Does milk consumption contribute to cardiometabolic health and overall diet quality?

Canadian Journal of Cardiology 32 (2016) 1026–1032

Review

Does Milk Consumption Contribute to Cardiometabolic Health and Overall Diet Quality?

Benoît Lamarche, PhD,[a] D. Ian Givens, PhD,[b] Sabita Soedamah-Muthu, PhD,[c] Ronald M. Krauss, MD,[d] Marianne Uhre Jakobsen, PhD,[e] Heike A. Bischoff-Ferrari, MD, DrPH,[f] An Pan, PhD,[g] and Jean-Pierre Després, PhD[h]

[a] *Institute of Nutrition and Functional Foods, School of Nutrition, Laval University, Québec City, Québec, Canada*

[b] *Food Production and Quality Division, Faculty of Life Sciences, University of Reading, Reading, United Kingdom*

[c] *Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands*

[d] *Children's Hospital Oakland Research Institute, Oakland, CA, USA*

[e] *Department of Epidemiology, School of Public Health, Aarhus University, Copenhagen, Denmark*

[f] *Department of Geriatrics and Aging Research, University of Zurich and University Hospital Zurich, Zurich, Switzerland*

[g] *Department of Epidemiology and Biostatistics, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China*

[h] *Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec, and Department of Kinesiology, Faculty of Medicine, Université Laval, Québec City, Québec, Canada*

ABSTRACT

Although milk consumption is recommended in most dietary guidelines around the world, its contribution to overall diet quality remains a matter of debate in the scientific community as well as in the public domain. This article summarizes the discussion among experts in the field on the place of milk in a balanced healthy diet. The evidence to date suggests at least a neutral effect of milk intake on health outcomes. The possibility that milk intake is simply a marker of diets higher in nutritional quality cannot be ruled out. This review also identifies a number of key research gaps pertaining to the impact of milk consumption on health. These need to be addressed to better inform future dietary guidelines.

RÉSUMÉ

Bien que dans le monde entier la plupart des lignes directrices en matière d'alimentation recommandent la consommation de lait, sa contribution à la qualité globale du régime alimentaire reste un sujet de controverse dans le milieu scientifique ainsi que dans la sphère publique. Cet article résume les discussions entre les experts de ce domaine sur la place du lait dans un régime alimentaire sain et équilibré. Les données probantes disponibles à ce jour suggèrent pour le moins que la consommation de lait a un effet neutre sur la santé. La possibilité que la consommation de lait soit simplement un marqueur des régimes alimentaires de qualité nutritionnelle supérieure ne peut pas être exclue. Cette revue identifie également plusieurs lacunes importantes de la recherche concernant les effets de la consommation de lait sur la santé. On doit remédier à ces lacunes pour mieux orienter les futures lignes directrices en matière d'alimentation.

Primordial and primary prevention is essential for improving the cardiovascular health of the population in years to come.[1] Primordial prevention hinges on the American Heart Association's "Life's Simple Seven," which targets 4 health behaviours (diet quality, physical activity, smoking, and body weight) and 3 health factors (cholesterol and glucose levels and blood pressure). Nutritional quality in this paradigm is assessed using 5 criteria: (1) fruit and vegetable consumption, (2) fish consumption, (3) intake of whole grain cereal products, (4) salt intake, and (5) consumption of sugar-sweetened beverages (SSBs).[2] Although the contribution of each of these foods to cardiovascular health is widely accepted, the extent to which other foods, such as milk, contribute to the overall nutritional quality of diets remains uncertain. Indeed, despite the fact that milk/dairy consumption is recommended in most dietary guidelines around the world, the role and place of these commodities in a healthy/balanced diet has given rise to

Received for publication November 27, 2015. Accepted December 23, 2015.

Corresponding author: Dr Benoît Lamarche, Institute of Nutrition and Functional Foods, Laval University, 2440, Boul Hochelaga, Québec G1V 0A6, Canada. Tel.: +1-418-656-2131 ×4355; fax: +1-418-656-5877.

E-mail: benoit.lamarche@fsaa.ulaval.ca

See page 1031 for disclosure information.

http://dx.doi.org/10.1016/j.cjca.2015.12.033

a highly polarized debate within scientific, media, and public circles. On the positive side, milk contributes a significant proportion of daily requirements for protein and calcium at a population level.[3] When fortified, milk also contributes to vitamin D intake. As discussed further on, calcium, vitamin D, and dairy proteins are key nutrients for bone health.[4,5] Adequate vitamin D status has also been associated with a lower risk of some cancers and mortality,[6,7] but conclusive evidence awaits the results from ongoing large trials of vitamin D supplementation. Milk consumption also contributes to dietary intake of magnesium, potassium, phosphorus, vitamin B_{12}, riboflavin, and vitamin A.

In addition to having potential biological and physiological effects per se, what milk displaces in the diet (for example SSBs or sugary juice) is a key consideration because it may yield further effects on health. Finally, reduced-fat milk consumption has been associated with a prudent dietary pattern in epidemiologic studies,[8] raising the possibility that milk intake may simply be a marker of a high-quality diet, having no favorable effect per se.

