

Comprehensive Review of the Impact of Dairy Foods and Dairy Fat on Cardiometabolic Risk^{1–3}

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ABSTRACT

Because regular-fat dairy products are a major source of cholesterol-raising saturated fatty acids (SFAs), current US and Canadian dietary guidelines for cardiovascular health recommend the consumption of low-fat dairy products. Yet, numerous randomized controlled trials (RCTs) have reported rather mixed effects of reduced- and regular-fat dairy consumption on blood lipid concentrations and on many other cardiometabolic disease risk factors, such as blood pressure and inflammation markers. Thus, the focus on low-fat dairy in current dietary guidelines is being challenged, creating confusion within health professional circles and the public. This narrative review provides perspective on the research pertaining to the impact of dairy consumption and dairy fat on traditional and emerging cardiometabolic disease risk factors. This comprehensive assessment of evidence from RCTs suggests that there is no apparent risk of potential harmful effects of dairy consumption, irrespective of the content of dairy fat, on a large array of cardiometabolic variables, including lipid-related risk factors, blood pressure, inflammation, insulin resistance, and vascular function. This suggests that the purported detrimental effects of SFAs on cardiometabolic health may in fact be nullified when they are consumed as part of complex food matrices such as those in cheese and other dairy foods. Thus, the focus on low-fat dairy products in current guidelines apparently is not entirely supported by the existing literature and may need to be revisited on the basis of this evidence. Future studies addressing key research gaps in this area will be extremely informative to better appreciate the impact of dairy food matrices, as well as dairy fat specifically, on cardiometabolic health. *Adv Nutr* 2016;7:1041–51.

Keywords: dairy, milk, yogurt, cheese, cholesterol, blood pressure, triglyceride, apolipoprotein B, inflammation

Introduction

Reducing LDL cholesterol concentrations along with managing high blood pressure (BP)⁸ are considered to be key targets for the prevention and treatment of cardiovascular disease (CVD) (1, 2). Several lines of evidence indicate that lifestyle factors, including poor diet and sedentary lifestyle, are also key modifiable risk factors for CVD and type 2 diabetes (T2D). The CVD-related dietary guidelines proposed by many health organizations traditionally have

been focused on nutrients that raise or reduce plasma LDL cholesterol concentrations (3). Low-fat dairy products are advocated in most dietary guidelines to limit the consumption

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⁸ Abbreviations used: BP, blood pressure; CVD, cardiovascular disease; CRP, C-reactive protein; DASH, Dietary Approaches to Stop Hypertension; MetS, metabolic syndrome; NCEP, National Cholesterol Education Program; RCT, randomized controlled trial; T2D, type 2 diabetes; VCAM-1, vascular cell adhesion molecule 1.

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of the cholesterol-raising SFAs contained in regular and high-fat dairy products.

However, the Institute of Medicine has suggested that the benefits of reducing LDL cholesterol concentration by statin treatment may not be extrapolated to the effect of dietary change on this risk factor (4). This is possibly the case as well for BP. Thus, analysis of a larger spectrum of risk factors may provide insightful information on how diet modifications likely affect CVD risk. Beyond increased LDL cholesterol concentrations and BP, low HDL cholesterol, high TGs (fasting and postprandial), high apoB, and small, dense LDL also may contribute on their own to increasing coronary artery disease risk (5, 6). Subclinical inflammation is recognized as a key feature of the atherosclerotic process (7), and several markers of subclinical inflammation, such as C-reactive protein (CRP) and IL-6, have been associated with an increased risk of coronary artery disease (8, 9). Vascular dysfunction (10) and impaired coagulation processes (11, 12), as well as insulin resistance (13), also have been identified as key cardiometabolic disease risk factors. The association between each of these risk factors and CVD risk is reviewed briefly in the **Supplemental Material**. Thus, there is a need for an extensive and comprehensive assessment of the impact of dairy food consumption on traditional and emerging cardiometabolic disease risk factors that is based on data from randomized controlled trials (RCTs) to help better inform future recommendations regarding dairy consumption and cardiovascular health. This paper reviews the evidence from RCTs that assessed the impact of consuming various types of dairy foods on a wide array of cardiometabolic disease risk factors.

Methods

This review is based primarily on data from meta-analyses of RCTs and from individual RCTs conducted in disease-free individuals. We specifically selected meta-analyses and RCTs that assessed the impact of total dairy consumption and of specific dairy foods (i.e., high- and low-fat products, milk, cheese, and yogurt) on cardiometabolic disease risk factors. Studies that have compared the impact of various dairy foods (e.g., cheese, milk, and yogurt) on cardiometabolic disease risk factors also were considered. Studies retained were those in which nonmodified dairy products were considered as the treatment per se, as opposed to being the control arm of the experiment. The following MeSH terms in PubMed were used for the literature search, with no restriction on publication date: “dairy product,” “milk,” “cheese,” and “yogurt or yoghurt,” in combination with “low-density lipoprotein,” “high-density lipoprotein,” “non high-density lipoprotein cholesterol,” “apolipoprotein B,” “apolipoprotein A-I,” “triglyceride,” “small dense LDL or LDL particle size,” “glucose,” “insulin or insulin resistance or HOMA,” “fibrinogen,” “Lp(a),” “inflammation or C-reactive protein or cytokine,” “vascular function or flow mediated dilation or peripheral arterial tone,” or “adhesion molecules.” Abstracts or articles published in languages other than English were not considered. The quality of identified meta-analyses and RCTs was assessed in broad terms on the basis of study design and duration, level of control of diets, and sample size.

Dairy and Cardiometabolic Disease Risk Factors LDL cholesterol

Dairy foods. Benatar et al. (14) meta-analyzed data from 9 RCTs that compared the impact of high- and low-fat dairy intake on plasma LDL cholesterol concentrations. To be included in the analysis, studies had to be RCTs of increased dairy consumption (low- and/or high-fat) for ≥ 1 mo without

additional dietary interventions. Increased total dairy consumption (mean increase of 3.6 servings/d) had no significant impact on LDL cholesterol concentrations compared with low dairy consumption. Increased consumption of both low-fat dairy (foods with $<1\%$ fat) and high-fat dairy (full-fat milk, cheese, butter, cream, and ice cream) also had no significant impact on LDL cholesterol concentrations (14). We showed in a recent RCT that consumption of 3 servings/d for 4 wk of commercially available dairy foods (30 g regular-fat cheddar cheese, 175 g 1.5%-fat yogurt, or 375 mL 1%-fat milk) slightly but significantly increased LDL cholesterol in healthy men and women compared with a dairy-free diet (Δ LDL cholesterol: $+0.08$ mmol/L, $P = 0.04$) (15). The magnitude of LDL cholesterol changes in this recent RCT is consistent with results from the meta-analysis by Benatar et al. (14), and therefore is unlikely to modify its conclusions that an increased intake of total dairy has no significant impact on LDL cholesterol concentrations.

The impact of milk consumption per se on LDL cholesterol concentrations has been documented in a few RCTs. Barr et al. (16) conducted a parallel-arm RCT in which subjects were instructed to either maintain their usual milk and dairy intake or to increase their milk consumption (1% fat) over a period of 12 wk. Postintervention LDL cholesterol concentrations were similar between the milk group and the control group. Beavers et al. (17) showed that consumption of reduced-fat milk for 4 wk had no impact on LDL cholesterol concentrations compared with intake of a soy beverage in postmenopausal women. We showed in a controlled feeding study in 27 postmenopausal women that 2%-fat milk consumption (3.2 servings, 800 mL/2000 kcal) for 6 wk had no significant effect on LDL cholesterol concentrations compared with a milk-free control diet (18). Data from these 3 RCTs suggest that milk intake per se has no effect on LDL cholesterol concentrations.

