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Review

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

Short title

Milk and cardiometabolic health

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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. This paper 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 higher nutritional quality diets 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.

75-word summary

This paper provides a perspective on the place of milk in a balanced/healthy diet. The evidence to date suggests a neutral effect of milk intake *per se* on several health-related outcomes. The possibility that milk intake is simply a marker of higher nutritional quality diets cannot be ruled out and needs to be further examined in future studies.

Introduction

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 four health behaviors (diet quality, physical activity, smoking, body weight) and three health factors (cholesterol, glucose 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] While the contribution of each of these foods to cardiovascular health is widely accepted, the extent to which other foods, such as milk, contribute to 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 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 below, 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[6] and of mortality,[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 as it may yield further effects on health. Finally, reduced-fat milk consumption has been associated with a prudent dietary pattern in epidemiological 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 regular 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 while increasing markedly in many South Asian and East Asian countries.

The International Chair on Cardiometabolic Risk (see Supplementary material) convened a group of experts to assess the evidence linking milk intake with health. Data from epidemiological 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 geographical location. There was a unanimous sense that milk intake *per se* was not associated with the risk of clinical outcomes such as total CVD, CHD, stroke and type 2 diabetes. Several meta-analyses on the topic support this conclusion. Soedamah-Muthu *et al*[11] have examined the dose-response relationship between milk intake and overall CVD incidence in a meta-analysis of four cohort studies published prior to 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]=0.94 per 200 mL/d, 95% confidence interval [CI] 0.89-0.99). However, this was not substantiated in a subsequent meta-analysis of cohort studies combining data from more than 330,000 individuals by O'Sullivan *et al*[12] who have reported no significant association between milk intake and CVD mortality (RR=0.96 per 200 mL/d, 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 have shown 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-up for 11 to 20 years.[14] The study revealed a significant increase in the risk of CVD mortality with milk consumption among both women (RR per 200g/d = 1.15, 95%CI 1.12-1.19) and men (RR=1.05, 95%CI 1.03-1.07). The authors have been 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 recent 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=1.00 per 200 mL/d, 95% CI 0.96-1.04) or stroke (RR=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 non-linear 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. non consumers=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 have been associated with a reduced risk of CHD in a meta-analysis by Chowdury *et al*.[18] Recent data from the Swedish studies in males and females[14] are at odds with previous nested case-control data from the same cohorts, 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 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 reflects variations in milk intake remains uncertain.

In sum, while the association between milk intake and CVD risk and morbidity remains uncertain to a certain degree, the evidence so far from existing meta-analyses and subsequent cohort studies points towards 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 to 14 studies and 167,000 to 459,790 individuals[21-24] have been relatively consistent in showing no significant association between milk intake and the risk for type 2 diabetes (RR ranging from 0.87 to 0.95, 95%CI ranging from 0.69 to 1.67 depending on whether total, low fat or whole fat milk was considered). Using a Mendelian randomization approach in a cohort of 97,811 Danish individuals, Bergholdt *et al*[25] have shown that milk intake as assessed by genetic variations related to lactose tolerance was also not associated with lower 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 as costs of treating a hip-fracture patient are about three 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) while a trend toward a benefit in men was suggested (RR=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 also among women (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 to 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 to 1.03) or hip fracture (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, while 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 (four 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 non-vertebral 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 due to reduced sunshine exposure. A recent individual participant data pooled analysis of 11 double-blind RCTs with 30,000 seniors has shown that high doses of supplemented vitamin D (median = 800 IU/20μg daily) reduces risk of hip fracture by 30% (hazard ratio [HR]=0.70, 95% CI 0.58-0.86) and of any non-vertebral 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 so far but 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 benefits on 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 LDL-C concentrations and blood pressure is considered to be the primary clinical intervention for reducing CVD risk. However, LDL 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-analysis of RCTs have shown that dietary SFA increase plasma LDL-C compared with carbohydrates, MUFA and PUFA.[34] However, SFA from dairy may have no effect on LDL particle number and on cholesterol levels.[35, 36] In fact, studies have shown that SFA from dairy tend to increase levels of larger, but not of smaller LDL particles in contrast with carbohydrates, which increase smaller LDL.[37] The clinical significance of this increase in large LDL with consumption of SFA from dairy remains to be determined.

Drouin-Chartier *et al*[38] have shown in a small randomized controlled feeding trial that consumption of four 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 a RCT involving 158 overweight and obese men and women, neither high protein nor SFA from dairy affected insulin sensitivity or plasma LDL-C, HDL-C and 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 favorable lipid profile, and 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 partly 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 favorable effects on cardiometabolic risk factors and on immune function.[41, 42] However, these data have not yet been replicated in human studies.[43] While 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 seven 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 increments of 200g/d of milk were associated with a significant 4% reduction in the risk of hypertension (RR=0.96, 95%CI 0.94-0.98). On the other hand, Benetar *et al*[45] in a meta-analysis of seven RCTs published prior to 2013 could not confirm a significant blood pressure lowering effect of total dairy intake on systolic and diastolic blood pressures. Meta-analyses of RCTs showed inconsistent results regarding the impact of probiotic fermented milk with favorable[46] as well as neutral effects[47] on systolic and diastolic BP. More recently, Drouin-Chartier *et al*[48] have shown in a RCT involving 76 mild to moderate hypertensive subjects that daily consumption of milk (low-fat), yogurt (low-fat) and cheese (regular fat) for a total of 3 servings/d significantly reduced mean daytime systolic blood pressure (-2 mm Hg, P=0.05) in men but not in women in comparison to 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[49] and longitudinal[50] cohort studies have shown significant inverse relationships between dairy product intake and measures of arterial stiffness, 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 sum, 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 favorable effect of dairy/milk intake on blood pressure. But several key questions remain, as discussed in the following section.