On the potentially negative side, consumption of full-fat milk contributes to saturated fat intake.[3] Allergies and other forms of intolerance to milk protein and lactose are also seen as barriers to milk consumption.[9] Finally, milk production is facing significant challenges related to sustainability, not only from an economic profitability perspective but also because of environmental and societal concerns.[10]

Revisiting the place and role of milk in the diet is therefore an important and timely topic, especially considering that milk consumption is deep rooted in many occidental cultures and is increasing markedly in many South Asian and East Asian countries.

The International Chair on Cardiometabolic Risk (*International Chair on Cardiometabolic Risk and Lifestyle Risk Factors* section of the Supplementary Material) convened a group of experts to assess the evidence linking milk intake with health. Data from epidemiologic studies and randomized controlled trials (RCTs) were reviewed. The consistency of associations across countries and across various health outcomes such as coronary heart disease (CHD), stroke, and type 2 diabetes was discussed. Challenges in assessing the association between milk intake and health were discussed, and knowledge gaps requiring future research were identified.

Milk Consumption and Health Outcomes

Cardiovascular diseases

The perspective on milk and health varied minimally among the experts, despite differences in areas of interest, expertise, and geographic location. There was a unanimous sense that milk intake per se was not associated with a risk of clinical outcomes such as total cardiovascular disease (CVD), CHD, stroke, and type 2 diabetes. Several meta-analyses on the topic support this conclusion. Soedamah-Muthu et al.[11] examined the dose-response relationship between milk intake and overall CVD incidence in a meta-analysis of 4 cohort studies published before 2011 based on data from a combined sample of 13,518 individuals. Increased consumption of milk was associated with a slightly reduced risk of CVD (composite relative risk [RR] per 200 mL/d, 0.94; 95% confidence interval [CI], 0.89-0.99). However, this was not substantiated in a subsequent meta-analysis by O'Sullivan et al.,[12] of cohort studies combining data from more than 330,000 individuals; they reported no significant association between milk intake and CVD mortality (RR per 200 mL/d, 0.96; 95% CI, 0.81-1.13). A number of important cohort studies have been published subsequent to these meta-analyses. For example, data from the Japan Collaborative Cohort comprising a total of 94,980 Japanese adults aged 40-79 years followed over a period of 19 years showed that drinking milk 1-2 times a month vs never drinking milk was associated with lower mortality from CVD in men (RR, 0.89; 95% CI, 0.82-0.98) but not in women (RR, 0.99; 95% CI, 0.89-1.08).[13] Among the very few reports of a positive association between milk intake and risk of total CVD is a recent publication from the Swedish Mammography Cohort and the Cohort of Swedish Men involving slightly more than 100,000 individuals who were followed for 11-20 years.[14] The study revealed a significant increase in the risk of CVD mortality with milk consumption among both women (RR per 200 g/d, 1.15; 95% CI, 1.12-1.19) and men (RR per 200g/d, 1.05; 95% CI, 1.03-1.07). The authors were very careful in formulating their conclusions by emphasizing the importance of confounding issues and reverse causation to explain the discordance between their findings and those from other groups.[14] More recently, Larsson et al.[15] in their meta-analysis of the association between milk intake and all-cause mortality concluded that there was no consistent association between milk consumption and mortality, including mortality from CVD, and that additional prospective studies were needed.

Soedamah-Muthu et al.[11] further examined the dose-response association between milk consumption and risk of CHD specifically (data from 259,162 men and women) and stroke (data from 375,381 men and women). Increased milk intake showed no significant association with the risk of CHD (RR per 200mL/d, 1.00; 95% CI, 0.96-1.04) or stroke (RR, RR per 200 mL/d, 0.87; 95% CI, 0.72-1.07). In a meta-analysis of 15 prospective cohort studies (n = 28,138 stroke events among 764,635 participants), Hu et al.[16] reported no significant linear association between milk intake and the risk of stroke. However, a highly significant nonlinear dose-response relationship between milk intake and risk of stroke was observed, with the lowest risk found in the groups consuming 200 mL/day (RR vs nonconsumers, 0.82; 95% CI, 0.79-0.86) and 300 mL/day (RR, 0.83; 95% CI, 0.79-0.86).

Milk fat intake can be ascertained using the plasma concentrations of fatty acids that are found specifically in dairy fat, primarily C15:0 and C17:0.[17] This approach is based on the premise that humans have a very low endogenous production of these fatty acids. Levels of C17:0 in plasma were associated with a reduced risk of CHD in a meta-analysis by Chowdhury et al.[18] Recent data from Swedish studies in men and women are at odds with previous nested case-control data from the same cohorts,[14] according to which milk fat intake assessed by plasma concentrations of the fatty acids C15:0 and C17:0 was inversely correlated with risk factors for metabolic syndrome and inversely associated with the risk of myocardial infarction in women but not in men.[19] It must be stressed that the use of such biomarkers of dairy fat intake has been challenged recently based on data indicating active metabolic pathways potentially influencing C15:0 and C17:0 levels in

Table 1. Summary of the association between milk consumption and risk of disease and clinical outcomes

Outcome	Association with milk intake
Total CVD	Uncertain
CHD	Neutral
Stroke	Neutral
Type 2 diabetes	Neutral
Fractures	Neutral

CHD, coronary heart disease; CVD, cardiovascular disease.

humans.[20] However, it must be kept in mind that even in its regular fat form, milk contributes a small proportion of total dietary fat. The extent to which variations in plasma concentrations of C15:0 and C17:0 reflect variations in milk intake remains uncertain.

