatty acids in milk fat are saturated and of these there is consensus that 4:0, 6:0, 8:0, 10:0 and 18:0 have no effect on circulating cholesterol. Of the saturated fatty acids in milk fat, lauric (12:0), myristic (14:0) and palmitic (16:0) acid have been shown to increase plasma concentrations of total cholesterol and LDL-cholesterol when added as dietary supplements [10]. The pattern of changes of circulating cholesterol in different lipoprotein fractions, however, is an important consideration since further advances in this area have established that lauric, myristic and palmitic acid may also result in increases in circulating HDL-cholesterol [11], a change that is associated with a reduced risk of CHD.

It is important to also recognize that individuals do not consume saturated fatty acids, or milk fat, as a dietary entity, but rather as fats in foods as part of an overall diet and investigations of the relationship of dairy product consumption and CVD also challenge the appropriateness of previous recommendations. As highlighted in this supplement, considering milk fat and dairy products within the context of overall health is a key consideration and in general, the available evidence does not provide support for the conclusion that consumption of dairy products adversely affects the risk of CVD. Clearly, the education of the public that fatty acids are not equal is required.

There is also increased recognition that foods contain 'bioactive' components that can affect health, and scientists are being asked to clarify the role of specific foods and food components in health maintenance and disease prevention [5]. Consequently, the bioactive properties of a number of components in milk have been examined with regard to a range of health-related variables. Of special interest are the components associated with the prevention of chronic human diseases and results have demonstrated that milk contains specific proteins, peptides and fatty acids that are bioactive, while the production of fermented milk products also has been shown to have the potential to elicit beneficial effects on health-related variables. A partial list of the bioactive components in dairy products is highlighted in Table 1.

This supplement reflects the intellectual input from the invited speakers and their review of the scientific evidence related to the impact of dairy product consumption and milk fat in human diets on overall health and the risk of CVD. Additional information can be found in German et al. [13], which presents an overview of this symposium, general consensus of the invited speakers, thoughtful discussions of the conference participants, and future suggestions for milk fat-human health research. The symposium was convened with over 50 internationally recognized experts in dietary fats and human health and addressed topics and issues related to:

- The collective body of scientific evidence on the effects of dairy food consumption from cohort studies on CVD, diabetes and cancer,
- The effects of dairy fats within different foods on plasma lipoproteins,
- The effects of dairy products on non lipid risk factors for CVD,
- The role of dairy products as essential contributors of micronutrients in reference food patterns and what effects recommending further reductions in dairy food consumption, to attain saturated fatty acid intake targets, would have on nutrient status at a population level,
- The importance of recognising that saturated fatty acids in the diet come in a package along with other nutrients and are not consumed as a single dietary entity and the difficulty and inappropriateness of divorcing any discussion of dairy fat from dairy foods,
- Identify areas of scientific agreement regarding the health effects of saturated fatty acids in milk and milk consumption per se on human health, as well as areas for further research,
- Consider whether the current body of science for milk fat and CVD is consistent with current dietary recommendations which propose reducing dairy fat consumption as a means of reducing intake of saturated fatty acids.

Table 1. Partial List of Bioactive Components in Milk That Have Human Health Implications. Adapted from Bauman et al. [12]

Milk fat components	Milk protein components	Other
Conjugated linoleic acids	Whey proteins	Calcium
Omega-3 fatty acids	Casein	Lactose
Oleic acid	Lactoferrin	Vitamins A, D & K
Vaccenic acid	Peptides	Oligosaccharides
Sphingolipids	Milk fat-globule membrane proteins	Nucleosides
Butyric acid		Probiotics
13-methyltetradecanoic acid		Potassium
		Phosphorus

In summary, this symposium provided a unique opportunity for researchers and experts from around the world with expertise in the area of milk, fats and human health to come together and review the available scientific evidence relating dairy products and milk fat to CVD risk. The information presented at this symposium and reviewed in this supplement highlight that despite the contribution of dairy products to the saturated fatty acid composition of the diet there is no clear evidence that dairy food consumption is consistently associated with a higher risk of CVD. Given the diversity of available dairy foods of widely differing composition and their contribution to nutrient intake within the population, recommendations to reduce dairy food consumption irrespective of the nature of the dairy product should be made with caution.

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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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Key words: milk, dairy, heart disease, stroke, diabetes, cancer, survival

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 $\geq$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 Dairy almost daily	Smoking, alcohol, BMI, education, diabetes, hypertension, area
Lamarche [37]	2,000 Males	13 year	217 IHD events	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] (males)	1,340	366	Dietary 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

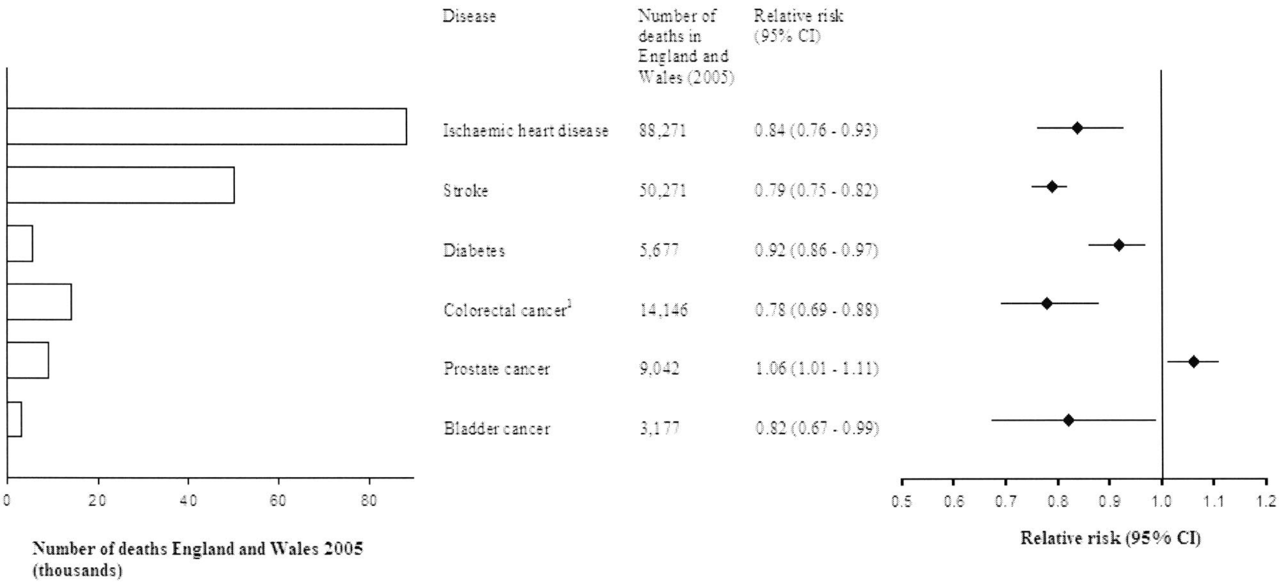

Fig. 1. The numbers of deaths in England and Wales in 2005 from various causes, and the risks for these causes in the subjects with the highest milk/dairy consumption, relative to the risk in the subjects with the lowest milk/diary consumption. RR estimates used for all cancers are those in Table 6,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

Effects of Dairy Fats within Different Foods on Plasma Lipids

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This review considers within the epidemiology of dairy fats and cardiovascular risk including the effects of 1. Fats within different dairy foods, 2. Specific dairy fatty acids including ruminant *trans* fats (TFA), conjugated linoleic acid (CLA), myristic acid and 3. The influence of metabolic syndrome.

Key teaching points:

- Population studies show strong associations between dairy fat, but less consistently between dairy food, and coronary heart disease (CHD).
- Consumption of cheese may not increase CHD risk and the association with milk is uncertain.
- Of dairy foods, butter raises low density lipoprotein cholesterol (LDL-C) most consistently, probably through its myristic and palmitic acid content.
- Cheese appears not to raise LDL-C and yoghurt inconsistently.
- Ruminant TFA may have effects on LDL-C similar to that of industrial TFA but the amounts eaten are probably too small to be of concern.
- The major ruminant CLA does not lower LDL-C.
- Dairy food consumption may modify favourably the metabolic syndrome.

INTRODUCTION

This review will focus primarily on whether the foods in which dairy fats are eaten may modify the responses in plasma lipid concentrations. The major foods for which data are available include milk and cream, butter, cheese and other fermented foods notably yoghurt.