Investigating the impact of cheese intake on LDL cholesterol concentrations is of relevance, considering the contribution of this dairy food to total dietary SFA intake in the population (19). Thorning et al. (20) showed that substituting cheese for meat or carbohydrates had no significant effect on post diet LDL cholesterol concentrations in postmenopausal women. Yogurt consumption per se for 6 wk in a large RCT comprising 90 healthy women was also shown to have no effect on LDL cholesterol concentrations compared with a dairy-free control diet (21).

Dairy fat. To our knowledge, studies that specifically compared the impact of high- and low-fat dairy foods on LDL cholesterol concentrations are scarce. In a crossover RCT in healthy men and women, consumption of a high-fat dairy and Dietary Approaches to Stop Hypertension (DASH)-type diet did not increase LDL cholesterol significantly compared with a low-fat dairy and DASH diet (22). Steinmetz et al. (23) conducted a parallel-arm RCT in which subjects consumed skimmed milk or whole-fat milk (236 mL/1000 kcal) for 6 wk. Postintervention LDL cholesterol concentrations were significantly lower in the skimmed milk group than in the

whole-fat milk group (mean \pm SE: 2.64 ± 0.19 compared with 2.96 ± 0.21 mmol/L, respectively, $P = 0.001$).

Dairy food matrix. De Goede et al. (24) conducted a meta-analysis of 5 RCTs that compared the effect of cheese and butter consumption on blood lipids. Data from 4 of the 5 RCTs were pooled for the specific analysis of LDL cholesterol. For a similar intake of SFAs, serum LDL cholesterol concentrations were significantly lower after cheese consumption than after butter consumption (Δ LDL cholesterol: -0.22 mmol/L; 95% CI: $-0.29, -0.14$ mmol/L). Consistent with this observation, LDL cholesterol concentrations after consumption of 40 g dairy fat from cheese/d tended to be lower than after consumption of a similar amount of dairy fat from butter [median (IQR): 3.7 mmol/L (3.3–3.9 mmol/L) compared with 3.9 mmol/L (3.5–4.1 mmol/L); $P = 0.07$] (25). Overall, these data suggest that constituents of cheese may attenuate the LDL cholesterol-raising effect of SFAs in normolipidemic subjects (Table 1). Our search did not retrieve any study that compared the impact of liquid and solid dairy products on LDL cholesterol concentrations.

Summary. Data from one meta-analysis and from additional RCTs are fairly consistent in suggesting that increasing consumption of dairy products, irrespective of fat content and form, and in the absence of other dietary change, has no effect on LDL cholesterol concentrations in healthy individuals (Table 1). The consumption of milk, cheese, or yogurt also may be relatively neutral in terms of impact on LDL cholesterol, although data remain limited to draw definitive conclusions at this point. The extent to which substitution of high-fat dairy for low-fat dairy influences LDL cholesterol concentrations also needs further assessment (Table 1). Additional RCTs are needed to address these knowledge gaps. Finally, data from RCTs also reinforce the importance of considering the food matrix from which dietary fat is provided and its impact on cardiometabolic disease risk factors, including LDL cholesterol.

HDL cholesterol

Dairy foods. The meta-analysis of RCTs by Benatar et al. (14) suggested that high compared with low dairy intake has no impact on HDL cholesterol concentrations. This was also the case when both low- and high-fat dairy foods were analyzed separately. In subsequent RCTs, total dairy product consumption was also shown to have no effect on HDL cholesterol concentrations (15, 22).

In a parallel-arm RCT, increasing consumption of 1%-fat milk by 750 mL/d for 12 wk had no impact on HDL cholesterol concentrations (week 12 compared with baseline, mean \pm SD: 1.43 ± 0.42 compared with 1.44 ± 0.46 mmol/L), whereas maintaining usual milk and dairy consumption was associated with an increase in HDL cholesterol (mean \pm SD: 1.42 ± 0.38 compared with 1.38 ± 0.37 mmol/L; between-group comparison, $P = 0.02$) (16). Also consistent with the meta-analysis by Benatar et al. (14), we showed that consumption of milk (800 mL/2000 kcal) for 6 wk in fully controlled feeding conditions had no effect on plasma

HDL cholesterol concentrations in postmenopausal women compared with a milk-free diet (18). Consumption of a diet containing 96–120 g cheese/d for 2 wk increased HDL cholesterol concentrations compared with a high-carbohydrate diet (mean \pm SE: 1.39 ± 0.07 compared with 1.30 ± 0.06 mmol/L, $P < 0.05$), but not compared with a high-meat diet (mean \pm SE: 1.39 ± 0.07 compared with 1.42 ± 0.07 mmol/L, $P > 0.05$) (20). This study highlighted the importance of considering the foods replaced by dairy in a dairy-free diet, because this may greatly influence the observed effect of dairy consumption on cardiometabolic health. Finally, one RCT showed that consumption of yogurt for 6 wk had no impact on HDL cholesterol concentrations compared with a yogurt- and dairy-free diet (21).

Dairy fat. The crossover RCT by Chiu et al. (22) showed no difference in HDL cholesterol concentrations between a high-fat dairy and DASH diet and a low-fat dairy and DASH diet. Consumption of whole-milk for 6 wk was also shown to have no effect on HDL cholesterol compared with skimmed milk (23).

Dairy food matrix. In their meta-analysis of 5 RCTs, de Goede et al. (24) showed that HDL cholesterol concentrations were slightly but significantly lower after cheese consumption than after butter consumption (Δ HDL cholesterol: -0.05 mmol/L; 95% CI: $-0.09, -0.02$ mmol/L). This is consistent with the notion that the food matrix may influence the cholesterol-raising effect of SFAs, with greater effects seen with butter than with cheese.

Summary. There is relatively robust evidence suggesting that total dairy intake has no impact on HDL cholesterol concentrations (Table 1). However, studies on the impact of specific dairy foods (e.g., milk, cheese, or yogurt) on HDL cholesterol concentrations are limited and have provided mixed results. The evidence pertaining to the impact of high-fat dairy compared with reduced-fat dairy products on HDL cholesterol concentrations is also limited, but data so far suggests that consumption of dairy fat per se has no impact on HDL cholesterol concentrations (Table 1). Finally, the HDL cholesterol-raising impact of dietary SFAs may be attenuated when they are consumed as part of more complex foods, such as cheese, compared with butter. Because cholesterol represents only one of several features of HDL, additional studies are needed to assess the impact of dairy foods and dairy fat on HDL functions that have been associated with the risk of CVD, beyond just HDL cholesterol concentrations (26).

Fasting TGs

Dairy foods. To our knowledge, there is currently no meta-analysis of the impact of total dairy consumption on fasting TG concentrations. Eight RCTs were identified, of which 6 had a parallel design (27–32) and 2 had a crossover design (15, 22). These trials generally compared the impact of ≥ 3 servings dairy/d [e.g., from Abdullah et al. (15): 30 g regular-fat cheddar cheese, 175 g 1.5%-fat yogurt, and 375 mL 1%-fat

TABLE 1 Summary of the evidence on the impact of dairy product consumption on cardiometabolic risk factors¹