In summary, although the association between milk intake and CVD risk and morbidity remains uncertain to a degree, the evidence so far from existing meta-analyses and subsequent cohort studies points toward a neutral association between milk intake and CHD risk (Table 1). More studies are warranted to provide a more definitive answer to this question.

Type 2 diabetes

Four meta-analyses combining data from 4-14 studies and 167,000-459,790 individuals have been relatively consistent in showing no significant association between milk intake and the risk for type 2 diabetes (RR, ranging from 0.87-0.95; 95% CI, ranging from 0.69-1.67, depending on whether total, low-fat, or whole-fat milk was considered).[21-24] Using a mendelian randomization approach in a cohort of 97,811 Danish individuals, Bergholdt et al.[25] showed that milk intake as assessed by genetic variations related to lactose tolerance was also not associated with the risk of type 2 diabetes. Taken together, current data pertaining to the risk of type 2 diabetes suggest no association with milk intake.

Bone/muscle health

The unique sets of nutrients provided by milk are believed to be beneficial for bone and muscle strength. This is a topic of particular significance in aging populations because costs of treating a patient with hip fracture are about 3 times greater than those of caring for a person without a history of hip fracture.[26] In a meta-analysis of large cohort studies including 195,102 women and 75,149 men, milk intake was not significantly associated with the risk of hip fracture in women (RR per glass of milk per day, 0.99; 95% CI, 0.96-1.02), whereas a trend toward a benefit in men was suggested (RR per glass of milk per day, 0.91; 95% CI, 0.81-1.01).[27] Notably, after excluding the influential Swedish cohort study by Michaelsson et al.,[28] there was a marginally significant 5% reduction of hip fracture risk per glass of milk intake per day in women as well (pooled RR, 0.95; 95% CI, 0.90-1.00; $P = 0.049$).[27] A more recent analysis of another Swedish cohort (104,000 individuals) suggested, in fact, a small increase in the risk of any fracture (RR, 1.02; 95% CI, 1.00-1.04) or of hip fracture (RR, 1.09; 95% CI, 1.05-1.13) per glass of milk intake among women but no association for the risk of all fractures (RR, 1.01; 95% CI, 0.99-1.03) or hip fractures (RR, 1.03; 95% CI, 0.99-1.07) in men.[14] The extent to which the higher rates of hip fracture in these Swedish cohorts, compared with data from other studies,[27] may have influenced results is unclear.

Calcium from foods including milk is found mainly in the form of calcium phosphate, whereas most studies on supplementation have used either calcium citrate or calcium carbonate. This is important because the different forms of calcium have highly variable bioavailability and, hence, potentially different effects on bone health.[29] It has been suggested that milk intake may plausibly reduce fracture risk through its specific calcium content and the potential synergistic effect of vitamin D in promoting calcium and phosphate absorption. In the most recent meta-analysis, calcium supplementation was shown to reduce the risk of total fracture (RR, 0.89; 95% CI, 0.81-0.96) and vertebral fracture (RR, 0.86; 95% CI, 0.74-1.00) but not hip (RR, 0.95; 95% CI, 0.76-1.18) or forearm fracture (RR, 0.96; 95% CI, 0.85-1.09). However, in the RCTs at lowest risk of bias (4 studies; N = 44 505), there was no effect of calcium supplementation on risk of fracture at any site. In another meta-analysis based on 4 double-blind RCTs,[30] no significant overall benefit of calcium supplementation on risk of nonvertebral fractures was observed. In fact, a possible adverse effect of calcium supplementation on hip fracture risk was found (among 6504 individuals and 139 hip fractures: pooled RR, 1.64; 95% CI, 1.02-2.64).[30]

Milk may reduce fracture risk through vitamin D fortification. Much of Europe, however, does not add vitamin D to milk. This is of particular concern in Northern European countries (including Sweden), where endogenous production of vitamin D by the skin is limited because of reduced exposure to sunshine. A recent individual participant data pooled analysis of 11 double-blind RCTs with 30,000 seniors showed that high doses of supplemented vitamin D (median, 800 IU/20 μg daily) reduces risk of hip fracture by 30% (hazard ratio [HR], 0.70; 95% CI, 0.58-0.86) and of any nonvertebral fracture by 14% (HR, 0.86; 95% CI, 0.76-0.96).[31] Benefits at the highest level of vitamin D intake were fairly consistent across subgroups defined by age group, type of dwelling, baseline 25-hydroxyvitamin D level, and calcium intake.[31]

To summarize, the association between milk intake and bone strength and fractures appears to be neutral, but this needs to be substantiated further through cohort studies and RCTs (Table 1). Additional mechanistic studies are also needed to better understand how milk affects bone strength and if, and to what extent, vitamin D fortification is critical to support milk's benefits for bone.