In order to place the published findings into perspective it will be helpful to consider also:

1. The epidemiology of dairy fats generally in the context of cardiovascular risk.
2. Effects of similar amounts of dairy fat within the four major foods as above.
3. The effects of specific dairy fatty acids
4. Whether the presence of metabolic syndrome and obesity alters the conclusions derived from studying healthy and lean subjects.
5. Specific dairy fats:
   a. Myristic acid, a major dairy fatty acid
   b. Conjugated linoleic acid
   c. Ruminant *trans* fatty acids
6. Conclusions

NUTRITIONAL EPIDEMIOLOGY RELATING TO DAIRY FATS

Information in humans has been derived from prospective cohort studies, case-control studies, and metabolic studies. The first two streams provide associations with disease states primarily that of coronary heart disease, whereas the metabolic studies provide mechanistic insights. These three sources of evidence have been placed in the hierarchy of evidence. Each is robust within the limitations of the methodology. However the best kind of evidence, intervention trials are unavailable thus reducing the power of overall conclusions.

Dairy Fat and Coronary Heart Disease

Most prospective cohort studies have followed populations that are mostly healthy at the beginning over many years

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documenting clinical events and relating events to dietary information obtained initially and often several times during the study's progression. The methodology used has been mostly of the food frequency variety that documents the number and size of serves of individual foods. Obvious limitations of the methodology are the subjective assessment of amount, reliability of memory and accurate knowledge of the composition of foods. The coefficients of variation differ for different nutrients and can be quite large. From this it probably follows that compounding groups of foods provides a better index of a true association with disease outcome than relying on an individual food. Thus it has been a more consistent finding that including low-fat dairy foods within a pattern of eating based on wholegrain foods, fish, vegetables, nuts and fruits and lean poultry provides a more reliable conclusion than examining the role of dairy foods alone. Parameters that define intakes of dairy fats are strengthened in studies that measure plasma fatty acids that are representative of such fats.

Cross-sectional studies of populations have demonstrated that total dairy fat consumption was associated with cardiovascular outcomes. Turpeinen reported a significant relationship between dairy food consumption and CHD mortality across 22 western countries in a paper that discussed the benefits of lowering cholesterol levels [1]. Probably the most influential of the earlier population studies, by Artaud-Wild and co-workers [2] described the strong association between consumption of dairy foods and CHD mortality in 40 countries. They postulated that differences in CHD among those populations could be explained to a large degree by differences in saturated fat and cholesterol intakes. Correlation coefficients between individual dairy foods and CHD mortality were for milk (0.51) and for butterfat (0.44) both highly significant. By contrast, the consumption of monounsaturated fat and polyunsaturated fat were significantly negatively correlated. They noted that Finland and France were clear outliers, the former showing a high and the latter a low mortality for CHD relative to saturated fat consumption. Interestingly, the consumption of cheese was found not to be related to CHD. Renaud and de Lorgerlil [3] also observed a significant correlation between dairy fat intakes and CHD mortality among western countries but noted that this association required omission of cheese consumption.

The largest of the prospective cohort nutritional studies has been the Nurses' Health Study which quantified the rising relative risk for future CHD events from consuming increasing amounts of saturated fat and *trans* fats and conversely the falling risk as mono- and polyunsaturated fat consumption increased. When the data from this study were analysed from the perspective of individual saturated fatty acids, major longer-chain fatty acids in dairy fats, myristic and lauric were significantly correlated with CHD risk [4]. The shorter fatty acids in dairy fat, C6:0 -C10:0 were not linked to CHD. The risk ratio was 1.07 for the short chain fatty acids but 1.41 for myristic (C:14) and lauric (C12:) combined ($P<0.001$). Combining the intakes of four high-fat dairy products (milk, butter, cheese, ice cream), those women who ate on average 2.93 serves daily (highest quartile) versus those eating the least resulted in an increased risk ratio of 1.22 (or a 22% rise in risk of CHD) with a P value of 0.001 for trend across the quartiles. A late follow-up of the Seven Countries study has also confirmed the adverse outcomes among consumers of high-fat dairy foods [5]. Although the studies quoted above have meticulously attempted to exclude confounding factors these can never be completely accounted for and may at times reflect a predominantly healthy or a less healthy lifestyle. Such factors include other major risk factors, environmental factors and behavioural characteristics of the individuals being studies.

It should be noted that the studies which have observed an adverse association between dairy food and CHD events represented estimates of total dairy fat. Thus it is not surprising that studies of one dairy food such as milk that contains relatively little fat compared with that in other dairy products have not uniformly shown an adverse link to CHD or stroke. Further some, but not other dairy foods were associated with adverse outcomes. Moss and Freed [6] reported a significant association with consumption of full-fat milk but not with yoghurt or cheese in a study across European countries over a 5 year period nearly 20 years ago. The frequent failure of cheese to be linked to CHD events is interesting, because as will be discussed later, the effect of cheese appears to differ from some other dairy foods on cardiovascular risk factors.

Nevertheless there is also persuasive evidence against a link between milk consumption and cardiovascular events. A large prospective cohort study in Scotland observed an apparently protective effect among men who drank one-third of pint (189 ml) of milk daily versus those who drank less or none [7]. As noted above such an intake would deliver very little dairy fat. A similar interpretation can be placed on a much smaller case-control study in which people who consumed on average one cup of milk daily subsequently appeared to have fewer events, though not significantly so [8]. These and other studies, a mixture of prospective and case-control studies, some that included probably too few subjects for reliable interpretation, have been collected in a meta-analysis that on the whole did not find adversely against milk consumption [9].

Conclusion. A reasonable conclusion from the epidemiology and intervention trials would be that when dairy fat is eaten in substantial amounts there is a strong association with future or current cardiovascular events. When individual dairy foods are evaluated, the evidence against milk is equivocal but may reflect the relatively small contribution to overall fat consumption. Of interest however is the frequent exclusion of cheese consumption as a factor in the overall effect of dairy fat.

EFFECTS OF DAIRY FOODS ON PLASMA LIPOPROTEINS

Consideration of individual dairy foods is likely to be of greater importance than that of dairy fat. Different dairy foods are compositionally unlike one another and some such as cheese, milk and yoghurt are complex foods. Components other than fat may confer beneficial or adverse characteristics to each food. Individual foods lend themselves to investigation of mechanisms of their components.

Butter

Of all dairy foods the influence of butter fat on plasma lipids is least controversial. In metabolic studies butter fat has frequently been the "positive control" in that its low density cholesterol (LDL-C) raising effect is mostly predictable. That the quality of dairy fat in terms of its fatty acid composition influences LDL-C has been demonstrated least equivocally in human dietary studies that compared conventional dairy foods with similar foods obtained by substituting unsaturated fatty acids for saturated fatty acids. This had been achieved through technology that ensured lipids in bovine feed were protected from hydrogenation in the rumen. When dairy foods from the two sources were eaten by individuals, the plasma total cholesterol and LDL-C concentrations were significantly higher with the foods derived from unaltered milk [10]. The respective LDL-C levels were 4.49mmol/L with conventional dairy foods and 4.25mmol/L with unsaturated dairy foods; baseline LDL-C was 3.95mmol/L also emphasising the magnitude of the LDL-C raising effect of conventional dairy fat.

Cheese

The apparent exception of cheese consumption as a link to cardiovascular disease observed in epidemiological studies may reflect its lesser LDL-C raising effect compared with butter. Recently, over a period of one year three studies independently came to that conclusion. The studies were carried out in Norway, Denmark and Australia using different types of cheese but otherwise a surprisingly similar design in that cheese provided 20% fat energy. Dr Tholstrup studied milk, butter and cheese containing similar amounts of fat in 14 young men, each test period lasting three weeks [11]. Lactose was added to the butter and cheese periods and protein was added during the butter period to match those components in milk. LDL-C was lowest with cheese; milk led to a higher but non significant LDL-C concentration (+0.14mmol/L) whereas the difference between butter and cheese (+0.21mmol/L) was significant. Biong and associates compared butter with cheese in 22 subjects with moderately raised plasma cholesterol levels [12]. They added either calcium or egg white during two butter phases partially to offset the difference in calcium and protein. Total cholesterol was significantly higher with butter (+0.26mmol/L; $P = 0.04$), while the difference in LDL-C (+0.21) just failed statistical significance.