	Dairy foods compared with low-dairy or dairy-free diets					Dairy fat		Dairy matrix			
	Total dairy		High-fat		Low-fat	Milk	Cheese	Yogurt	High-fat vs. low-fat dairy	Whole vs. low-fat or skimmed milk	Cheese vs. butter
LDL cholesterol	No effect*	No effect*	No effect*	No effect*	No effect*	No effect [†]	No effect [§]	No effect [§]	No effect [§]	Increased [§]	Reduced*
HDL cholesterol	No effect*	No effect*	No effect*	No effect*	Uncertain [‡]	Uncertain [‡]	Uncertain [‡]	Uncertain [‡]	No effect [§]	No effect [§]	Reduced*
Fasting TGs	No effect*	No effect [§]	No effect [§]	No effect [§]	Uncertain [‡]	Uncertain [‡]	No effect [§]	No effect [§]	Reduced [§]	Uncertain [‡]	No effect*
Postprandial TGs	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]	No effect [§]	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]
LDL size	Undetermined [#]	No effect [§]	No effect [§]	Uncertain [‡]	Uncertain [‡]	No effect [§]	Undetermined [#]	Undetermined [#]	Increased [§]	Reduced [§]	Undetermined [#]
apoB	Undetermined [#]	No effect [§]	No effect [§]	No effect [§]	No effect [§]	No effect [§]	Undetermined [#]	Undetermined [#]	No effect [§]	No effect [§]	Undetermined [#]
Non-HDL cholesterol	Undetermined [#]	No effect [§]	No effect [§]	No effect [§]	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]	No effect [§]	Undetermined [#]	Undetermined [#]
Cholesterol ratios	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]	No effect [§]	No effect [§]	Reduced [§]	No effect [§]	No effect [§]	Undetermined [#]
Inflammation	No effect*	No effect*	No effect*	No effect*	No effect [§]	No effect [§]	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]
Insulin resistance	Uncertain [‡]	Undetermined [#]	Undetermined [#]	Uncertain [‡]	No effect [§]	No effect [§]	No effect [§]	Undetermined [#]	No effect [§]	Undetermined [#]	Undetermined [#]
Blood pressure	No effect*	No effect*	No effect*	No effect*	No effect [§]	No effect [§]	Undetermined [#]	Undetermined [#]	No effect [§]	Undetermined [#]	No effect [§]
Vascular function	No effect [§]	Undetermined [#]	Undetermined [#]	No effect [§]	No effect [§]	No effect [§]	Undetermined [#]	Undetermined [#]	Undetermined [#]	Undetermined [#]	No effect [§]

¹Data from studies that assessed the impact of high-fat compared with low-fat cheese, high-fat compared with milk or yogurt, milk compared with butter or yogurt, and yogurt compared with butter on cardiometabolic risk factors are very limited and discussed in the text only. *Based on data from ≥ 1 meta-analysis. [†]Consistent results reported in ≥ 3 randomized controlled trials. [‡]Reported in < 3 randomized controlled trials; data need to be interpreted with caution. [§]Effects remain uncertain, available randomized controlled trials having yielded mixed results. [#]No randomized controlled trials on this topic.

milk] to ≤ 1 daily serving dairy products in various forms and with various fat content. Intervention duration varied from 3 wk (22) to 3 y (27). Despite the fact that subjects' characteristics in these studies were diverse, results are highly consistent in showing no effect of dairy consumption on fasting TG concentrations.

The impact of milk consumption per se on fasting TG concentrations has been evaluated in only a few RCTs, to our knowledge, and results are mixed. One trial reported that increasing usual consumption of dairy by 750 mL 1%-fat milk/d for 12 wk increased fasting TGs compared with baseline values (mean \pm SD: 1.57 ± 0.93 compared with 1.45 ± 0.83 mmol/L), whereas maintaining usual intake had no impact on TGs during the same period (mean \pm SD: 1.43 ± 0.71 compared with 1.46 ± 0.69 mmol/L; between-group comparison, $P = 0.002$) (16). Elsewhere, 2 studies showed no impact of milk consumption on fasting TG concentrations (17, 18). Finally, increased consumption of cheese (20) and yogurt (21) compared with dairy-free diets were shown to have no impact on fasting TG concentrations.

Dairy fat. In their crossover RCTs, Chiu et al. (22) showed that consumption of a DASH diet containing whole-fat milk and yogurt for 3 wk significantly reduced fasting TG concentrations compared with a DASH diet with skimmed milk and yogurt (mean \pm SE: 1.15 ± 0.04 compared with 1.32 ± 0.04 mmol/L, $P < 0.05$). On the other hand, consumption of buttermilk (2 L/d) for 3 wk was shown to have no impact on fasting TG concentrations compared with skimmed milk (2.5 L/d) (33). Similar conclusions were drawn from a small crossover RCT comprising 8 healthy men in whom consumption of whole-fat milk or skimmed milk for 6 wk had no impact on fasting TG concentrations (23). On the other hand, consumption of skimmed milk (500 mL/d) for 2 wk was shown to reduce fasting TG concentrations compared with whole-milk consumption in 14 normolipidemic subjects (34).

Dairy food matrix. The meta-analysis of 4 RCTs by de Goede et al. (24) reported no difference in fasting TG concentrations between cheese and butter consumption. Consistent with this observation, consumption of 40 g dairy fat from cheddar cheese/d for 4 wk had no significant impact on fasting TG concentrations compared with 40 g dairy fat from butter/d in a group of 19 hypercholesterolemic subjects (25).

Summary. Data from RCTs suggest that consumption of dairy foods in various forms and with different dairy fat content has no effect on fasting TG concentrations (Table 1). This assessment, however, is based on a relatively small number of RCTs. It is also stressed that many of the available RCTs were conducted on a very limited number of subjects. Change in fasting TG concentrations was generally not considered the primary outcome in most of these studies, and the quality of the RCTs in many instances was considered to be low. Therefore, there is a lack of good-quality evidence to properly

assess the impact of dairy intake on fasting plasma TG concentrations. Additional studies with larger sample sizes, proper controls, and change in fasting TG concentrations as primary outcome are warranted. Finally, there is fairly robust data indicating that the dairy food matrix does not influence the effect of dairy fat on fasting TG concentrations (Table 1).

Postprandial TGs

Dairy foods. To our knowledge, the literature on the impact of dairy food consumption on postprandial TG concentrations is very limited. A crossover RCT conducted in 16 overweight and obese men compared the postprandial TG response to 4 different meals, all comprising butter cake (168 g) and 1 of the following 4 beverages: 1) 500 mL water plus 29 g lactose; 2) 500 mL water, 29 g lactose, and 2.3 g calcium; 3) 500 mL water plus 29 g lactose, 1.3 g calcium, and 23.4 g milk protein; and 4) 500 mL 0%-fat milk (35). There was no significant difference in the postprandial TG response between the 4 meals. In the study by Thorning et al. (20) involving 14 postmenopausal women, consumption of a high-fat cheese diet for 2 wk compared with high-carbohydrate or high-meat diets had no significant impact on the TG concentrations measured 3 h after intake of breakfast meals that had a macronutrient and food composition similar to that of the intervention period just completed.

Summary. Limited data from RCTs suggest that acute consumption of milk and cheese has no significant impact on postprandial TG concentrations compared with various control foods (Table 1). However, this assessment is based on only 2 RCTs. To our knowledge, no high-quality RCT has yet evaluated the impact of dairy food or dairy fat per se on postprandial TGs as the main outcome. Thus, there is a need for additional studies to better understand the acute and chronic impact of dairy consumption in general on postprandial TG concentrations, a key risk factor for CVD (36).

LDL particle size

Dairy foods. Van Meijl et al. (37) assessed the impact of low-fat dairy foods (500 mL low-fat milk and 150 g low-fat yogurt) compared with carbohydrate-rich control products (600 mL fruit juice and 3 fruit biscuits) on LDL particle size in 35 overweight and obese subjects. The low-fat dairy diet had no effect on LDL size and LDL particle number compared with the control diet (37). Chiu et al. (22) showed that consumption of a high-fat dairy and DASH diet for 3 wk had no impact on LDL particle size, whereas consumption of the low-fat dairy and DASH diet reduced LDL particle size compared with the control diet (mean \pm SE: 22.1 ± 0.0 compared with 22.2 ± 0.0 nm, $P < 0.05$). Finally, consumption of 2%-fat milk (800 mL/2000 kcal) for 6 wk had no effect on LDL particle size compared with a milk-free diet in postmenopausal women (18).