Cardiometabolic risk factors

Data from observational cohort studies are fairly consistent with data from RCTs, which in general suggest a neutral effect of milk consumption on cardiometabolic risk factors. Lowering plasma low-density lipoprotein cholesterol (LDL-C) concentrations and blood pressure is considered to be the primary clinical intervention for reducing CVD risk. However, LDLs are heterogeneous in size and density, and smaller LDL particles have been reported to be associated with an overall atherogenic dyslipidemic phenotype generally associated with an increased risk of CHD.[32] Data also suggest that LDL particle number may be more important than LDL-C concentration in determining the risk of CHD.[33] Meta-analyses of RCTs have shown that dietary saturated fatty acids (SFAs) increase plasma LDL-C compared with carbohydrates, monounsaturated fatty acids, and polyunsaturated fatty acids.[34] However, SFAs from dairy may have no effect on LDL particle number and cholesterol levels.[35,36] In fact, studies have shown that SFAs from dairy tend to increase levels of larger, but not smaller, LDL particles, in contrast to carbohydrates, which increase smaller LDLs.[37] The clinical significance of this increase in large LDLs with consumption of SFAs from dairy remains to be determined.

In a small randomized controlled feeding trial, Drouin-Chartier et al.[38] showed that consumption of 4 cups of partly skimmed milk (2% fat) for 6 weeks vs no milk had virtually no impact on a wide spectrum of cardiometabolic risk factors in postmenopausal women, including LDL-C and other lipid risk factors, markers of vascular function, and markers of inflammation. In an RCT with 158 overweight and obese men and women, neither high protein nor SFAs from dairy affected insulin sensitivity or plasma LDL-C, high-density lipoprotein cholesterol, or triglyceride concentrations.[39]

There has been some evidence that specific fatty acids found in dairy fat may be associated with health benefits. For example, trans-palmitoleate (trans 16:1n-7) is a trans fatty acid found primarily in dairy fat, and its blood phospholipid concentrations have been associated with lower insulin resistance, a more favourable lipid profile, and a reduced incidence of diabetes,[40] but results have not been consistent.[18] Vaccenic acid, a trans fatty acid found in dairy fat but also in partially hydrogenated vegetable oil, has also drawn the attention of the research community. Several studies in animals have shown that intake of vaccenic acid may have favourable effects on cardiometabolic risk factors and immune function.[41,42] However, these data have not yet been replicated in human studies.[43] Although of interest, studying the health impacts of individual trans fatty acids specific to dairy fat will not fully resolve the question of how milk as a complex food influences health.

The association between milk intake and hypertension/blood pressure has been quite consistent in observational cohort studies. The meta-analysis of 7 cohort studies by Soedamah-Muthu et al.[44] assessed the dose-response association between milk intake and the risk of hypertension. Based on data from 47,647 individuals, each increment of 200g/d of milk was associated with a significant 4% reduction in the risk of hypertension (RR, 0.96; 95% CI, 0.94-0.98). In contrast, Benatar et al,[45] in a meta-analysis of 7 RCTs published before 2013, could not confirm a significant blood pressure−lowering effect of total dairy intake on systolic and diastolic blood pressure. Meta-analyses of RCTs showed inconsistent results regarding the impact of probiotic fermented milk, with favourable as well as neutral effects on systolic and diastolic blood pressure.[46,47] More recently, Drouin-Chartier et al.[48] showed in an RCT with 76 patients with mild to moderate hypertension that daily consumption of milk (low fat), yogurt (low fat), and cheese (regular fat) for a total of 3 servings per day significantly reduced mean daytime systolic blood pressure (−2 mm Hg; $P = 0.05$) in men but not in women when compared with a dairy-free control diet. Because most of the existing RCTs have assessed the impact of total dairy rather than milk per se on blood pressure, more studies on this topic are clearly needed.

Both cross-sectional and longitudinal cohort studies have shown significant inverse relationships between dairy product intake and measures of arterial stiffness,[49,50] which has been proposed to be a more holistic marker of vascular health and predictor of cardiovascular events and mortality than blood pressure per se.[51] This remains controversial, however, and more clinical studies assessing the impact of milk intake on arterial stiffness are clearly warranted to pursue this hypothesis.

In summary, it appears that milk consumption per se may have relatively neutral effects on a wide spectrum of cardiometabolic risk factors, which overall is consistent with data from observational cohort studies. One exception pertains to a potentially favourable effect of dairy/milk intake on blood pressure. However, several key questions remain, as discussed in the following section.