Nestel et al. [13] studied 19 subjects, 13 of whom were clearly hypercholesterolemic. Following a reduced-fat run-in period of two weeks, either cheese or butter was randomly assigned, each for four weeks in a cross-over design. Total cholesterol levels for run-in, butter and cheese were respectively 5.6, 6.1 and 5.8 mmol/L (ANOVA across the groups $P<0.01$). The difference in LDL-C between butter and cheese among the hypercholesterolemic subjects was significant, $P < 0.05$, for butter 4.4 and for cheese 3.9 mmol/L.

No satisfactory explanations are available for the relatively minor LDL-C raising effect of cheese. The higher calcium content of cheese has been partly discounted in the Norwegian study in which the addition of calcium during the butter period partially compensated for that in cheese. The addition of protein and lactose during butter periods reduced the likely involvement of those constituents in the differential effect on lipids. Fermentation remains a strong candidate although which constituents of cheese (lipids or protein) had been altered sufficiently to reduce the LDL-C raising effect is unknown. However since yoghurts also appear to have a lesser cholesterol raising effect, fermentation remains a strong clue. A review of studies that had compared fermented and non-fermented dairy products concluded that the former probably raised LDL-C less [14]. The lipid globules are differently packaged in cheese, milk and butter; whether that influences their metabolic fates upon absorption is unknown. Among changes produced by fermentation that of vitamin K_2 or menaquinone has become interesting since a large prospective study in the Netherlands found that the consumption of the vitamin was associated with significantly less CHD [15].

Yoghurt and Fermented Milk

The effect of yoghurt on plasma lipids appears to be as interesting as that of cheese. However the results of many studies have left a confusing picture, albeit only a few trials have been sufficiently large or appropriately designed to enable conclusions [14]. Two of the better designed trials both of which are negative for a benefit, will be briefly described although there appear to be almost similar numbers of studies that report benefit as those which do not. Thompson et al. [16] reported a well controlled trial in which six groups of subjects consumed either one of four control milks (with varying fat content) versus two that were fermented. One was yoghurt with *L. bulgaricus* and *S. thermophilus* and the other buttermilk containing *S. cremoris* and *S. lactis.* Three week test periods showed that the fermented products did not influence plasma lipid concentrations when compared with control milk of similar fat content. The study by De Roos [17] also failed to detect a difference in any plasma lipid in a comparison of a test yoghurt (*L. acidophilus*) versus a control yoghurt containing a starter culture.

The hypotheses underlying a potential LDL-C reduction with fermented milks is based on establishing an appropriate gut microbial population that may increase production of short-chain fatty acids (to reduce cholesterol synthesis) or to deconjugate and thereby reduce the reabsorption of bile acids. The difficulties in testing the hypotheses are reflected in the variable designs of the studies that include:

The testing of subjects with low/normal LDL-C

Variable bacterial strains and uncertain colonisation of the gut

Variable fat content of products

Addition of prebiotics in some studies

Duration; it may be necessary to test for longer periods (one study showed a significant rise in HDL-C over a six-month period [18]).

Milk

Studies carried out several decades ago had suggested that the consumption of large volumes of milk may reduce serum cholesterol levels. Such studies distorted the overall pattern of food intake and were thus difficult to control. More recently comparisons of skim and whole milk or with butter demonstrated substantially lower LDL-C levels with skim milk [19,20]. In a study referred to above, the consumption of whole milk raised LDL-C by an amount not distinguishable from that of butter [11]. Other studies have been less convincing although as pointed out before, milk contains <4% fat that may be insufficient to show an effect on LDL-C in a trial. That nevertheless implies that modest consumption of milk would be expected to have at most a minor effect on plasma cholesterol but does not indicate, as claimed by some, that there are significant LDL-C lowering compounds in milk.

INDIVIDUAL DAIRY FATTY ACIDS

Myristic Acid

Of the major saturated fatty acids found in milk, myristic acid that accounts for about 10% of dairy fat predominates in its impact on LDL-C. Zock et al. [21] had demonstrated this in a comparison with another major saturated fatty acid, palmitic acid that contributes about one-quarter to dairy fat. In the study using dairy foods that had been modified through rumen technology [10], myristic acid was reduced by a third and palmitic acid almost halved; oleic acid was the main unsaturated fatty acid in the feed and hence in the milk. The concentration of LDL-C was significantly reduced when the modified dairy products were substituted for conventional products. Although meta-analyses of the effects on LDL-C of individual fatty acids identifies the strong LDL-C raising effect of myristic acid [22], an occasional dietary trial in which amounts of myristic acid that are conventionally eaten had been tested, has failed to confirm an adverse effect [23]. Further, a study in which the fatty acids in plasmas of healthy young subjects were measured, myristic acid (as a surrogate of dairy consumption) was inversely related to the LDL-C level [24].

Conjugated Linoleic Acid

The major conjugated linoleic acid in milk, the *cis*-9, *trans*-11 isomer which is derived from vaccenic acid has been extensively investigated in recent years. It has not lived up to expectations, with most studies failing to show an effect on LDL-C. Dairy products enriched with as much as 3g of CLA daily, far more than could be obtained from eating dairy foods, failed to influence plasma lipids [25]. (A minor isomer, *trans*-10, *cis*-12 CLA has also been tested repeatedly and shown in some studies actually to raise LDL-C [26] and to increase the oxidant burden in plasma). In one study in which the CLA content was enriched by rumen technology to provide 1.42g/d of *cis*-9, *trans*-11 CLA also failed to affect plasma lipids [27]. A similarly produced modified butter that provided substantial amounts of CLA (4.22g/d) also failed to affect plasma lipids [28].

Ruminant *Trans* Fatty Acids

Industrially produced *trans* fatty acids (TFA), used to harden oils, have been shown to raise LDL-C and another atherogenic lipoprotein Lp(a), and to lower HDL-C [29]. These fats have been largely removed from dietary fats in most countries. Although not tested directly, it has been assumed that the TFA produced in ruminants may not induce similar adverse effects on plasma lipids. Two recent studies have shown this assumption to be erroneous. In a well designed trial, a large amount of industrial TFA was compared with a similar amount of ruminant TFA and also with smaller amounts of ruminant TFA such as may be derived from average consumption of dairy foods [30]. Industrial TFA led to higher LDL-C than with moderate amounts of ruminant TFA. However high intakes of ruminant TFA resulted in an increase in LDL-C and a decrease in HDL-C. Chardigny et al. [31] also observed an LDL-C increase when women, but not men consumed ruminant TFA but an increase in HDL-C was also found. The conclusion is that there may not be a significant difference between TFA produced industrially or from ruminants but that neither leads to demonstrable increments in plasma LDL-C when consumed in amounts available from current foods in most countries.

DAIRY FOODS AND THE METABOLIC SYNDROME

Although outside the scope of the current review, the rapidly increasing prevalence of the metabolic syndrome that may equate in risk to that for CHD justifies a brief comment on recent studies. Two large cross-sectional data from the Netherlands and from the USA respectively, suggested an inverse trend between consumption of some dairy foods and the presence of the metabolic syndrome although some of the findings were counter-intuitive. The USA National Health and Nutritional Examination for the years 1999-2004 found that the intake of whole milk and yoghurt was inversely associated with metabolic syndrome whereas the opposite applied with skim milk or cheese consumption [32]. The consumption of whole milk was particularly linked with lower blood pressure, potentially important as high blood pressure is an important component of the syndrome. However the consumption of total dairy foods was positively associated with metabolic syndrome and obesity (a cardinal component) in men. The Hoorn study in the Netherlands confirmed the finding of fewer cases of metabolic syndrome in people consuming milk and yoghurt (with lower blood pressure again to the fore), whereas cheese intake led to greater body mass index [33]. Further, a large prospective cohort study (as opposed to cross-sectional data), in overweight adults with insulin resistance syndrome has reported that increased consumption of dairy foods was associated with fewer components of the syndrome (dyslipidemia, hypertension and glucose homeostasis), and reduced risk of future diabetes [34].

