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Potential Cardiometabolic Health Benefits of Full-Fat Dairy: The Evidence Base

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ABSTRACT

Since their inception in 1980, the Dietary Guidelines for Americans have promoted low- or fat-free dairy foods. Removing fat from dairy does not reduce putatively beneficial nutrients per serving, including calcium, vitamin D, and potassium. Additionally, links between saturated fat and dietary cholesterol intakes with cardiovascular disease risk have helped to sustain the view that low-fat dairy foods should be recommended. Emerging evidence shows that the consumption of full-fat dairy foods has a neutral or inverse association with adverse cardiometabolic health outcomes, including atherosclerotic cardiovascular disease, type 2 diabetes, and associated risk factors. Thus, although low-fat dairy is a practical, practice-based recommendation, its superiority compared with full-fat dairy is not obviously supported by results from recent prospective cohort studies or intervention trials. To evaluate the emerging science on full-fat dairy, a group of nutrition experts convened to summarize and discuss the scientific evidence regarding the health effects of consuming full-fat dairy foods. Future studies should focus on full-fat dairy foods (milk, yogurt, and cheese) in the context of recommended dietary patterns and consider meal composition and metabolic phenotype in assessing the relation between full-fat dairy consumption and cardiometabolic health. *Adv Nutr* 2020;00:1–15.

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Introduction

Cardiovascular disease (CVD) is the leading cause of death globally and in the United States, where it accounts for ∼1 of every 3 deaths (1). The incidence and prevalence of type 2 diabetes (T2D) have increased in recent years and the CDC estimates that >100 million US adults are now living with diabetes or prediabetes (2). Atherosclerotic cardiovascular disease (ASCVD), T2D, and related conditions and risk factors, including hypertension, dyslipidemia, obesity, and insulin resistance, have established associations and, in some cases, causal effects with lifestyle factors such as dietary intake, physical activity, sleep adequacy, and smoking (3–6). According to the Global Burden of Disease Study 2013, diet was the largest contributing risk factor across the leading causes of death in the United States (7). Consequently, accurate public health messaging related to dietary intake and disease risk by both government and academic organizations is paramount.

Dietary guidelines should deliver a clear message that accurately reflects the current scientific evidence base. The Dietary Guidelines for Americans (DGA) are published every 5 y by the US Departments of Health and Human Services and Agriculture to help guide Americans in making healthy dietary choices and serve as the foundation for national nutrition policies and programs. In the last several versions of the DGA, there has been a notable shift from recommending specific nutrients to dietary patterns, with more of an emphasis on foods. However, the 2015–2020 DGA continue to specifically recommend the consumption of low-fat and fat-free dairy as part of a healthy eating pattern to reduce the risks of metabolic syndrome, diabetes, CVD, and obesity (8). Historically, this low-fat and fat-free dairy recommendation in the DGA was based on the nutrient density of dairy foods and evidence that removing some or all of the fat from dairy does not alter its nutrient-rich composition as a source of nutrients of concern, including calcium, vitamin D, and potassium, but doing so lowers energy density. For several decades, concern over saturated fat and dietary cholesterol intakes has reinforced that recommendations should aim to minimize the consumption of full-fat dairy and thus supported the promotion of low-fat and fat-free dairy foods (8).

Such conclusions have not primarily considered evidence of whole dairy foods in relation to health outcomes, but instead relied primarily on extrapolations of the health effects of single nutrients and food components studied in isolation. As nutrition research has increasingly focused on dietary patterns (9), it has become apparent that the food matrix (the food structure and nutrients therein) (10) and other dietary components affect the bioactive properties of food. For instance, the biological effects of dietary fats depend on fatty acid chain length and the food matrix, among other factors (11). The net health effects of dietary saturated fat remain inconclusive (12, 13), likely due to the fact that the food source impacts its biological effects (14–16) and that any food or substance may have beneficial effects on some aspects of physiology and deleterious effects on others. Thus, the health effects of a whole food cannot always be fully predicted based on fatty acid profile alone (17). Dairy foods, in particular, have complex food matrices and multiple bioactive components beyond saturated fat and cholesterol, including proteins, lipids, micronutrients (calcium, vitamin D, potassium, and magnesium), and probiotics (in fermented dairy foods such as cheese and yogurt), that impact metabolic health (10, 18). Results from a growing body of evidence, including recent large and well-controlled studies, systematic reviews, and meta-analyses of both observational studies and randomized controlled trials (RCTs), suggest that full-fat dairy foods, particularly yogurt and cheese, do not exert the detrimental effects on cardiometabolic health as previously predicted on the basis of their sodium and saturated fat contents (19). To expand upon this emerging science, a group of nutrition experts convened to summarize and discuss the health effects of full-fat dairy foods. The purpose of this article is to provide a review of the observational and experimental evidence related to full-fat dairy food consumption in relation to cardiometabolic health, as well as to address current knowledge gaps and future research needed to inform health messaging.