Table 2. Key knowledge gaps related to milk and health and research opportunities

- Do regular/full fat and reduced/nonfat milk products have similar or different effects on health outcomes?
- To what extent are potential health effects of milk consumption modulated by the foods it is replacing in the diet?
- What is the impact of milk consumption on other vascular-related disease outcomes such as peripheral arterial disease, chronic kidney disease and cognitive decline?
- Does milk powder have similar health properties as liquid milk?
- How do different cattle feeding practices, which modify the fatty acid profiles of dairy fat, influence the effect of milk on health?
- Do age, weight status, sex, and ethnicity influence the impact of milk consumption on health?
- Is the effect of milk consumption on health outcomes similar among populations with traditionally low vs high intakes?

Complexities in Assessing the Impact of Milk on Health and Research Opportunities

Assessing the effect of milk consumption on health is complex and requires further studies to address several important questions relevant to clinical practice and public health (Table 2).

Effect of replacement foods

One of the key aspects to consider when assessing the place of milk in a healthy dietary pattern is to consider what it displaces in the diet. This issue requires considerable attention because the impact of milk per se on health cannot be fully dissociated from that of the foods it replaces. Data from a 6-month RCT indicated that isocaloric replacement of milk by SSBs increases fat storage in the liver, muscle, and visceral fat.[52] Results from observational cohort studies based on modelling of dietary data are consistent with this in suggesting that "substituting" SSBs for milk is associated with an increased risk of weight gain.[53] Data from 2 large US cohort studies have shown that compared with 1 serving per day of red meat, 1 serving per day of dairy including milk was associated with an 11% (95% CI, 5%-17%) lower risk of stroke in men and women and a 13% (95% CI, 6%-19%) lower risk of CHD in women.[54,55] In contrast, dairy consumption in place of fish was associated with a higher risk of CHD in women.[55] However, as emphasized earlier, milk may not be comparable to other solid sources of protein in the context of hydration and protein functionality. This issue deserves more consideration in future studies so that the impact of solid vs liquid foods on health can be assessed separately, according to their specific contribution to the overall diet.

Factors affecting nutrient composition of milk

Other aspects to consider pertain to seasonal and feeding practice—related variations in milk nutrient content. For example, indoor feeding of dairy cows increases the SFA content of fat in milk by almost 10% compared with outdoor feeding at high altitudes.[56] Accordingly, studies in Europe and the United States have documented seasonal changes in the fat content of milk,[57,58] with a decrease in the proportion of SFAs and an increase trans fatty acids during the grazing season. However, the statistically significant differences in the fatty acid content of milk between seasons and regions in the United States appeared to be minor from an overall human nutrition perspective, with SFA profiles that were numerically similar.[58] Assessment of food intake in observational cohort studies certainly does not capture such variation in milk nutrient composition, whether important or not. Hence, the extent to which accounting for such variation in milk nutrient profile will enhance our understanding of the impact of milk consumption on health is uncertain. Whether a reduced-SFA milk is healthier than unmodified milk is certainly an area with great research potential.[59]

Whole milk (3.25% fat) in most observational cohort studies has generally been considered a high/regular-fat product, which may be inappropriate considering that other full-fat dairy such as cheese contains as much as 40%-45% fat. This is a significant shortcoming in several of the existing studies on milk and health. To better address this limitation, future studies should also examine how different types of milk based on fat content, but also perhaps on other aspects such as fermentation and vitamin D fortification, relate to cardiometabolic health.

Geographic considerations

Vitamin D fortification of milk is not systematic in Europe but is so in the United States and Canada. The extent to which this leads to inconsistent associations between milk intake and health is unclear. Consumption of milk is highly variable around the world, with trends toward reduced consumption in North America and increased consumption in Asia,[60] where consumption has traditionally been very low. It will be challenging for ongoing observational cohort studies in these populations to account for acute upward and downward trends in milk/dairy consumption. Asian countries are also important consumers of milk protein powders. The impact of this nonliquid form of milk on health is poorly characterized compared with its liquid parent. Lactose intolerance also needs to be factored in when assessing the impact of milk intake on health in Asian countries.

Other disease outcomes

Further research is needed to document how milk consumption influences vascular-related disease outcomes other than heart disease and stroke, eg, peripheral arterial disease, chronic kidney disease, and cognitive decline.[61] The extent to which weight status, age, ethnicity, and sex modify the impact of milk consumption on health outcomes also needs further consideration. The expert panel did not discuss the impact of milk intake on cancer risk. Briefly, several reports and meta-analyses of observational cohort studies have been conducted on this topic, suggesting no detrimental effect of milk consumption on the risk of a variety of cancers,[62-64] with the exception perhaps of prostate cancer,[65] although this has not been a consistent finding.[66]

Table 3. Key summary points

- Milk consumption is part of many cultures and is recommended in most dietary guidelines around the world
- Evidence available to date suggests that milk has a neutral effect on most cardiovascular outcomes, whereas milk intake may be associated with a lower risk of hypertension
- Important research gaps need to be addressed to better understand the impact of milk intake on health

Conclusions

Although in principle, RCTs would be the optimal means of assessing the impact of milk consumption per se on clinical outcomes such as CVD, type 2 diabetes, or cancer, such studies are for the most part not practicable, and hence it is necessary to rely on high-quality observational cohort studies as well as on smaller-scale clinical studies of milk effects on surrogates of disease outcome such as cardiometabolic risk factors. The available body of evidence is relatively consistent in supporting a neutral effect of milk intake on multiple health outcomes (Table 3). This raises the question about the relevance of including milk (and dairy) as part of the guidelines for promoting healthy eating. However, milk consumption does contribute to the intake of several important nutrients, and this needs to be factored in when considering the place of milk in current dietary guidelines.