CONCLUSIONS

1. Population studies, both cross-sectional and prospective cohort studies consistently show an association between dairy fat consumption and increased risk for coronary heart disease.
2. Milk consumption has been claimed not to increase the risk of CHD but this may reflect the lower fat intake from milk than from butter.
3. Dairy fat per se, best exemplified by butter, consistently raises LDL-C.
4. Consumption of myristic acid, a major fatty acid in dairy fat generally raises LDL-C.
5. Cheese appears to be an exception in that its impact on CHD is less than that of butter consumption and its intake leads to only small increments in LDL-C. However it appears to be associated with increased risk of metabolic syndrome and of obesity in cross-sectional surveys.
6. Other fermented dairy foods including yoghurt show an inconsistent effect on LDL-C that probably reflects the nature and functionality of the fermenting bacteria.
7. The major conjugated linoleic acid present in milk has no effects on plasma lipids even in amounts that are greater than can be consumed from conventional dairy foods.
8. The characteristic *trans* fatty acids in milk exert effects on plasma lipids not unlike those of industrial *trans* fatty acids; however in amounts likely to be consumed it probably poses no risk.
9. Cross-sectional data from several large studies suggests that consumption of some dairy foods, whole milk and yoghurt, are associated with lower prevalence of metabolic syndrome.
10. Long-term robust trials of individual dairy foods, both full-cream and fat-reduced, are needed to establish their roles in promoting CHD risk including LDL-C.
11. The components in cheese and in yoghurt that appear to modify the response in LDL-C concentration require systematic study.
12. The role of dairy foods in modifying the risk from metabolic syndrome should be established.

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Review

Review of the Effect of Dairy Products on Non-Lipid Risk Factors for Cardiovascular Disease

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Key words: dairy foods, hypertension, inflammation, diabetes, obesity

The association between dairy food consumption and the risk of cardiovascular disease (CVD) has been a topic of intense debate over the years. Recent data suggest that individuals who consume dairy foods, particularly low fat products, are less likely to develop CVD than those who have a lower intake of these foods. We are also just beginning to understand how various components of the complex dairy food matrix affect several risk factors for CVD. The objective of this review is to provide an overview of the effects of dairy foods *per se* and of some of their components on non lipid CVD risk factors. Focus will be on blood pressure, inflammation, insulin resistance and type 2 diabetes, obesity and the metabolic syndrome. While the impact of dairy foods on blood pressure appears to be beyond debate, their effects on body weight and other non lipid risk factors need to be further substantiated. However, the purported inverse association between dairy foods, particularly low fat dairy products, and the metabolic syndrome is suggestive of cardiovascular benefits that may go well beyond the effect of dairy fat on blood cholesterol.

Key teaching points:

- The data on the beneficial blood pressure lowering effect of dairy foods are convincing.
- The association between dairy food consumption and the metabolic syndrome is promising.
- The impact of dairy foods on inflammation, oxidative stress and type 2 diabetes needs to be further substantiated.
- Overall, the data suggest that dairy foods may have cardiovascular benefits that may go well beyond the effect of dairy fat on blood cholesterol.

INTRODUCTION

Studies describing the association between dairy food consumption and the risk of cardiovascular disease (CVD) have been inconsistent. In large epidemiological studies, consumption of high fat dairy products has been associated with an increased CVD risk, while intake of low fat dairy foods has not [1]. On the other hand, a recent survey of publications available on this topic has suggested that a high vs. a low consumption of any type of milk was not associated with an increased risk of CVD [2]. This apparent lack of association between dairy food consumption and CVD risk in many studies may appear as being counterintuitive since dairy products contribute significantly to the intake of saturated fatty acids, a key LDL cholesterol-raising dietary factor. Yet, we are just beginning to unravel and appreciate the complexity of the dairy food matrix, and its effects on several other CVD risk factors. At the same time, there is a growing recognition of the contribution of risk factors unrelated to LDL to the pathophysiology of CVD [3]. This review intends to provide an overview of the effects of dairy foods *per se* and of some of their individual components on non lipid CVD risk factors such as blood pressure, inflammation, insulin resistance and type 2 diabetes, obesity and the metabolic syndrome.

DAIRY FOODS AND BLOOD PRESSURE

The association between elevated blood pressure and the risk of CVD is beyond debate and several large-scale clinical

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trials have been convincing in demonstrating that reducing blood pressure using various pharmacological agents significantly reduces the incidence of CVD in most patients [4]. There is also accumulating evidence indicating that diet may be a significant factor to consider in strategies for high blood pressure prevention. In that regard, several health organizations around the world advocate the importance of restricting sodium intake and limiting alcohol intake [4] to reduce the risk of hypertension. It is also generally recommended to consume diets that are reduced in saturated fat and cholesterol, and that emphasize fruits, vegetables and low-fat dairy products, dietary and soluble fibre, whole grains and protein from plant sources [4].

The recommendation regarding the intake of low-fat dairy products as a means to prevent hypertension is based on a large body of evidence. In the first National Health and Nutrition Examination Survey (NHANES I) comprising more than 10,000 participants, low consumption of milk products was associated with a high incidence of hypertension [5]. The prevalence of hypertension in Puerto Rico has also been shown to be twice as high in middle-aged men who drank no milk as in middle-aged men who drank at least 1 L milk/day [6]. The consumption of milk has been shown to be lower in hypertensive than normotensive subjects in an Italian population studies as well [7].

In a prospective cohort of 28,886 US women aged ≥45 years followed over a period of 10 years, a high intake of low fat dairy products (top vs. lowest quintile) was associated with a significant 11% reduction in the risk of developing hypertension [8]. Interestingly, this reduction in risk was also significant across quintiles of dietary calcium and dietary vitamin D, but was not across quintiles of calcium or vitamin D supplements. The association between intake of low-fat dairy products and incident hypertension was significantly attenuated after adjustment for dietary calcium but not after adjustment for vitamin D. Finally, intake of high fat dairy products showed no association (positive or negative) with the risk of hypertension in multivariate analysis. This large study in middle-aged and older women emphasized the notion that high fat and low fat dairy products may not similarly affect blood pressure and hence, the risk of CVD [8]. Interestingly, two prospective studies have found that the inverse association between calcium intake and stroke was stronger for dairy calcium than for non-dairy calcium [9,10]. It must be stressed that the apparently beneficial impact of dairy food consumption on hypertension and stroke has not been seen in all epidemiological studies [11,12].

Perhaps one of the most acknowledged intervention studies on the association between dairy foods and blood pressure is the multicentre Dietary Approach to Stop Hypertension (DASH) study [13]. In DASH, the diet rich in fruits and vegetables and low-fat dairy products reduced systolic blood pressure by 5 mmHg more and diastolic pressure by 3.0 mmHg more than the control diet. About 50% of the magnitude in these reductions was ascribed to the dairy foods *per se* in the DASH diet. It has been estimated that a population-wide reduction in systolic or diastolic blood pressure of the magnitude observed with the DASH diet would reduce incident coronary heart disease by approximately 15% and stroke by approximately 27% [14].

Calcium is thought to be one of the main nutrients responsible for the impact of dairy products on blood pressure [15]. High salt diets have been shown to be calciuretic, thereby exacerbating the physiological impact of calcium-deficient diets. One of the consequences of this is an increase in 1,25-dihydroxyvitamin D, which *per se* contributes to elevate calcium levels in vascular smooth muscle cells, thereby increasing peripheral vascular resistance and blood pressure. Thus, dietary calcium is thought to reduce blood pressure mainly through suppression of 1,25-dihydroxyvitamin D [16]. Other minerals such as magnesium and potassium may also regulate blood pressure, but their individual contributions have been difficult to isolate and quantify because they most frequently occur in foods that are also rich in calcium [17].

Both casein and whey proteins are a rich source of specific bioactive peptides, which have been shown to have angiotensin-I-converting enzyme inhibitory effect, a key process in blood pressure control [18]. Studies have also suggested that certain peptides derived from milk proteins may modulate endothelin-1 release by endothelial cells, thereby partly explaining the anti-hypertensive effect of milk proteins [19].

DAIRY FOODS AND INFLAMMATION

Inflammation and oxidative stress are being increasingly recognized as key etiological factors in the development of atherosclerosis and subsequent CVD [20]. C-reactive protein (CRP), a non-specific protein of the acute inflammation phase, has been proposed to be a new cardiovascular biomarker of atherosclerosis and its complications [21]. Studies have shown that individuals with elevated CRP concentrations (>3.0 mg/L) are more vulnerable to develop CVD than those with constitutive CRP concentrations below 1.0 mg/L [22]. CRP is produced mainly by the liver, where its synthesis by hepatocytes is stimulated by interleukin-6 (IL-6), also an inflammatory cytokine [23]. Tumor necrosis factor- α, soluble intercellular adhesion molecule, homocystein and fibrinogen are other biomarkers of the pro-inflammatory and pro-thrombotic processes associated with an increased risk of CVD [20,24]. Monocyte chemoattractant protein (MCP)-1 is an adipocytokine thought to be involved in the development of the obesity-associated insulin resistance and atherosclerosis [25]. A recent study has shown that tumor necrosis factor-α, interleukin-6, and monocyte chemoattractant protein-1 gene expression were markedly decreased in the adipose tissue of ap2-agouti mice fed a high-calcium or a high dairy diet, with a corresponding diet-induced increase in adiponectin expression compared with the basal diet [26]. Consistent with these findings, twenty-four weeks of feeding a high-dairy eucaloric diet and hypocaloric diet in overweight men and women led to clinically meaningful reductions in plasma CRP (11% and 29% respectively) and to reciprocal increase in plasma adiponectin concentrations (8% and 18% respectively) [26]. These data suggested that dietary calcium may suppress adipose tissue oxidative and inflammatory stress associated with obesity. They also emphasized that dairy foods may beneficially alter circulating CRP and adiponectin levels independently of changes in body weight. However, the extent to which these mechanisms *per se* underlie some of the apparent cardioprotective properties of dairy foods remains to be more thoroughly demonstrated.