Dairy fat. In the RCT by Chiu et al. (22), LDL peak diameter after the high-fat dairy and DASH diet was significantly greater than after the low-fat dairy and DASH diet (mean \pm SE: 22.3 ± 0.0

compared with 22.1 ± 0.0 nm, $P < 0.05$). Consuming nonfat milk (500 mL/d) for 2 wk was shown to increase LDL size in a small group of 14 healthy normolipidemic Japanese subjects (34).

Summary. Evidence regarding the impact of dairy consumption on LDL particle size remains scarce and uncertain, and thus needs to be interpreted with caution (Table 1). Data that compared specifically the impact of low- and high-fat dairy foods on LDL particle size are also very limited. To best of our knowledge, no study has yet documented how the dairy food matrix (for example, cheese compared with butter) influences the impact of dairy fat on LDL particle size. This is of interest because dietary SFAs have been shown to increase LDL particle size (38). More studies therefore are needed to further assess the impact of dairy food consumption on various features of the LDL particle size phenotype.

apoB

Dairy foods. Chiu et al. (22) showed that consumption of a DASH diet comprising either high-fat dairy products or low-fat dairy products had no impact on apoB concentrations compared with a control diet low in dairy products. Consumption of a National Cholesterol Education Program (NCEP) diet incorporating 1%-fat milk (800 mL/2000 kcal) for 6 wk also had no effect on plasma apoB concentrations in postmenopausal women compared with a dairy-free NCEP diet (18). Similar results were observed in postmenopausal women who consumed a high-cheese diet or a high-carbohydrate or high-meat diet for 2 wk each (20).

Dairy fat. Data from Chiu et al. (22) indicated that consumption of the high-fat dairy and DASH diet had no significant effects on apoB concentrations compared with a low-fat dairy and DASH diet. Similarly, Steinmetz et al. (23) showed that consumption of skimmed milk for 6 wk compared with whole-fat milk had no significant effect on apoB concentrations.

Summary. Available data suggest that total dairy food consumption has no significant impact on apoB concentrations. These findings are based on only a few RCTs, and data therefore must be interpreted with caution until additional studies corroborate these results. To our knowledge, no study has yet documented the effect of the dairy food matrix on apoB concentrations.

Non-HDL cholesterol

To our knowledge, the study by Chiu et al. (22) is the only one to have assessed the impact of dairy consumption on non-HDL cholesterol concentrations. Consumption of the high-fat dairy and DASH and low-fat dairy and DASH diets for 3 wk had no significant impact on non-HDL cholesterol concentrations compared with the control diet, which was low in dairy foods. Non-HDL cholesterol concentrations were also similar after the high-fat dairy and low-fat dairy DASH diets (22). This study suggests that consumption of high-fat dairy and low-fat dairy per se has no impact on non-HDL cholesterol concentrations. This needs to be substantiated by additional

studies on dairy and lipids, which can easily and systematically report the change in this important cardiometabolic outcome at no additional cost.

Cholesterol ratios

Dairy foods. We identified 3 RCTs that evaluated the impact of the inclusion or exclusion of dairy foods on cholesterol ratios. In postmenopausal women, consumption of 2%-fat milk (800 mL/2000 kcal) for 6 wk in the context of an NCEP prudent diet had no significant impact on the total-to-HDL cholesterol ratio compared with a milk-free NCEP diet (18). Consumption of a diet high in cheese for 2 wk also had no effect on the LDL-to-HDL cholesterol and total-to-HDL cholesterol ratios compared with diets high in carbohydrates or protein from meat in postmenopausal women (20). Finally, yogurt consumption for 6 wk led to a small but significant reduction in the total-to-HDL cholesterol ratio compared with a yogurt-free diet [Δ compared with baseline (mean \pm SD): -0.01 ± 0.01 compared with 0.01 ± 0.02 , $P < 0.01$] (21).

Dairy fat. Steinmetz et al. (23), in a small study of 8 men aged 20–36 y, showed that consumption of skimmed milk for 6 wk had no significant impact on the non-HDL-to-HDL cholesterol ratio compared with whole milk consumption.

Summary. The impact of dairy food consumption on cholesterol ratios may vary according to the type of dairy foods, with a beneficial reduction being observed in the case of yogurt, and neutral effects being reported for milk and cheese. However, considering that total dairy consumption has been shown to have a very limited impact on LDL cholesterol or HDL cholesterol concentrations, it is expected that it will also have limited effects on cholesterol ratios. Further studies on this particular outcome are needed so that more robust conclusions can be drawn (Table 1).

Inflammation

Dairy foods. In a systematic review of RCTs published before June 2012, we concluded that dairy consumption has no adverse effect on circulating inflammatory biomarkers in overweight and obese adults (39). This is consistent with data from the meta-analysis of 6 RCTs by Benatar et al. (14), which also concluded that high dairy consumption had no impact on plasma CRP concentrations compared with low dairy consumption. Benatar et al. (14) also reported no difference between low- and high-fat dairy with regard to their impact on CRP concentrations. Three RCTs have been published since then. Despite heterogeneity in study designs, results between studies were highly consistent (40–42). Consumption of a combination of low- and high-fat dairy products (40, 41) or low-fat dairy only (42) had no impact on inflammatory gene expression (40, 41) or on blood concentrations of inflammatory biomarkers (CRP, adiponectin, IL-1 β , IL-6, monocyte chemoattractant protein 1, and TNF- α) (40–42) compared with low dairy intake in overweight or obese subjects.

Three RCTs evaluated the impact of milk consumption per se on markers of inflammation. A 28-d parallel-arm RCT in 31 postmenopausal women showed no difference in skeletal muscle gene expression of TNF- α , IL-1 β , and IL-6 after consumption of 3 daily servings (720 mL/d) of a commercially available low-fat milk compared with 3 daily servings (732 mL/d) of a commercially available vanilla soy beverage (43). In a randomized, crossover, controlled-feeding RCT in 27 postmenopausal women, we showed that consumption of 2%-fat milk (800 mL/2000 kcal) for 6 wk compared with a milk-free diet had no impact on plasma CRP and adiponectin concentrations (18). Finally, consumption of a high-fat dairy meal comprising cheese and butter was shown to significantly reduce the postprandial CRP AUC compared with a high-fat nondairy meal supplemented with high-fat milk (mean \pm SD: -0.04 ± 0.5 compared with -0.5 ± 0.6 mg/L \times 6 h, $P < 0.05$) (44). However, AUCs for the 2 dairy meals were not different from the high-fat nondairy control meal, and no difference was observed in postprandial IL-6, TNF- α , and endotoxin concentrations in test meals.

Dairy fat. With the use of a crossover study design, Nestel et al. (45) compared the impact of a low-fat dairy diet (skimmed milk and 1%-fat yogurt) with 2 regular-fat dairy diets, 1 of which included fermented products (full-fat yogurt and cheddar cheese) and the other of which included no fermented products (butter, cream, and ice cream) on inflammatory biomarkers in 12 overweight and obese subjects. The concentrations of most of the biomarkers investigated were statistically comparable between diets, with the exception of plasma IL-6 concentrations, which were significantly higher after the regular-fat nonfermented dairy diet than after the low-fat dairy diet (mean \pm SE: 7.0 ± 0.9 compared with 6.2 ± 0.7 pg/mL, $P < 0.05$) (45). Although changes in biomarkers associated with inflammation, oxidative stress, or atherogenesis were identified a priori as primary outcome measures, the small sample size in that study limits its overall scope.