This review also identifies key research gaps that need to be addressed in the future (Table 2). It will be important to determine the intrinsic health properties of milk (eg, vitamin D fortification vs no fortification) vs the effects mediated through foods it replaces or displaces in the diet. In this regard, the difference between regular-fat and reduced-fat milk in influencing health outcomes needs to be specifically documented. The extent to which nutrient variations in milk, including milk SFAs, influence its association with health outcomes also needs consideration. Potential variations by sex, obesity status, and geographic locations regarding the impact of milk intake on health are poorly understood. Finally, the possibility that milk intake is simply a marker of diets with good nutritional quality cannot be ruled out, and this concept needs further research as well. Addressing these research gaps will help resolve the place of milk in the healthy eating paradigm, hence contributing to better informed evidence-based dietary guidelines.

Acknowledgements

The authors wish to thank Frank B. Hu, Professor of Nutrition and Epidemiology at the Harvard T. H. Chan School of Public Health, for his insightful comments and critical review of the manuscript.

Funding Sources

The International Chair on Cardiometabolic Risk supported the meeting and the travel of researchers who coauthor the paper. No other funding was provided to support this review.

Disclosures

Please see the *Disclosures* section of the Supplementary Material.

References

1. Weintraub WS, Daniels SR, Burke LE, et al. Value of primordial and primary prevention for cardiovascular disease: a policy statement from the American Heart Association. Circulation 2011;124:967-90.
2. Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic impact goal through 2020 and beyond. Circulation 2010;121:586-613.
3. Huth PJ, Fulgoni VL, Keast DR, et al. Major food sources of calories, added sugars, and saturated fat and their contribution to essential nutrient intakes in the U.S. diet: data from the National Health and Nutrition Examination Survey (2003-2006). Nutr J 2013;12:116.
4. Dawson-Hughes B, Mithal A, Bonjour JP, et al. IOF position statement: vitamin D recommendations for older adults. Osteoporos Int 2010;21:1151-4.
5. Sanders KM, Nowson CA, Kotowicz MA, et al. Calcium and bone health: position statement for the Australian and New Zealand Bone and Mineral Society, Osteoporosis Australia and the Endocrine Society of Australia. Med J Aust 2009;190:316-20.
6. Liao Y, Huang JL, Qiu MX, et al. Impact of serum vitamin D level on risk of bladder cancer: a systemic review and meta-analysis. Tumour Biol 2015;36:1567-72.
7. Garland CF, Kim JJ, Mohr SB, et al. Meta-analysis of all-cause mortality according to serum 25-hydroxyvitamin d. Am J Public Health 2014;104:e43-50.
8. Duffey KJ, Steffen LM, Van Horn L, et al. Dietary patterns matter: diet beverages and cardiometabolic risks in the longitudinal coronary artery risk development in young adults (cardia) study. Am J Clin Nutr 2012;95:909-15.
9. Barr SI. Perceived lactose intolerance in adult Canadians: a national survey. Appl Physiol Nutr Metab 2013;38:830-5.
10. von Keyserlingk MA, Martin NP, Kebreab E, et al. Invited review: sustainability of the US dairy industry. J Dairy Sci 2013;96:5405-25.
11. Soedamah-Muthu SS, Ding EL, Al-Delaimy WK, et al. Milk and dairy consumption and incidence of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. Am J Clin Nutr 2011;93:158-71.
12. O'Sullivan TA, Hafekost K, Mitrou F, et al. Food sources of saturated fat and the association with mortality: a meta-analysis. Am J Public Health 2013;103:e31-42.
13. Wang C, Yatsuya H, Tamakoshi K, et al. Milk drinking and mortality: findings from the Japan collaborative cohort study. J Epidemiol 2015;25:66-73.
14. Michaelsson K, Wolk A, Langenskiold S, et al. Milk intake and risk of mortality and fractures in women and men: cohort studies. BMJ 2014;349:g6015.
15. Larsson SC, Crippa A, Orsini N, et al. Milk consumption and mortality from all causes, cardiovascular disease, and cancer: a systematic review and meta-analysis. Nutrients 2015;7:7749-63.
16. Hu D, Huang J, Wang Y, et al. Dairy foods and risk of stroke: a meta-analysis of prospective cohort studies. Nutr Metab Cardiovasc Dis 2014;24:460-9.
17. Abdullah MM, Cyr A, Lepine MC, et al. Recommended dairy product intake modulates circulating fatty acid profile in healthy adults: a multi-centre cross-over study. Br J Nutr 2015;113:435-44.