DAIRY FOODS AND TYPE 2 DIABETES

The incidence of type 2 diabetes is increasing at an alarming rate worldwide, with more than 1 million new cases per year diagnosed in the United States alone [27]. Type 2 diabetes on its own is an important risk factor for CVD and several studies have shown that patients with type 2 diabetes have a two to four-fold greater risk of CVD than non diabetic individuals [28]. Although the incidence of CVD events in patients with diabetes seems to have declined over the past decade [29], implementation of preventive strategies is often inadequate [30]. In addition to being associated with a dysfunctional glucose-insulin homeostatis, type 2 diabetes also encompasses typical dyslipidemic and pro-inflammatory/pro-thrombotic states that contribute to the increased risk of CVD, on their own as well as in combination [31]. Lifestyle changes including dietary modifications are proposed as the primary target for the prevention and treatment of type 2 diabetes [32] and this has been reinforced recently by two important studies that have shown that lifestyle changes can be as efficient (and perhaps even more efficient) that pharmacological therapy in preventing the onset of type 2 diabetes in high risk individuals [33,34].

In that regard, it appears that dairy foods may have interesting anti-diabetes properties. Observational studies have been relatively consistent in showing association between low vitamin D status, calcium or dairy intake, and prevalent type 2 diabetes. A recent review of these studies indicated that the prevalence of type 2 diabetes was 64% lower among non-blacks for highest vs. lowest 25-hydroxyvitamin D intake [35]. Inverse associations with incident type 2 diabetes have also been observed. Specifically, highest vs. lowest combined vitamin D and calcium intake has been associated with an 18% reduction in incident type 2 diabetes while highest vs. lowest dairy intake may reduce the risk of type 2 diabetes by 14% [35].

The available literature suggests that the reduction in the risk of type 2 diabetes associated with combined vitamin D and calcium supplementation may be significant only in populations at high risk such as those with glucose intolerance [35]. It is stressed, however, that the available evidence relating dairy foods, calcium and vitamin D to type 2 diabetes is limited. Most observational studies are cross-sectional and did not adjust for important confounders, while intervention studies were generally short in duration and had limited statistical power due to small sample size. Thus, it is generally agreed that more data are required, particularly from controlled clinical studies, to quantify the efficacy of dairy products in modulating the risk of type 2 diabetes.

DAIRY AND OBESITY/METABOLIC SYNDROME

While it is clearly established that elevated plasma cholesterol levels contribute significantly to the risk of CVD [36,37] it is also being increasingly recognized that other risk factors also play a major role in the pathophysiology leading to CVD [38]. In that context, the metabolic syndrome has been the topic of intense research and debate over the last 15 years, leading to the identification of a series of additional metabolic disturbances that are most frequently found in combination rather than in isolation [3]. Thus, the insulin resistant state and the typical dyslipidemia (high plasma triglyceride and low HDL-cholesterol levels) that characterize the metabolic syndrome are also most likely to be accompanied by increased number of reduced size LDL particles, a pro-inflammatory, pro-oxidative and pro-thrombotic state, impaired postprandial lipid metabolism and abdominal obesity [39]. It has been suggested that approximately one-quarter of the adult American population has the metabolic syndrome, with an even greater figure (45%) in adult individuals above the age of 65 years [40]. Weight management through diet and exercise is thought to be one of the key strategies for an optimal management of the risk of developing the metabolic syndrome [3].

The replacement of starchy carbohydrates with protein from lean meat and low-fat dairy products has been suggested to enhance satiety, thereby facilitating weight control [41] but this remains an issue of debate [42–45]. Dairy calcium *per se* is thought to promote weight loss [46] and facilitate weight management. Zemel et al. [47] have shown that calcium as well as dairy supplementation can accentuate body weight loss during dietary restriction in obese individuals characterized by low-to-very-low calcium consumption at baseline. It has been hypothesized that high calcium diets may increase fat breakdown and preserve metabolism during caloric restriction, thereby modulating weight and fat loss [46]. In vitro studies of human adipocytes have demonstrated a key role of intracellular calcium in regulating lipid metabolism and triglyceride storage. Specifically, increased intracellular calcium has been shown to stimulate lipogenic gene expression and lipogenesis and to suppress lipolysis [46]. It is also thought that dairy sources of calcium may exert a greater effect than calcium supplements in attenuating weight and fat gain and accelerating fat loss.

In many studies, dairy consumption has been inversely associated with the occurrence of one or several facets of the metabolic syndrome. Recent data from the National Health and Nutrition Examination Survey 1999–2004 data based on sample sizes of 4519 for the metabolic syndrome and 14618 for obesity have revealed a significant inverse association between intake of whole milk, yogurt, calcium, and magnesium and metabolic disorders [48]. Specifically, odds ratios (OR) for one more daily serving of yogurt and 100 mg Mg were 0.40 for the metabolic syndrome and 0.83 for obesity (all significant). The opposite was found for intakes of cheese, low-fat milk, and phosphorus. Ethnic differences in risk factors related to the metabolic syndrome, such as body mass index and systolic blood pressure, were partly explained by variations in dairy-related nutrients. The authors suggested that various dairy products may have differential associations with metabolic disorders, including obesity. They also suggested that ethnic differences in dairy consumption may explain in part the ethnic disparities in metabolic disorders in the US population [48].

The association between dairy consumption and metabolic syndrome has also been investigated in a sample of 827 Tehranian adults aged 18–74 y [49]. Subjects in the highest quartile of dairy consumption had significantly lower odds of having enlarged waist circumference (OR = 0.63), hypertension (OR = 0.71), and metabolic syndrome (OR = 0.69). However, the OR values were weaker after adjustment for calcium intake. This study is consistent with the concept that dairy consumption is inversely associated with the risk of having metabolic syndrome and further suggests that part of this relationship may be attributed to calcium [49]. The association between calcium and dairy products and metabolic syndrome has also been noted in a study with 10,006 women participating in the Women's Health Study [50]. Finally, in the CARDIA study that involved 3,157 adults aged 18–30 years, consumption of $\geq$5 servings/d of dairy products vs. $<$1.5servings/d was associated with a 70% reduction in the risk of having the metabolic syndrome over a period of 10 years [51].

It must be stressed that the association between dairy food intake and prevalent or incident metabolic syndrome has not been consistently shown. In an elderly Dutch population, higher dairy consumption has not been associated with lower weight or with a more favorable profile of risk factors associated with the metabolic syndrome, except for a modest association with lower blood pressure [52].

CONCLUSIONS

While the impact of dairy foods on blood pressure appears to be beyond debate, their effects on body weight and other non-lipid risk factors need to be further substantiated. Nevertheless, the purported inverse association between dairy foods, particularly low-fat dairy products, and incidence of the metabolic syndrome is suggestive of cardiovascular benefits that may go well beyond the effect of dairy fat on blood cholesterol. The potential impact of dairy foods on inflammation and oxidative stress is also consistent with this hypothesis. These associations may explain why intake of dairy products in most epidemiological studies has not been associated with an increased cardiovascular risk. Although further research is required to better understand the impact of dairy foods on non-lipid risk factors, there is accumulating evidence that a high intake of low fat dairy products may in fact be beneficial from a heart health perspective.