Summary. Updating results from existing systematic reviews with data from more recent RCTs confirms that short-term consumption of dairy products in various forms and with various fat content has no impact on systemic inflammation, as measured by circulating biomarkers or inflammatory gene expression (Table 1). The extent to which longer-term dairy consumption may influence inflammatory processes needs to be investigated.

Insulin resistance

Dairy foods. Turner et al. (46) recently published a systematic review of RCTs that assessed the impact of dairy consumption on plasma glucose and insulin concentrations, as well as on the HOMA-IR index. Studies targeted in this systematic review were those in which only dairy intake was altered, with no other lifestyle or dietary change. Four of the studies reviewed reported a favorable effect of dairy consumption on

insulin sensitivity (47–50), 5 showed no effect (28, 31, 32, 37, 51), and 1 study found unfavorable effects (52). Studies with a duration >12 wk were more likely to see favorable effects of dairy intake on insulin sensitivity than those with a shorter duration (46). Important differences in methodologies, sample size, and type of dairy consumed limited the ability to conclusively determine a role for dairy in modulating glucose and insulin homeostasis and insulin sensitivity (46).

The impact of low-fat dairy food consumption per se on insulin resistance was evaluated in 3 RCTs. Van Meijl and Mensink (29) reported that consumption of low-fat milk and yogurt for 8 wk compared with a dairy-free control diet had no significant impact on glucose and insulin concentrations. Rideout et al. (47) conducted a crossover RCT in free-living conditions in which subjects consumed 4 servings low-fat dairy products (1 serving = 250 mL milk or 175 g yogurt or 50 g cheese) or ≤ 2 servings low-fat dairy products daily for periods of 6 mo. Both fasting insulin concentrations and the HOMA-IR index were lower after the high-dairy period than after the low-dairy period (mean \pm SD insulin: 14.8 ± 2.4 compared with 16.2 ± 3.7 μ U/mL; mean \pm SD HOMA-IR: 3.4 ± 0.9 compared with 3.8 ± 1.3 ; $P < 0.05$ for both). Conversely, Turner et al. (53) reported that consumption of a diet supplemented with low-fat dairy (milk, yogurt, or custard) for 4 wk compared with a diet rich in protein from red meat significantly increased fasting insulin concentrations (mean \pm SD: 6.64 ± 4.1 compared with 5.47 ± 2.4 mU/L, $P < 0.05$) and HOMA-IR index (mean \pm SD: 1.55 ± 1.0 compared with 1.30 ± 0.7 , $P < 0.05$) in 47 overweight adults (53). The Matsuda index was also lower after the dairy diet, whereas fasting glucose and the Stumvoll index were not different between the dairy and the red meat diets.

We showed that milk consumption (800 mL/2000 kcal; 2% fat) compared with a milk-free control diet had no significant impact on fasting glucose and insulin concentrations and on Cederholm and Matsuda insulin sensitivity indexes in postmenopausal women (18). Similar results were observed in the RCT by Thorning et al. (20), in which consumption of a diet rich in cheese had no significant impact on the HOMA-IR index and on fasting and postprandial insulin and glucose concentrations compared with diets high in proteins or carbohydrates.

Summary. In sum, short-term intervention studies provide a mixed portrait regarding the impact of dairy consumption on insulin resistance, with no evidence, however, of detrimental effects (Table 1). On the other hand, prolonged exposure to dairy in RCTs may induce favorable changes in glucose and insulin homeostasis, which would be consistent with epidemiologic data that related dairy intake to a reduced risk of T2D (54). The impact of dairy fat per se or of different dairy food matrices on insulin sensitivity has not been evaluated so far, to our knowledge. Additional high-quality studies with insulin resistance as primary outcome are needed to substantiate this relation.

BP

Dairy foods. The DASH study (55) provided the first indirect evidence that dairy consumption may reduce BP. However, because of differences in macronutrient composition of the various diets in the original DASH trial, the specific contribution of dairy to BP-lowering with the DASH diet, estimated to be 50%, remains uncertain (56). In their meta-analysis, Benatar et al. (14) reported no significant effect of total dairy intake on systolic and diastolic BP. Additional RCTs in hypertensive subjects provided mixed results regarding the impact of high dairy intake compared with low or no dairy over periods of 4–5 wk on BP outcomes (57–59). Two studies saw no effect of dairy intake on systolic and diastolic BP (57, 58), whereas we reported that consumption of 3 daily servings of regular-fat dairy (30 g regular-fat cheddar cheese/d, 175 g 1.5%-fat yogurt/d, and 375 mL 1% fat milk/d) significantly reduced mean daytime systolic BP compared with a dairy-free control diet in men (mean \pm SD: 142 ± 10 compared with 144 ± 10 mm Hg, $P = 0.05$) (59). Unexpectedly, mean daytime diastolic BP was higher after the dairy diet than after the control phase in women (mean \pm SD: 85 ± 9 compared with 84 ± 8 mm Hg, $P = 0.05$), but not in men (59).

In the meta-analysis of RCTs by Benatar et al. (14), the impact of low- and high-fat dairy consumption on systolic BP and diastolic BP was also not significant (14). Consistent with this observation, recent RCTs that compared the impact of low- or high-fat dairy consumption with dairy-free diets reported either no effect (47, 60) or a small beneficial effect (22) on BP outcomes.

A limited number of RCTs assessed the impact of milk consumption per se on BP. Barr et al. (16) reported no difference in systolic or diastolic BP between subjects who consumed milk for 12 wk and a control group that did not consume milk over the same period of time. We showed that milk consumption (800 mL/2000 kcal; 2% fat) for 6 wk as part of an NCEP diet tended to reduce mean BP more than an NCEP milk-free diet in postmenopausal women [(mean difference) Δ compared with baseline: -4.1% compared with -1.1% , $P = 0.07$] (18).

Dairy fat. In a crossover RCT, 45 normotensive subjects consumed low-fat or whole-fat milk and yogurt as part of their regular diet for 8-wk periods (61). There was no difference in systolic and diastolic BP between the diets with low-fat and whole-fat dairy, suggesting that there was no impact of dairy fat on BP. In the RCT by Chiu et al. (22), consumption of a high-fat dairy and DASH diet had no effect on BP compared with the low-fat dairy and DASH diet.

Dairy food matrix. The impact of consuming equal amounts of SFAs from cheese and butter on BP outcomes were compared in a crossover RCT involving 49 men and women (62). Authors reported no difference in systolic or diastolic BP between the diet supplemented with cheese and the diet supplemented with butter. Schlienger et al. (63) showed in a parallel-arm RCT that consumption of 30 g camembert

cheese/d for 5 wk had no impact on BP outcomes compared with consuming 250 mL full-fat yogurt/d in 159 hypercholesterolemic men and women.

Summary. Evidence from short-term RCTs suggests that dairy food consumption, irrespective of type and fat content, has no significant effect on BP outcomes (Table 1). Reconciling data from prospective cohort studies—which suggest that total dairy, low-fat dairy, and milk intake is associated with a reduced risk of hypertension (54)—with this apparent neutral effect of dairy intake based on data from RCTs is challenging. One potential explanation for such discrepant results is that dairy consumption may attenuate the unfavorable effects of other foods on BP over the long term, a phenomenon that cannot be appreciated in shorter-term RCTs. It is also possible that dairy consumption per se nullifies the increase in BP seen in many individuals with aging and with weight gain, thereby being associated with a protective effect on BP change and, hence, on the risk of hypertension in the longer term. This hypothesis also needs to be investigated in future studies.