18. Chowdhury R, Warnakula S, Kunutsor S, et al. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. Ann Intern Med 2014;160:398-406.
19. Warensjo E, Jansson JH, Cederholm T, et al. Biomarkers of milk fat and the risk of myocardial infarction in men and women: a prospective, matched case-control study. Am J Clin Nutr 2010;92:194-202.
20. Jenkins B, West JA, Koulman A. A review of odd-chain fatty acid metabolism and the role of pentadecanoic acid (c15:0) and heptadecanoic acid (c17:0) in health and disease. Molecules 2015;20:2425-44.
21. Tong X, Dong JY, Wu ZW, et al. Dairy consumption and risk of type 2 diabetes mellitus: a meta-analysis of cohort studies. Eur J Clin Nutr 2011;65:1027-31.
22. Chen M, Sun Q, Giovannucci E, et al. Dairy consumption and risk of type 2 diabetes: 3 cohorts of us adults and an updated meta-analysis. BMC Med 2014;12:215.
23. Gao D, Ning N, Wang C, et al. Dairy products consumption and risk of type 2 diabetes: systematic review and dose-response meta-analysis. PLoS One 2013;8:e73965.
24. Aune D, Norat T, Romundstad P, et al. Dairy products and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. Am J Clin Nutr 2013;98:1066-83.
25. Bergholdt HK, Nordestgaard BG, Ellervik C. Milk intake is not associated with low risk of diabetes or overweight-obesity: a mendelian randomization study in 97,811 Danish individuals. Am J Clin Nutr 2015;102:487-96.
26. Haentjens P, Autier P, Barette M, et al. The economic cost of hip fractures among elderly women. A one-year, prospective, observational cohort study with matched-pair analysis. Belgian hip fracture study group. J Bone Joint Surg Am 2001;83-A:493-500.
27. Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, et al. Milk intake and risk of hip fracture in men and women: a meta-analysis of prospective cohort studies. J Bone Miner Res 2011;26:833-9.
28. Michaelsson K, Melhus H, Bellocco R, et al. Dietary calcium and vitamin D intake in relation to osteoporotic fracture risk. Bone 2003;32:694-703.
29. Bischoff-Ferrari HA, Staehelin HB. Importance of vitamin d and calcium at older age. Int J Vitam Nutr Res 2008;78:286-92.
30. Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, et al. Calcium intake and hip fracture risk in men and women: a meta-analysis of prospective cohort studies and randomized controlled trials. Am J Clin Nutr 2007;86:1780-90.
31. Bischoff-Ferrari HA, Willett WC, Orav EJ, et al. A pooled analysis of vitamin D dose requirements for fracture prevention. N Engl J Med 2012;367:40-9.
32. Lamarche B, Tchernof A, Moorjani S, et al. Small, dense low-density lipoprotein particles as a predictor of the risk of ischemic heart disease in men. Prospective results from the Quebec cardiovascular study. Circulation 1997;95:69-75.

33. Sniderman AD, Lamarche B, Contois JH, et al. Discordance analysis and the Gordian Knot of LDL and non-HDL cholesterol versus apoB. Curr Opin Lipidol 2014;25:461-7.

34. Mensink RP, Katan MB. Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. Arterioscler Thromb 1992;12: 911-9.

35. Rosqvist F, Smedman A, Lindmark-Mansson H, et al. Potential role of milk fat globule membrane in modulating plasma lipoproteins, gene expression, and cholesterol metabolism in humans: a randomized study. Am J Clin Nutr 2015;102:20-30.

36. Thorning TK, Raziani F, Bendsen NT, et al. Diets with high-fat cheese, high-fat meat, or carbohydrate on cardiovascular risk markers in overweight postmenopausal women: a randomized crossover trial. Am J Clin Nutr 2015;102:573-81.

37. Dreon DM, Fernstrom HA, Campos H, et al. Change in dietary saturated fat intake is correlated with change in mass of large low-density-lipoprotein particles in men. Am J Clin Nutr 1998;67:828-36.

38. Drouin-Chartier JP, Gagnon J, Labonte ME, et al. Impact of milk consumption on cardiometabolic risk in postmenopausal women with abdominal obesity. Nutr J 2015;14:12.

39. Chiu S, Williams PT, Dawson T, et al. Diets high in protein or saturated fat do not affect insulin sensitivity or plasma concentrations of lipids and lipoproteins in overweight and obese adults. J Nutr 2014;144:1753-9.

40. Mozaffarian D, Cao H, King IB, et al. Trans-palmitoleic acid, metabolic risk factors, and new-onset diabetes in U.S. adults: a cohort study. Ann Intern Med 2010;153:790-9.

41. Jacome-Sosa MM, Borthwick F, Mangat R, et al. Diets enriched in trans-11 vaccenic acid alleviate ectopic lipid accumulation in a rat model of nafld and metabolic syndrome. J Nutr Biochem 2014;25:692-701.