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Review

Dairy Products as Essential Contributors of (Micro-) Nutrients in Reference Food Patterns: An Outline for Elderly People

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The nutrient richness of dairy products is widely recognized, but mainly low fat or skimmed versions are generally advocated given the proportion of saturated fatty acids in milk fat. The question arises how to appraise this nutrient richness relative to the contribution of the saturated fraction of dairy fat. We reviewed available data - collected from elderly people - on nutrient contributions by dairy products in The Netherlands, on the relevance of nutrients specifically supplied by dairy products and shown to be associated with ageing-related functional losses, and from prospective studies in selected elderly populations in Europe on the impact of dietary and lifestyle factors on morbidity and mortality. In the current daily food pattern of older adults in The Netherlands dairy products provide significant to substantial amounts of protein and a number of minerals and vitamins relevant for healthy ageing. Especially in the frail elderly it will be difficult to replace dairy products by other foods. Dietary advice should focus on an adequate supply of energy, protein and micronutrients rather than on avoiding saturated fats. For the younger healthy 65 + we estimated that including lower fat dairy products rather their whole fat equivalents, may help to improve the dietary pattern. However, prospective analyses on morbidity and mortality do not suggest that moderate dietary intake of dairy products is associated with increased cardiovascular disease risk in this age group. In dietary risk-benefit analyses the ultimate perspective should be the nutritional status, the risk profile of the target group and the place of the foods in the dietary pattern. Such analyses need more sophisticated methods than currently available and applied in this paper. In Europe initiatives have been taken to develop such methods.

Key teaching points:

- Dairy products provide significant to substantial amounts of protein and a number of minerals and vitamins relevant for healthy ageing.
- Prospective analyses on morbidity and mortality in selected elderly populations in Europe do not suggest that moderate dietary intake of dairy products is associated with increased cardiovascular disease risk in this age group.
- With regard to dairy products intake by the frail elderly, dietary advice should primarily focus on an adequate supply of energy, protein and micronutrients rather than on general recommendations aiming to limit intakes, mostly of fat.
- Given the nutrient density of dairy products, a balanced dietary advice for the aged population should take into account the nutritional status, the risk profile of the target group and the place of the dairy foods in the dietary pattern.

INTRODUCTION

The nutrient richness of dairy products is widely recognized and therefore they are often part of national food-based dietary guidelines [1]. However, low fat or skimmed versions are generally advocated due to global recommendations to decrease intake of saturated fatty acids in view of reported adverse effects on blood lipid risk markers for cardiovascular disease [2,3]. Due to the proportion of saturated fatty acids in milk fat, the intake of normal liquid milk has declined or

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stagnated over the last decade, especially in Europe and North America [4,5]. However, consumers, but also nutritionists, tend to forget that milk contains important nutrients, such as protein, calcium, zinc and B-vitamins.

A diversity of dairy foods of widely differing composition is processed from cows' milk. The fat content in these products varies widely, from ~82% in butter to virtual absence in 0% fat dairy drinks. On average, bovine milk contains about 33 g of lipids per litre. Approximately 95% of the lipid fraction consists of triacylglycerols with fatty acids of different length (4 to 24 C-atoms), degree of saturation and positional specificity on the glycerol backbone [6]. The residual fraction of milk lipids consists of diacylglycerol (~2%), cholesterol (<0.5%), phospholipids (~1%), and free fatty acids (<0.5%). Milk fat is present as highly complex globules with structural properties distinct from other biological sources of fats; complex phospholipids make up a highly glycosylated and protein-embedded plasma membrane around each milk fat globule. During processing, the array of nutrients in the raw milk is distributed over the various process streams, depending on e.g. fat solubility, heat stability, shearing forces, binding characteristics for specific milk proteins, use of specific ferments [7]. The nutrient density is therefore not a simple function of the fat content [8,9].

The fat fraction contributes very much to the creaminess and thus the palatability and popularity of dairy products. The saturated fat content of the milk fat is not constant, but dependent on the feeding regime of the cows. On average 66% of the milk fat consists of saturated fatty acids, whereby it should be noted, with respect to cardiovascular disease risk, that not all saturated fats have the same effect on blood lipids as intermediate markers of risk [3], and that the matrix in which they are contained may influence the disease risk as well [9,10].

The purpose of this paper is to consider the benefits of the nutrient richness of dairy products, and their contribution to healthy dietary patterns, versus the risk from the intake of milk fat, and thus saturated fats, in the perspective of the ageing population. These considerations are based on available data from nutrient contributions by dairy products in The Netherlands, the relevance of specific dairy nutrients to possible functional losses while ageing and prospective analyses on morbidity and mortality of the influence of dietary and lifestyle factors in selected elderly populations in Europe.

NUTRIENT CONTRIBUTION OF DAIRY PRODUCTS TO DAILY FOOD PATTERNS IN THE NETHERLANDS

The contribution of milk (products) and cheese to daily intake of selected nutrients has been calculated from the third Dutch National Food Consumption Survey [11], allowing comparisons between age groups. Table 1 shows the comparison between the total population and the age category above 65

Table 1. Contribution (%) of Dairy Products to the Daily Intake of Energy, Macro- and Micronutrients; Data Derived from Dutch National Food Consumption Surveys (DNFCS) in 1997/1998 [11] and 2003 [12]

Energy and nutrients	DNFCS 1998 Total population (n = 5958)		DNFCS 1998 Older adults (65+)				DNFCS 2003 Young adults (19–30)	
			Men (n = 185)		Women (n = 236)		Men (n = 352)	Women (n = 398)
	milk (products)	cheese	milk (products)	cheese	milk (products)	cheese	all dairy products	
Energy	11.1	4.5	10.3	4.7	11.9	4.6	13.9	15.3
Protein	17.8	8.3	16.7	8.8	19.4	8.4	24.1	26.5
Fat	9.1	8.9	9.7	8.8	9.2	8.6	17.6	18.8
Saturated fat	14.9	14.0	13.5	13.5	14.0	13.1	30.4	31.4
Calcium	47.7	21.1	45.8	23.6	54.8	20.2	65.6	62.6
Magnesium	15.0	2.6	14.2	2.7	15.7	2.6	15.1	17.0
Zinc	15.6	9.7	14.8	10.0	16.3	9.2	24.8	26.7
Selenium	10.5	6.9	9.3	5.4	11.0	5.5	12.5	13.9
Retinol	8.0	8.2	6.8	6.7	7.8	7.4	14.6	15.5
Vitamin D	5.1	4.1	3.9	3.2	4.4	3.5	9.2	10.2
Vitamin B_1	10.0	0.7	9.0	0.7	10.4	0.7	12.7	13.0
Vitamin B_2	45.5	3.7	42.8	3.7	47.1	3.4	45.1	47.7
Vitamin B_6	9.0	1.1	13.0	1.1	9.8	1.0	10.1	12.0
Vitamin B_{11}	7.9	1.1	6.5	0.1	8.0	0.1	11.1	13.5
Vitamin B_{12}	34.7	2.4	28.0	2.0	33.9	2.2	33.5	36.7

The 1998 DNFCS data were based on records for two sequential days of food items noted in a diary; the 2003 data were based on computer-assisted 24-h diet recall interviews by trained dieticians on two independent days. The 1998 data for vitamins B_{11} and B_{12} were calculated by the authors.

years. Evident are the substantial contributions of dairy products to the intake of calcium (69–75%), vitamins B_2 (riboflavin; 46–50%) and B_{12} (cobalamin; 30–37%), protein (~25%) and zinc (~25%). Lower, but still significant contributions, can be noted for dietary intake of magnesium (17–18%), vitamins B_6 (pyridoxal phosphate; 10–14%), B_1 (thiamin; 10–11%) and B_{11} (B_9, folic acid; 6–9%), retinol (7–8%), vitamin D (7–9%) and selenium (14–17%). Contributions to the intake of energy, fat and saturated fat were 15–16%, ~18% and 27–29%, respectively. A more recent intake assessment on these nutrients for younger adults (19–30 yrs) has been reported in 2003 [12]. From Table 1 it can be concluded that nutrient contributions through dairy intake in The Netherlands are rather similar in young(er) adults and adults above 65 yrs of age. Such a similarity is also present in current recommendations on food based dietary guidelines where intakes of 450–650 ml and 20–30 g for milk (products) and cheese respectively are recommended for each of the three age categories of 19–50, 50–70 and over 70 yrs. These food based dietary guidelines aim to promote balanced food and nutrient intake, whereby saturated fat content is one of the limiting criteria to classify foods as "preferred foods".

During the 1998 Dutch National Food Consumption Survey the relative contributions of full fat, semi-skimmed and skimmed milk were 18, 53 and 29% respectively. Today the contribution of semi-skimmed milk in The Netherlands has increased to about 85%. The average cheese consumption, predominantly as full-fat Gouda cheese, amounted to 27 g/d, with above average intakes (~35 g/d) for the age categories 19–50 and 50–70 yrs, and with men eating more cheese than women. Average butter intake was 3 g/d, with above average consumption (up to 7 g/d) for the age categories over 50 yrs.