Vascular function

Dairy foods. In a large RCT involving men and postmenopausal women at risk of metabolic syndrome (MetS), a difference in dairy intake of 250 g milk and yogurt/d and of 20 g cheese/d between a high-dairy group and a low-dairy group was associated with significantly reduced plasma vascular cell adhesion molecule 1 (VCAM-1) concentrations in women but not in men (28). Plasma E-selectin also was significantly reduced after the dairy diet, but only in subjects from Norway in this multicenter study (28). It must be stressed that the difference in dairy consumption between the dairy group and the control group was rather small (<2 servings dairy/d), thereby limiting the potential impact of the intervention per se on outcome measures associated with endothelial function.

Two other RCTs reported no effect of low-fat dairy consumption on markers of endothelial function (37, 60). Data from Maki et al. (60), however, suggested that low-fat dairy consumption may improve vascular function in prehypertensive subjects with endothelial dysfunction at baseline (mean \pm SE reactive hyperemia index: 2.32 ± 0.19 compared with 1.50 ± 0.04 , $P = 0.002$), but this was based on a subanalysis of only 14 hypertensive subjects.

We showed that consumption of 2%-fat milk (800 mL/2000 kcal) for 6 wk had no impact on intercellular adhesion molecule 1, VCAM-1, endothelin, and E-selectin concentrations compared with a milk-free diet in postmenopausal women (18). In a crossover RCT, 19 adults with MetS consumed low-fat milk (475 mL) or an isocaloric volume of rice drink after an overnight fast. The postprandial flow-mediated dilation response was unchanged after consumption of the low-fat milk, but was significantly deteriorated after consumption of the rice drink (64). These data suggest that acute intake of low-fat milk maintains the integrity of vascular endothelial function in individuals with MetS compared with a nondairy drink (64).

Dairy food matrix. Nestel et al. (65) tested how the fermented status of dairy products influences the postprandial change in biomarkers associated with vascular function in overweight subjects. Twelve participants consumed single breakfasts containing a control low-fat milk or 45 g fat from butter, cream, yogurt, or cheese after an overnight fast. The various dairy matrices had no differential effects on surrogate markers of vascular function in that study (VCAM-1 and intercellular adhesion molecule 1).

Summary. Evidence suggests that intake of total dairy, low-fat dairy, and milk has no effect on vascular function. However, the small number of studies so far precludes us from drawing definite conclusions regarding the impact of dairy consumption on biomarkers of vascular function or on vascular function per se (Table 1). Favorable effects may be observed in individuals with deteriorated vascular function at baseline, but this needs to be substantiated and confirmed by additional studies of good quality.

Interpretation and Conclusions

Despite the fact that dairy products are an important part of most dietary guidelines around the world, research over the last decades has provided some discordant information as to their role in health. Because regular-fat dairy products contribute significantly to dietary fat and SFA intake, and because SFAs are considered to be involved in the etiology of CVD, many guidelines advocate consumption of low-fat dairy products as opposed to regular-fat products. This recommendation remains controversial to many (66), and this creates confusion for the public.

To the best of our knowledge, this review represents one of the most comprehensive assessments of the impact of dairy food consumption on a large spectrum of cardiometabolic disease risk factors. The following key points can be emphasized:

- 1) Data do not support a detrimental impact of total dairy or high-fat dairy consumption on lipid-related cardiometabolic disease risk factors. In most cases, evidence points toward no effect of dairy consumption on such risk factors. Results from RCTs on lipid-related cardiometabolic disease risk factors are consistent with results from meta-analyses of prospective cohort studies, which suggest no detrimental association between dairy consumption and cardiovascular-related clinical outcomes (54).
- 2) Data suggest that the cholesterol-raising effects of SFAs are attenuated when provided in complex foods such as milk, cheese, or yogurt. Increasing evidence suggests that the combination of dairy bioactive peptides, minerals, and fat constitutes a complex matrix that may limit the cholesterol-raising effect of SFAs. Studies that compared cheese and butter provide key evidence to support this concept.
- 3) Data from several RCTs have shown that dairy foods and dairy fat consumption have no impact on low-grade

systemic inflammation, measured by several surrogate markers. Whereas RCTs are usually conducted over a relatively short period of time, the long-term effect of dairy consumption on inflammation needs further investigation, considering the positive association between milk consumption and IL-6 concentrations reported in a recent large observational prospective cohort study (67).

- 4) Data from RCTs suggest that dairy consumption has no impact on insulin resistance and glucose and insulin homeostasis in the short term, but may be beneficial in the long term. To some extent, these results are consistent with large prospective cohort studies associating total dairy, low-fat dairy, cheese, and yogurt to a reduced risk of T2D, and total dairy and milk consumption to a reduced risk of MetS (54). Additional well-designed RCTs with long interventions are needed to confirm these effects from a cardiometabolic standpoint.
- 5) The impact of dairy food consumption, and of dairy fat per se, on hemostatic function remains undetermined. Studies on this specific topic are warranted.
- 6) Data from RCTs that have evaluated the impact of dairy consumption on either BP or vascular function are very consistent in showing mostly a null effect, irrespective of the dairy food matrix or fat content. These results are not consistent with epidemiologic studies that have associated total dairy, low-fat dairy, and milk consumption with a reduced risk of hypertension (54). As emphasized above, the study of the long-term impact of dairy consumption on BP or vascular function is challenging. The hypothesis that dairy consumption may prevent the age- and body weight gain-related increase in BP needs to be ascertained with the use of proper study designs.

We purposefully did not comment on the diet of the control arm in the various RCTs described in this review because of important heterogeneity between studies. It is obvious that foods used to substitute dairy products in the control low-dairy or dairy-free diets would affect the results and their interpretation. The design of the control arm in future RCTs on dairy foods needs to be thought out carefully to ensure that foods consumed in replacement of dairy reflect consumers' choices and dietary habits. We also purposefully did not review the extensive literature pertaining to the effect of dairy consumption on body weight. This is indeed a huge area of research on its own. Although some of the available literature relating dairy intake to clinical outcomes and cardiometabolic disease risk may have been confounded by concurrent variations in body weight and body fat, we believe that this is unlikely to have significantly skewed the association between dairy and health. Also, this review was not intended to be systematic. Thus, we did not evaluate potential publication bias and have not performed meta-analyses of existing data. One must keep in mind that many of the cardiometabolic disease risk factors investigated

in the RCTs reviewed here were investigated as secondary or tertiary outcomes, as opposed to being considered the primary outcome variable. This implies that study design and sample sizes in these RCTs may have provided inadequate settings to properly document the impact of dairy intake on many of these cardiometabolic outcomes. Interpretation of studies in which many cardiometabolic outcomes are investigated together and simultaneously must be made with great caution.

A large trial on dairy intake and clinical outcomes such as CVD and T2D is highly unlikely in the future. In that context, interpretation of the association between dairy (in any forms) and health will need to rely on indirect evidence from epidemiologic data, as well as a thorough understanding of their impact on the broadest array of recognized cardiometabolic disease risk factors, not just LDL cholesterol and BP. This review identified key research gaps that need to be addressed in the future.

We also believe that the focus on low-fat dairy products in the current guidelines is not entirely supported by the existing literature, because no evidence currently supports a detrimental effect of regular- or high-fat dairy products compared with low-fat dairy on a large spectrum of cardiometabolic disease risk factors. In that context, studies that compare the impact of low-fat dairy foods with their regular-fat versions are urgently needed to better address this important point and to better inform future dietary guidelines related to dairy consumption.