42. Blewett HJ, Gerdung CA, Ruth MR, et al. Vaccenic acid favourably alters immune function in obese JCR: LA-cp rats. Br J Nutr 2009;102: 526-36.

43. Gebauer SK, Chardigny JM, Jakobsen MU, et al. Effects of ruminant trans fatty acids on cardiovascular disease and cancer: a comprehensive review of epidemiological, clinical, and mechanistic studies. Adv Nutr 2011;2:332-54.

44. Soedamah-Muthu SS, Verberne LD, Ding EL, et al. Dairy consumption and incidence of hypertension: a dose-response meta-analysis of prospective cohort studies. Hypertension 2012;60:1131-7.

45. Benatar JR, Jones E, White H, et al. A randomized trial evaluating the effects of change in dairy food consumption on cardio-metabolic risk factors. Eur J Prev Cardiol 2014;21:1376-86.

46. Dong JY, Szeto IM, Makinen K, et al. Effect of probiotic fermented milk on blood pressure: a meta-analysis of randomised controlled trials. Br J Nutr 2013;110:1188-94.

47. Usinger L, Reimer C, Ibsen H. Fermented milk for hypertension. Cochrane Database Syst Rev 2012;4:CD008118.

48. Drouin-Chartier JP, Gigleux I, Tremblay AJ, et al. Impact of dairy consumption on essential hypertension: a clinical study. Nutr J 2014;13:83.

49. Crichton GE, Elias MF, Dore GA, et al. Relations between dairy food intake and arterial stiffness: pulse wave velocity and pulse pressure. Hypertension 2012;59:1044-51.

50. Livingstone KM, Lovegrove JA, Cockcroft JR, et al. Does dairy food intake predict arterial stiffness and blood pressure in men?: evidence from the Caerphilly prospective study. Hypertension 2013;61:42-7.

51. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol 2010;55:1318-27.

52. Maersk M, Belza A, Stodkilde-Jorgensen H, et al. Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: a 6-mo randomized intervention study. Am J Clin Nutr 2012;95:283-9.

53. Pan A, Malik VS, Hao T, et al. Changes in water and beverage intake and long-term weight changes: results from three prospective cohort studies. Int J Obes (Lond) 2013;37:1378-85.

54. Bernstein AM, Pan A, Rexrode KM, et al. Dietary protein sources and the risk of stroke in men and women. Stroke 2012;43:637-44.

55. Bernstein AM, Sun Q, Hu FB, et al. Major dietary protein sources and risk of coronary heart disease in women. Circulation 2010;122:876-83.

56. Kraft J, Collomb M, Mockel P, et al. Differences in CLA isomer distribution of cow's milk lipids. Lipids 2003;38:657-64.

57. Heck JM, van Valenberg HJ, Dijkstra J, et al. Seasonal variation in the Dutch bovine raw milk composition. J Dairy Sci 2009;92:4745-55.

58. O'Donnell-Megaro AM, Barbano DM, Bauman DE. Survey of the fatty acid composition of retail milk in the United States including regional and seasonal variations. J Dairy Sci 2011;94:59-65.

59. Livingstone KM, Lovegrove JA, Givens DI. The impact of substituting SFA in dairy products with MUFA or PUFA on CVD risk: evidence from human intervention studies. Nutr Res Rev 2012;25:193-206.

60. Wang Y, Li S. Worldwide trends in dairy production and consumption and calcium intake: is promoting consumption of dairy products a sustainable solution for inadequate calcium intake? Food Nutr Bull 2008;29: 172-85.

61. Fardet A, Boirie Y. Associations between food and beverage groups and major diet-related chronic diseases: an exhaustive review of pooled/meta-analyses and systematic reviews. Nutr Rev 2014;72:741-62.

62. Genkinger JM, Wang M, Li R, et al. Dairy products and pancreatic cancer risk: a pooled analysis of 14 cohort studies. Ann Oncol 2014;25: 1106-15.

63. Dong JY, Zhang L, He K, et al. Dairy consumption and risk of breast cancer: a meta-analysis of prospective cohort studies. Breast Cancer Res Treat 2011;127:23-31.

64. Ralston RA, Truby H, Palermo CE, et al. Colorectal cancer and non-fermented milk, solid cheese, and fermented milk consumption: a systematic review and meta-analysis of prospective studies. Crit Rev Food Sci Nutr 2014;54:1167-79.

65. Aune D, Navarro Rosenblatt DA, Chan DS, et al. Dairy products, calcium, and prostate cancer risk: a systematic review and meta-analysis of cohort studies. Am J Clin Nutr 2015;101:87-117.

66. Huncharek M, Muscat J, Kupelnick B. Dairy products, dietary calcium and vitamin D intake as risk factors for prostate cancer: a meta-analysis of 26,769 cases from 45 observational studies. Nutr Cancer 2008;60: 421-41.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at http://dx.doi.org/10.1016/j.cjca.2015.12.033.