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-mo RCT indicated that isocaloric replacement of milk by SSB increases fat storage in the liver, muscle, and visceral fat.[52] Results from observational cohort studies based on modeling 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 two large US cohort studies have shown that compared with 1 serving/day of red meat, 1 serving/day of dairy including milk was associated with an 11% (95%CI 5%-17%) lower risk of stroke in men and women[54] and a 13% (95%CI 6%-19%) lower risk of CHD in women.[55] In contrast, dairy consumption in place of fish was associated with a higher risk of CHD in women.[55] However, as emphasized above, 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 increases the SFA content of fat in milk by almost 10% compared with outdoor feeding at high altitudes.[56] Accordingly, studies in Europe[57] and in the USA[58] have documented seasonal changes in the fat content of milk, with a decrease in proportion of SFA 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 US appeared 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. In order 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.

Geographical considerations. Vitamin D fortification of milk is not systematic in Europe but is so in the USA 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 towards reduced consumption in North America and increased consumption in Asia,[60] where consumption has traditionally been very low. It will be challenging for on-going 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 non-liquid form of milk on health is poorly characterized compared to 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 needs to document how milk consumption influences vascular-related disease outcomes other than heart disease and stroke such as 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]

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-scaled 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 2**). This raises the question as to the relevance of including milk (and dairy) as part of guidelines 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 3**). It will be important to determine the intrinsic health properties of milk (for example vitamin D fortification vs. no fortification) vs. the effects mediated through foods it replaces or displaces in the diet. In that 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 SFA, influences its association with health outcomes also needs considerations. Potential variations by sex, obesity status and geographical locations regarding the impact of milk intake on health are poorly understood. Finally, the possibility that milk intake is simply a marker of good nutritional quality diets cannot be ruled out and this concept needs further research as well. Addressing these research gaps will help resolve the place of milk within the healthy eating paradigm, hence contributing to better informed, evidence-based dietary guidelines.

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Disclosures are provided as 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;124:967-990
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;21:1151-1154
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;190:316-320
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;36:1567-1572
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;95:909-915
9. Barr SI. Perceived lactose intolerance in adult canadians: A national survey. *Appl Physiol Nutr Metab*. 2013;38:830-835
10. von Keyserlingk MA, Martin NP, Kebreab E, et al. Invited review: Sustainability of the us dairy industry. *J Dairy Sci*. 2013;96:5405-5425
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;93:158-171
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;7:7749-7763
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;24:460-469

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;113:435-444

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;20:2425-2444

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;65:1027-1031

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;98:1066-1083

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;102:487-496

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;26:833-839

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;78:286-292

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;86:1780-1790

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;367:40-49

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;25:461-467
34. Mensink RP, Katan MB. Effect of dietary fatty acids on serum lipids and lipoproteins. A meta- analysis of 27 trials. *Arteriosclerosis & Thrombosis*. 1992;12:911-919
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;102:573-581
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;67:828-836
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;144:1753-1759
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;153:790-799

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;102:526-536

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;2:332-354

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

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;21:1376-1386

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;110:1188-1194

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;59:1044-1051

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;61:42-47

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;55:1318-1327

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;95:283-289

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;37:1378-1385

54. Bernstein AM, Pan A, Rexrode KM, et al. Dietary protein sources and the risk of stroke in men and women. *Stroke*. 2012;43:637-644

55. Bernstein AM, Sun Q, Hu FB, et al. Major dietary protein sources and risk of coronary heart disease in women. *Circulation*. 2010;122:876-883

56. Kraft J, Collomb M, Mockel P, et al. Differences in cla isomer distribution of cow's milk lipids. *Lipids*. 2003;38:657-664

57. Heck JM, van Valenberg HJ, Dijkstra J, et al. Seasonal variation in the dutch bovine raw milk composition. *J Dairy Sci*. 2009;92:4745-4755

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;29:172-185

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;72:741-762

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;25:1106-1115

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 nonfermented milk, solid cheese, and fermented milk consumption: A systematic review and meta-analysis of prospective studies. *Crit Rev Food Sci Nutr*. 2014;54:1167-1179

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;60:421-441

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

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

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

- Do regular/full fat and reduced/non-fat 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?

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, while milk intake may be associated with a lower risk of hypertension.
- However, important research gaps need to be addressed to better understand the impact of milk intake on health.