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References

1. Anderson TJ, Gregoire J, Hegele RA, Couture P, Mancini GB, McPherson R, Francis GA, Poirier P, Lau DC, Grover S, et al. 2012 update of the Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult. *Can J Cardiol* 2013;29:151–67.
2. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009;338:b1665.
3. Lamarche B, Couture P. It is time to revisit current dietary recommendations for saturated fat. *Appl Physiol Nutr Metab* 2014;39(12):1409–11.
4. Evaluation of biomarkers and surrogate endpoints in chronic disease. Washington (DC): The National Academies Press, 2010.
5. Lamarche B, Lewis GF. Atherosclerosis prevention for the next decade: risk assessment beyond low density lipoprotein cholesterol. *Can J Cardiol* 1998;14:841–51.
6. Leiter LA, Fitchett DH, Gilbert RE, Gupta M, Mancini GB, McFarlane PA, Ross R, Teoh H, Verma S, Anand S, et al. Cardiometabolic risk in Canada: a detailed analysis and position paper by the cardiometabolic risk working group. *Can J Cardiol* 2011;27:e1–33.
7. Libby P, Ridker PM, Hansson GK. Inflammation in atherosclerosis: from pathophysiology to practice. *J Am Coll Cardiol* 2009;54:2129–38.
8. Kaptoge S, Seshasai SR, Gao P, Freitag DF, Butterworth AS, Borglykke A, Di Angelantonio E, Gudnason V, Rumley A, Lowe GD, et al. Inflammatory cytokines and risk of coronary heart disease: new prospective study and updated meta-analysis. *Eur Heart J* 2014;35:578–89.
9. Buckley DI, Fu R, Freeman M, Rogers K, Helfand M. C-reactive protein as a risk factor for coronary heart disease: a systematic review and meta-analyses for the U.S. Preventive Services Task Force. *Ann Intern Med* 2009;151:483–95.

10. Ras RT, Streppel MT, Draijer R, Zock PL. Flow-mediated dilation and cardiovascular risk prediction: a systematic review with meta-analysis. *Int J Cardiol* 2013;168:344–51.
11. Danesh J, Lewington S, Thompson SG, Lowe GD, Collins R, Kostos JB, Wilson AC, Folsom AR, Wu K, Benderly M, et al. Plasma fibrinogen level and the risk of major cardiovascular diseases and nonvascular mortality: an individual participant meta-analysis. *JAMA* 2005;294:1799–809.
12. Erqou S, Thompson A, Di Angelantonio E, Saleheen D, Kaptoge S, Marcovina S, Danesh J. Apolipoprotein(A) isoforms and the risk of vascular disease: systematic review of 40 studies involving 58,000 participants. *J Am Coll Cardiol* 2010;55:2160–7.
13. Xun P, Wu Y, He Q, He K. Fasting insulin concentrations and incidence of hypertension, stroke, and coronary heart disease: a meta-analysis of prospective cohort studies. *Am J Clin Nutr* 2013;98:1543–54.
14. Benatar JR, Sidhu K, Stewart RA. Effects of high and low fat dairy food on cardio-metabolic risk factors: a meta-analysis of randomized studies. *PLoS One* 2013;8:e76480.
15. Abdullah MM, Cyr A, Lepine MC, Labonte ME, Couture P, Jones PJ, Lamarche B. Recommended dairy product intake modulates circulating fatty acid profile in healthy adults: a multi-centre cross-over study. *Br J Nutr* 2015;113(3):435–44.
16. Barr SI, McCarron DA, Heaney RP, Dawson-Hughes B, Berga SL, Stern JS, Oparil S. Effects of increased consumption of fluid milk on energy and nutrient intake, body weight, and cardiovascular risk factors in healthy older adults. *J Am Diet Assoc* 2000;100:810–7.
17. Beavers KM, Serra MC, Beavers DP, Hudson GM, Willoughby DS. The lipid-lowering effects of 4 weeks of daily soymilk or dairy milk ingestion in a postmenopausal female population. *J Med Food* 2010;13:650–6.
18. Drouin-Chartier JP, Gagnon J, Labonte ME, Desroches S, Charest A, Grenier G, Dodin S, Lemieux S, Couture P, Lamarche B. Impact of milk consumption on cardiometabolic risk in postmenopausal women with abdominal obesity. *Nutr J* 2015;14:12.
19. Huht PJ, Fulgoni VL, Keast DR, Park K, Auestad N. 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.
20. Thorning TK, Raziani F, Bendsen NT, Astrup A, Tholstrup T, Raben A. 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(3):573–81.
21. Sadrzadeh-Yeganeh H, Elmadfa A, Djazayeri A, Jalali M, Heshmat R, Chamary M. The effects of probiotic and conventional yoghurt on lipid profile in women. *Br J Nutr* 2010;103:1778–83.
22. Chiu S, Bergeron N, Williams PT, Bray GA, Sutherland B, Krauss RM. Comparison of the DASH (Dietary Approaches to Stop Hypertension) diet and a higher-fat DASH diet on blood pressure and lipids and lipoproteins: a randomized controlled trial. *Am J Clin Nutr* 2016;103:341–7.
23. Steinmetz KA, Childs MT, Stimson C, Kushi LH, McGovern PG, Potter JD, Yamanaka WK. Effect of consumption of whole milk and skim milk on blood lipid profiles in healthy men. *Am J Clin Nutr* 1994;59:612–8.
24. de Goede J, Geleijnse JM, Ding EL, Soedamah-Muthu SS. Effect of cheese consumption on blood lipids: a systematic review and meta-analysis of randomized controlled trials. *Nutr Rev* 2015;73:259–75.
25. Nestel PJ, Chronopoulos A, Cehun M. Dairy fat in cheese raises LDL cholesterol less than that in butter in mildly hypercholesterolaemic subjects. *Eur J Clin Nutr* 2005;59:1059–63.
26. Asztalos BF, Tani M, Schaefer EJ. Metabolic and functional relevance of HDL subspecies. *Curr Opin Lipidol* 2011;22:176–85.
27. Baran D, Sorensen A, Grimes J, Lew R, Karellas A, Johnson B, Roche J. Dietary modification with dairy products for preventing vertebral bone loss in premenopausal women: a three-year prospective study. *J Clin Endocrinol Metab* 1990;70:264–70.
28. Wennersberg MH, Smedman A, Turpeinen AM, Retterstol K, Tengblad S, Lipre E, Aro A, Mutanen P, Seljeflot I, Basu S, et al. Dairy products and metabolic effects in overweight men and women: results from a 6-mo intervention study. *Am J Clin Nutr* 2009;90:960–8.
29. van Meijl LE, Mensink RP. Low-fat dairy consumption reduces systolic blood pressure, but does not improve other metabolic risk parameters in overweight and obese subjects. *Nutr Metab Cardiovasc Dis* 2011;21:355–61.
30. Palacios C, Bertran JJ, Rios RE, Soltero S. No effects of low and high consumption of dairy products and calcium supplements on body composition and serum lipids in Puerto Rican obese adults. *Nutrition* 2011;27:520–5.
31. Crichton GE, Howe PR, Buckley JD, Coates AM, Murphy KJ. Dairy consumption and cardiometabolic health: outcomes of a 12-month crossover trial. *Nutr Metab (Lond)* 2012;9:19.
32. Benatar JR, Jones E, White H, Stewart RA. A randomized trial evaluating the effects of change in dairy food consumption on cardio-metabolic risk factors. *Eur J Prev Cardiol* 2013;21(11):1376–86.
33. Hussi E, Miettinen TA, Ollus A, Kostianen E, Ehnholm C, Haglund B, Huttunen JK, Manninen V. Lack of serum cholesterol-lowering effect of skimmed milk and butter milk under controlled conditions. *Atherosclerosis* 1981;39:267–72.
34. Hidaka H, Takiwaki M, Yamashita M, Kawasaki K, Sugano M, Honda T. Consumption of nonfat milk results in a less atherogenic lipoprotein profile: a pilot study. *Ann Nutr Metab* 2012;61:111–6.
35. van Meijl LE, Mensink RP. Effects of milk and milk constituents on postprandial lipid and glucose metabolism in overweight and obese men. *Br J Nutr* 2013;110:413–9.
36. Nordestgaard BG, Benn M, Schnohr P, Tybjaerg-Hansen A. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. *JAMA* 2007;298:299–308.
37. van Meijl LE, Mensink RP. Effects of low-fat dairy consumption on markers of low-grade systemic inflammation and endothelial function in overweight and obese subjects: an intervention study. *Br J Nutr* 2010;104:1523–7.
38. Desroches S, Lamarche B. Diet and low-density lipoprotein particle size. *Curr Atheroscler Rep* 2004;6:453–60.
39. Labonté ME, Couture P, Richard C, Desroches S, Lamarche B. Impact of dairy products on biomarkers of inflammation: a systematic review of randomized controlled nutritional intervention studies in overweight and obese adults. *Am J Clin Nutr* 2013;97:706–17.
40. Van Loan MD, Keim NL, Adams SH, Souza E, Woodhouse LR, Thomas A, Witbracht M, Gertz ER, Piccolo B, Bremer AA, et al. Dairy foods in a moderate energy restricted diet do not enhance central fat, weight, and intra-abdominal adipose tissue losses nor reduce adipocyte size or inflammatory markers in overweight and obese adults: a controlled feeding study. *J Obes* 2011;2011:989657.
41. Labonté ME, Cyr A, Abdullah MM, Lepine MC, Vohl MC, Jones P, Couture P, Lamarche B. Dairy product consumption has no impact on biomarkers of inflammation among men and women with low-grade systemic inflammation. *J Nutr* 2014;144(11):1760–7.
42. Jones KW, Eller LK, Parnell JA, Doyle-Baker PK, Edwards AL, Reimer RA. Effect of a dairy- and calcium-rich diet on weight loss and appetite during energy restriction in overweight and obese adults: a randomized trial. *Eur J Clin Nutr* 2013;67:371–6.
43. Serra MC, Beavers KM, Beavers DP, Willoughby DS. Effects of 28 days of dairy or soy ingestion on skeletal markers of inflammation and proteolysis in post-menopausal women. *Nutr Health* 2012;21:117–30.
44. Schmid A, Petry N, Walther B, Butikofer U, Luginbuhl W, Gille D, Chollet M, McTernan PG, Gijs MA, Vionnet N, et al. Inflammatory and metabolic responses to high-fat meals with and without dairy products in men. *Br J Nutr* 2015;113:1853–61.
45. Nestel PJ, Mellett N, Pally S, Wong G, Barlow CK, Croft K, Mori TA, Meikle PJ. Effects of low-fat or full-fat fermented and non-fermented dairy foods on selected cardiovascular biomarkers in overweight adults. *Br J Nutr* 2013;110:2242–9.
46. Turner KM, Keogh JB, Clifton PM. Dairy consumption and insulin sensitivity: A systematic review of short- and long-term intervention studies. *Nutr Metab Cardiovasc Dis* 2015;25(1):3–8.
47. Rideout TC, Marinangeli CP, Martin H, Browne RW, Rempel CB. Consumption of low-fat dairy foods for 6 months improves insulin resistance without adversely affecting lipids or bodyweight in healthy adults: a randomized free-living cross-over study. *Nutr J* 2013;12:56.