RELEVANCE OF SPECIFIC DAIRY NUTRIENTS FOR THE AGEING POPULATION

The SENECA survey on nutrition and the elderly has shown that dairy intakes may differ considerably between different regions in Europe [13]. Potential concerns were identified with respect to low dietary intakes of the vitamins D and B_{12}; furthermore, the status of these vitamins may also be influenced by insufficient sun exposure/skin synthesis and reduced absorption efficiency, respectively [14]. Together with calcium these nutrients appear to have the highest priority in terms of multiple health outcomes for the elderly population related to bone metabolism, muscle and brain function [15–19].

With calcium, vitamins B_{12}, vitamin D and protein, dairy products contain important nutrients in relation to bone health. Protein intake is associated with increased bone mineral mass and reduced incidence of osteoporotic fracture [20]. Calcium is a critical component of the bone structure, and plays, in conjunction with vitamin D intake/status, an important role in risk reduction of osteoporotic fractures [21,22]. Elevated plasma levels of homocysteine (Hcy) have been identified as independent risk factors for osteoporotic fractures [23,24]. Vitamin B_{12} was able to reduce Hcy levels. In the Longitudinal Ageing Study Amsterdam (men and women with a mean age of 76 years at baseline; 3 year follow-up period) where it was shown that high plasma levels of Hcy and low serum levels of vitamin B_{12}, and especially the combination of these parameters, are related to a 3 to 4-fold higher fracture risk; in women, but not in men; markers of bone strength, bone turnover as well as bone formation were affected [25].

Loss of body weight and/or skeletal muscle mass is common in older persons; inadequate intake of protein and energy may result in clinically relevant reductions in strength, exercise capacity and mobility [26]. Regular performance of resistance exercises and the habitual ingestion of adequate amounts of dietary protein from high-quality sources are two important ways for older persons to slow the progression of the age-related loss of skeletal muscle mass and function [27]. As there is increasing evidence that the anabolic response after a mixed meal may be blunted during ageing, consensus is growing that current protein recommendations may need modest upward adjustment [28]. It is not clear, however, whether and how synergy with resistance exercise can be achieved, especially for the frail elderly. Noteworthy in this respect is the finding from the Health ABC Study that the change in lean body composition amongst community-dwelling elderly (70–79 yrs) over a 3 years period was associated with habitual protein intake; the highest quintile of protein intake had ~40% reduced loss in total and non-bone appendicular lean mass compared with the lowest quintile [29].

Observational studies, vitamin deficiency states and homozygous gene defects related to the one-carbon metabolism have suggested that low plasma cobalamin and folate statuses, as well as elevated plasma homocysteine concentrations, as a functional indicator of their status, are associated with diminished cognitive performance in the elderly [30,31]. However, recent systematic reviews of both observational studies [32] and randomized trials [33] have concluded that the available evidence so far does as yet not allow for firm conclusions on functional cognition related benefits; the heterogeneity in study designs and methods applied is considered as the main problem in this respect [32–34].

There is strong evidence that elevated plasma HCy levels are causally related to cardiovascular disease risk [35,36]. The vitamins B_2, B_6, B_{11} and B_{12} are crucial factors in the re-methylation (recycling as methionine) and transsulfuration (formation of cysteine) pathways of HCy. Plasma HCy lowering is particularly responsive to intervention with B_{11} and to a lesser extent with B_{12} and B_6. However, twelve secondary prevention trials have so far not provided evidence for a clear vascular risk benefit of HCy lowering by one or a mix of these B-vitamins [37]. McNulty et al. [38] have also pointed to a possible role for riboflavin, in particular with respect to the genetic polymorphism for the enzyme methylenetetrahydrofolate reductase (MTHFR), which provides the substrate for the B_{12} dependent conversion of HCy into methionine. Individuals homozygous for the MTHFR gene variant 677C→T have reduced enzyme activity, resulting in elevated plasma HCy levels. Compared to subjects with genotype CC or CT, individuals with the TT genotype may be more sensitive to the supply and status of the various B-vitamins involved in HCy metabolism [39]. The prevalence of the TT-genotype varies geographically and with ethnicity, but may be as high as 30% when assessed in newborns [40].

Magnesium and calcium in milk and milk-based products may also contribute to beneficial effects on blood pressure, as these food items are also generally low in sodium and moderate in potassium content [41]. Population attributable risk (PAR) for the prevalence of increased systolic blood pressure due to dietary or lifestyle factors has been calculated for four European countries and the US, based on data from randomized controlled trials [42]. Low calcium and low magnesium intakes were associated with 2–8% and 4–8% PAR respectively; on the other hand, PAR% were higher for overweight (11–17%), excessive sodium intake (9–17%), low potassium intake (4–17%), physical inactivity (5–13%) and low intake of fish oil (3–16%). The inverse association between magnesium intake and blood pressure appears to be the strongest for magnesium obtained from foods rather than from supplements [43].

Zinc is needed for optimal functioning of the immune system and antioxidant stress responses. In elderly subjects cell-mediated immune dysfunction and increased oxidative stress are common [44]. Zinc deficiency is related to dietary habits. Supplementation with zinc (45 mg/d) in elderly subjects has been shown to reduce common infections over a 12 month period, coinciding with lowering of markers of inflammation and oxidative stress [45].

Selenium is incorporated as selenocysteine at the active sites of multiple selenoproteins. These proteins fulfil roles in thyroid function, muscle metabolism, antioxidant and immune defence [46]. The role of selenium in chronic disease has recently been reviewed by Boosalis [47] with respect to selenium status or supplementation. The author concluded that it is advisable for all individuals to maintain an adequate selenium status in relation to hypertension, cardiovascular disease, cancer and diabetes, but also cautioned with regard to careless use of selenium supplements. Arnaud et al. [48] presented evidence from a 9-year follow-up study of the EVA cohort, showing a longitudinal decrease of plasma selenium in a free-living elderly population (59–71 years at baseline), in line with a number of cross-sectional studies in Europe. Besides age, persistent obesity and occurrence of cardiovascular disease during follow-up augmented the longitudinal decline in plasma selenium. This suggests that plasma selenium changes may reflect requirements for oxidative stress response; the implication will be that increased supply of selenium may be needed during conditions of stress and/or disease.

It is evident that dairy products contain a number of important nutrients required for the maintenance of organs and tissues while ageing. However, dairy products are part of a dietary pattern and dysfunction of tissues and organs in general will occur gradually, thus, prospective studies analyzing the associations between dietary patterns and predictors of survival may reveal the relative contribution of dairy products.

DIETARY PATTERNS VERSUS FOOD ITEMS AS PREDICTORS OF SURVIVAL IN THE ELDERLY POPULATION

Numerous studies have shown that diet and lifestyle influence morbidity and mortality during the course of life. Ten-year mortality from all causes, or specifically from cardiovascular diseases or cancer, has been investigated in 1507 apparently healthy men and 832 women, aged 70 to 90 years in 11 European countries. In the so-called HALE-project (Healthy Ageing: a Longitudinal study in Europe; cohorts from both SENECA and FINE were combined for the analysis) adherence to a defined Mediterranean diet and healthful lifestyle (moderate alcohol use, physical activity and non-smoking) was associated with a more than 50% lower rate of all-causes and cause-specific mortality [49]. The Mediterranean Diet Score in this study was based on eight components: ratio of monounsaturated to saturated fat, legumes nuts and seeds, grains, fruit, vegetables and potatoes, meat and meat products, dairy products and fish. Intake of each component was adjusted to daily intakes of 2500 kcal (10.5 MJ) for men and 2000 kcal (8.5 MJ) for women. The sex specific median intake values were taken as cut-off points for scoring purposes, whereby meat and dairy products intake were scored as non-beneficial.