48. Zemel MB, Richards J, Milstead A, Campbell P. Effects of calcium and dairy on body composition and weight loss in African-American adults. *Obes Res* 2005;13:1218–25.
49. Stancliffe RA, Thorpe T, Zemel MB. Dairy attenuates oxidative and inflammatory stress in metabolic syndrome. *Am J Clin Nutr* 2011;94:422–30.
50. Pal S, Ellis V, Dhaliwal S. Effects of whey protein isolate on body composition, lipids, insulin and glucose in overweight and obese individuals. *Br J Nutr* 2010;104:716–23.
51. Hoppe C, Kristensen M, Boiesen M, Kudsk J, Fleischer Michaelsen K, Molgaard C. Short-term effects of replacing milk with cola beverages on insulin-like growth factor-I and insulin-glucose metabolism: a 10 d interventional study in young men. *Br J Nutr* 2009;102:1047–51.
52. Hoppe C, Molgaard C, Juul A, Michaelsen KF. High intakes of skimmed milk, but not meat, increase serum IGF-I and IGFBP-3 in eight-year-old boys. *Eur J Clin Nutr* 2004;58:1211–6.
53. Turner KM, Keogh JB, Clifton PM. Red meat, dairy, and insulin sensitivity: a randomized crossover intervention study. *Am J Clin Nutr* 2015;101:1173–9.
54. Drouin-Chartier JP, Brassard D, Tessier-Grenier M, Côté JA, Labonté M-È, Desroches S, Couture P, Lamarche B. Systematic review of the association between dairy product consumption and risk of cardiovascular-related clinical outcomes. *Advan Nutr* 2016;7:1026–40.
55. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997;336:1117–24.
56. Craddock SR, Elmer P, Obarzanek E, Vollmer W, Svetkey L, Swain M. The DASH diet and blood pressure. *Curr Atheroscler Rep* 2003;5:484–91.
57. Kynast-Gales SA, Massey LK. Effects of dietary calcium from dairy products on ambulatory blood pressure in hypertensive men. *J Am Diet Assoc* 1992;92:1497–501.
58. Hilpert KF, West SG, Bagshaw DM, Fishell V, Barnhart L, Lefevre M, Most MM, Zemel MB, Chow M, Hinderliter AL, et al. Effects of dairy products on intracellular calcium and blood pressure in adults with essential hypertension. *J Am Coll Nutr* 2009;28:142–9.
59. Drouin-Chartier JP, Giguère I, Tremblay AJ, Poirier L, Lamarche B, Couture P. Impact of dairy consumption on essential hypertension: a clinical study. *Nutr J* 2014;13:83.
60. Maki KC, Rains TM, Schild AL, Dicklin MR, Park KM, Lawless AL, Kelley KM. Effects of low-fat dairy intake on blood pressure, endothelial function, and lipoprotein lipids in subjects with prehypertension or stage 1 hypertension. *Vasc Health Risk Manag* 2013;9:369–79.
61. Alonso A, Zozaya C, Vazquez Z, Alfredo Martinez J, Martinez-Gonzalez MA. The effect of low-fat versus whole-fat dairy product intake on blood pressure and weight in young normotensive adults. *J Hum Nutr Diet* 2009;22:336–42.
62. Hjerpsted J, Leedo E, Tholstrup T. Cheese intake in large amounts lowers LDL-cholesterol concentrations compared with butter intake of equal fat content. *Am J Clin Nutr* 2011;94:1479–84.
63. Schlienger JL, Paillard F, Lecerf JM, Romon M, Bonhomme C, Schmitt B, Donazzolo Y, Defoort C, Mallmann C, Le Ruyet P, et al. Effect on blood lipids of two daily servings of Camembert cheese. An intervention trial in mildly hypercholesterolemic subjects. *Int J Food Sci Nutr* 2014;65(8):1013–18.
64. Ballard KD, Mah E, Guo Y, Pei R, Volek JS, Bruno RS. Low-fat milk ingestion prevents postprandial hyperglycemia-mediated impairments in vascular endothelial function in obese individuals with metabolic syndrome. *J Nutr* 2013;143:1602–10.
65. Nestel PJ, Pally S, MacIntosh GL, Greeve MA, Middleton S, Jowett J, Meikle PJ. Circulating inflammatory and atherogenic biomarkers are not increased following single meals of dairy foods. *Eur J Clin Nutr* 2012;66:25–31.
66. Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: a comprehensive review. *Circulation* 2016;133:187–225.
67. Michaëlsson K, Wolk A, Langenskiöld S, Basu S, Warensjö Lemming E, Melhus H, Byberg L. Milk intake and risk of mortality and fractures in women and men: cohort studies. *BMJ* 2014;349:g6015.