In its finale study, the SENECA survey on nutrition and the elderly has explored the predictive value for survival of Mediterranean diet scores in relation to single food items for 631 males and 650 females from northern and southern European towns [13]. Two Mediterranean Diet Scores (MDS) were used to calculate hazard ratios: the original MDS was based on scores using sex specific median cut-off values, whereas an adapted MDS took higher alcohol and meat/poultry intake for women into account as well as P25–P75 percentile values for optimal milk (products) intake for both sexes. The adapted MDS coincided with improved survival time, although the values in women did not reach statistical significance. In women, the use of the P25–P75 percentile for milk intake improved the hazard ratio versus the use of the median intake (P50) as cut-off value. When comparing hazard ratios in function of cut-off points used for milk (products) intake in northern or southern European regions, it was found that P25–P75 values gave more beneficial scores for women in both regions, yet for men this was not observed. This inconsistency could not be explained by variations in intake per study site. The P25–

P75 values for milk (products) intake were 144–474 g per day for men and 159–465 g per day for women. It should be pointed out that the available Eurocode food coding system was unable to distinguish between milk products varying in fat content.

The HALE population has also been investigated for the association of total cholesterol, HDL-, LDL- and VLDL-cholesterol and 10-year mortality from cardiovascular diseases and all-causes. During follow-up, 302 deaths were due to cardiovascular diseases. From the assessed lipid fractions only a significant inverse association was found between HDL-cholesterol and cardiovascular and all-cause mortality; the highest tertile had a significant lower risk of mortality from cardiovascular diseases (HR: 0.72, 95% CI: 0.54–0.95) and all-causes (HR: 0.80, 95% CI: 0.66–0.96), compared to the lowest tertile. These associations remained significant after adjustments for gender, age, education, BMI, smoking, study center and LDL- and VLDL-cholesterol [50]. Inverse associations between HDL-cholesterol levels and mortality from coronary artery disease, ischemic stroke or all-cause mortality have also been reported in other studies of elderly populations [51–53].

RISK-BENEFIT CONSIDERATIONS

In order to evaluate the benefit of nutrient richness of dairy products versus the intake of saturated fats for the ageing population the following aspects should be considered. It is important to realize that it is difficult to assess effects of single food items or food categories in population or community based prospective studies. Foods/food categories are part of a dietary pattern and to a certain extent influenced by cultural habits. For the European population we have taken the SENECA/HALE dataset as an example, but the predictive value of dietary patterns has also been explored in other datasets. Hereby it is evident that there is heterogeneity in approaches on how to assess dietary patterns and their impact on vitality and longevity. For example, the EPIC-Elderly study [54] has shown that an a *posteriori* dietary cluster analysis of the association between adherence to a plant-based diet and all-cause mortality is moderately positively associated (overall correlation of 0.621) with survival as assessed by scoring the diets *a priori* according to the Modified Mediterranean Diet Score. Yet, apparent associations were country-specific. In a Dutch study within the EPIC cohort, mortality rates were better when older women adhered to a healthy variant of the traditional Dutch diet, as compared to a type of Mediterranean diet [55]. Note that both types of diet were based on posteriori data analyses.

At a population level, it is important for nutrition research to address interactions between nutrients and also multiple effects of one nutrient with respect to health outcomes, as argued recently by Heaney [56], while challenging the prevailing nutrient by nutrient reductionist approach. He illustrated his argument with the interactions of protein, calcium and vitamin D regarding bone metabolism and health. Within the dairy matrix other examples may be the B-vitamins for cognitive performance or vascular health, or zinc, selenium and protein for antioxidant function.

A third consideration is that there are different health states ("consumer profiles") within the ageing population. In the context of this paper we will distinguish between the frail elderly and the care-independent elderly with due attention for respectively malnutrition and vitality.

Dairy Products for the Frail Elderly

With advancing age food intake may decline for a variety of reasons [57,58]. Changes in concentrations of and responses to sex and satiety hormones, as well as some neurotransmitters involved in food intake regulation, may contribute to the decline of appetite resulting in anorexia of ageing. Furthermore, sensory perception may change. Social and psychological factors, but also disease conditions and medications, may aggravate the physiological anorexia of ageing and lead to protein-energy malnutrition and weight loss. Malnutrition as the consequence of inadequate food intake is highly prevalent in elderly persons who need care. The resulting energy, protein and micronutrient deficiencies of the fragile elderly are preferably solved through the use of foods rather than food supplements. However, specific nutritional supplements for calcium and the vitamins B_{12} and D may be desirable due to dairy avoidance in the case of calcium, insufficient levels of vitamin D in dairy products or reduced absorption efficiency of food-bound vitamin B_{12} [59,60]. Fortification of milk with crystalline B_{12} has been shown as effective as capsules with crystalline B_{12} in improving the cobalamin status of mildly deficient females of 70 years and older, as assessed by levels of serum cobalamin and methylmalonic acid [61]. Vitamin D fortification of milks is quite common. Recently, equal vitamin D bioavailability was demonstrated when comparing vitamin D_3 fortified Cheddar and low-fat cheese with supplements in younger men and women (average age 30 yrs) [62]; sufficiently long nutrient stability in an industrial setting was verified as well for the cheeses [63].

The hedonic properties of dairy foods are important for feeding the frail elderly. Even slight differences between regular and micronutrient fortified foods in scores on pleasantness, desire to eat and attitude toward products may be perceived for a longer period of time [64]. The primary goal to improve the nutritional status of the frail elderly is to stimulate intake of nutrient dense foods. Due to their nutrient richness, the well appreciated palatability, and the variety of products that can be offered, dairy products provide excellent opportunities to achieve that goal. The choice for low or full fat versions is of lesser importance in this respect.

Dairy Products for the Care-Independent Elderly

The relative intakes of full fat, low fat or skimmed dairy products are not known for the SENECA/HALE studies. It is fair to assume, however, that the elderly populations have consumed full fat cheese as well as full fat milks and yoghurts. Yet, the available hazard analyses suggest that moderate dairy intake does not present increased risk for the elderly population. In order to explore in some more detail how the choice between full fat or lower or no fat dairy alternatives would impact saturated fat, energy and micronutrient intakes, we used the data of the Dutch Food Consumption Survey of 1997/1998 [12] to estimate shifts in intake for men and women over 65 years of age. We assumed for the daily consumption pattern of an average man or woman that milk products were either full fat or skimmed, and that the high fat cheeses (~31% of fat; the predominant consumed product at that time in The Netherlands) were fully replaced by lower fat cheeses (~18% fat). The result of this simplified approach is that men and women would have consumed 114 and 106 kcal less, respectively, when choosing the low(er) fat alternatives. For the intake of, respectively, fat and saturated fat, the reductions in grams per day were 16.1 and 9.8 for men, and 15.0 and 9.1 for women; expressed as percentage of daily energy intake the reductions in saturated fat intake were 2.8% for men and 3.0% for women. These are relevant reductions in dietary intake from a cardiovascular disease risk prevention point of view, although this should be viewed within the perspective of the risk profile of the consumer as well as other preventive measures such as changes in lifestyle and increased intake of fruits and vegetables [65]. The choice for lower fat dairy alternatives also impacted dietary intake of cholesterol (minus ~45 mg), calcium (plus ~135 mg) and retinol equivalents (minus ~150 μg). Although the reduction in retinol intake is relatively high, it is not expected that this will lead to intakes below recommended levels.

CONCLUSIONS AND OUTLOOK

The benefits of the nutrient richness of dairy products have been evaluated against the intake of saturated fats in the perspective of the ageing population. In the current daily food pattern of older adults in the Netherlands dairy products provide significant to substantial amounts of protein and a number of minerals and vitamins relevant for healthy ageing. Especially for the frail elderly, maintaining a healthy condition will depend on adequate food and energy intake, whereby the primary focus should be on the intake of nutrients rather than on avoiding saturated fats. For this purpose the dairy product category provides ample choice of palatable nutrient-dense foods.

The prospective analyses on morbidity and mortality of the influence of dietary and lifestyle factors in selected elderly populations in Europe [13] suggest that moderate dairy intake is not associated with increased cardiovascular risk, which is in line with a recent meta-analysis of cohort studies on milk drinking and ischemic heart disease and stroke [66]. Nevertheless, most prospective studies experience difficulty in obtaining more precise quantification of the differentiation of products within food categories in a pan-European perspective. Hopefully, the ongoing European projects on harmonisation and development of food composition databank systems [67] and alignment on micronutrient recommendations [68] will enable more refined analyses of prospective studies on morbidity and mortality in relation to dietary patterns.

The risk-benefit analysis in relation to foods and food ingredients also needs more sophisticated methods than the one we have applied in this paper on nutrient density and saturated fat intake. The European project BRAFO (Benefit-Risk Analysis of Foods), will develop a framework to quantitatively compare human health risks and benefits of foods and food compounds, using a common scale of measurement. Such a scale will most likely be based on duration and quality of life years with weighting of data quality and severity of effect using QALY or DALY-like methodology [69].

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