Current Status of Knowledge

This review was undertaken to evaluate the emerging science on full-fat dairy consumption and cardiometabolic health, with a focus on incident ASCVD [coronary heart disease (CHD) and stroke] and T2D, as well as biomarkers of cardiometabolic disease risk, including lipoprotein lipids, blood pressure, obesity, insulin sensitivity, and markers of inflammation. Given that extensive systematic reviews and meta-analyses have recently been published on the topic of dairy consumption and cardiometabolic disease (20–29), our aim was to further contribute to the evaluation of evidence by focusing specifically on data for full-fat dairy foods, including milk, yogurt, and cheese. This review will therefore summarize results from RCTs, prospective cohort studies, systematic reviews, and meta-analyses examining the relation between full-fat dairy consumption and cardiometabolic health and contrast these results with findings from studies of low-fat and fat-free dairy foods, when such data are available.

Observational evidence for full-fat dairy intake and cardiometabolic disease outcomes

RCTs are widely accepted as the gold standard for supporting causal relations between exposures and health outcomes. However, several practical and ethical considerations have limited the use of RCTs for studying the relations between dietary exposures and chronic disease outcomes (30). As a result, evidence relating dairy intake to clinical cardiometabolic endpoints is largely dependent on observational studies, as well as RCTs investigating effects on biomarkers of disease risk. In the absence of evidence from RCTs of clinical outcomes, prospective observational studies are heavily relied upon to inform dietary guidelines, although these have important limitations such as the potential for residual confounding (31), healthy/unhealthy user bias, and misclassification bias (30). Over the past several years, a growing body of evidence from prospective observational investigations has shown that higher consumption of full-fat dairy is not associated with increased risk of cardiometabolic outcomes, with most studies suggesting neutral or inverse relations between higher consumption of full-fat dairy and risks of cardiometabolic disease outcomes (**Table 1**) (20, 22–25, 32–42).

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Abbreviations used: ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; CHS, Cardiovascular Health Study; CRP, C-reactive protein; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; DGA, Dietary Guidelines for Americans; FFCC, full-fat Irish cheddar cheese; HF, heart failure; HTN, hypertension; OCFA, odd-chain SFA; RCT, randomized controlled trial; SRR, summary RR; T2D, type 2 diabetes.

TABLE 1 Evidence from prospective observational studies, meta-analyses, and systematic reviews on associations between full-fat dairy foods and T2D, CHD, and stroke[1]

Study (reference)	Study design	Dairy types	Results
T2D			
Soedamah-Muthu et al., 2018 (22)	Meta-analysis	Full-fat total dairy, yogurt, milk, and cheese	Nonlinear inverse association with incident T2D (RR: 0.86 at 80 g/d vs 0 g/d; 95% CI: 0.83, 0.90); no associations with total dairy, milk, and cheese
Gijsbers et al., 2016 (39)	Meta-analysis	High-fat dairy	No significant association of high-fat dairy intake with T2D risk (RR: 0.98 per 200 g/d; 95% CI: 0.93, 1.04); no association with milk or cheese individually
Drouin-Chartier et al., 2016 (25)	Systematic review	Total dairy	High-quality evidence supporting an inverse association between yogurt intake and T2D risk; high- to moderate-quality evidence for neutral associations between full-fat dairy and T2D risk
Morio et al., 2016 (43)	Review	Full-fat dairy	4 studies found no association between intake of full-fat dairy foods and T2D risk; 1 study showed an inverse relation
Total CVD			
Dehghan et al., 2018 (44)	Multinational prospective cohort	Whole-fat dairy (milk, yogurt, and cheese)	Inverse association between higher intake (>2 servings/d vs no intake) and major cardiovascular events (HR: 0.81; 95% CI: 0.77, 0.93)
Drouin-Chartier et al., 2016 (25)	Systematic review	Total dairy	High- to moderate-quality evidence for neutral associations between total dairy, cheese, and yogurt consumption and CVD risk
Visioli and Strata, 2014 (45)	Narrative review	Total dairy	The majority of published observational studies show no association between dairy intake and CVD risk
Kratz et al., 2013 (32)	Systematic review	Full-fat dairy	Modest inverse association between intake of full-fat dairy foods and CVD risk
Huth and Park, 2012 (33)	Systematic review	Total dairy	The majority of observational studies have failed to find an association between dairy foods and increased CVD risk, regardless of milk-fat levels
Rice et al., 2014 (46)	Review	Full-fat dairy	Inverse association between full-fat milk, cheese, and yogurt and CVD risk
Chen et al., 2017 (37)	Meta-analysis	Cheese	Inverse association between cheese intake and total CVD (high vs low intake—RR: 0.90; 95% CI: 0.82, 0.99)
Wu and Sun, 2017 (47)	Meta-analysis	Yogurt	No association (highest vs lowest category of consumption) between yogurt intake and incident CVD risk (RR: 1.01; 95% CI: 0.95, 1.08)
CHD			
Soedamah-Muthu et al., 2018 (22)	Meta-analysis	Total dairy, milk	No association between total dairy or milk intake and CHD risk
Guo et al., 2017 (23)	Meta-analysis	Total dairy, milk	No associated between total dairy (RR: 1.00; 95% CI: 0.98, 1.03) or milk (RR: 1.01; 95% CI: 0.97, 1.04)
Bechthold et al., 2017 (48)	Meta-analysis	Full-fat dairy foods	No difference in incident CHD risk for low- and full-fat dairy food intake
Chen et al., 2017 (37)	Meta-analysis	Cheese	Inverse association between cheese intake and CHD (high vs low intake—RR: 0.86; 95% CI: 0.77, 0.96)
Stroke			
Soedamah-Muthu et al., 2018 (22)	Meta-analysis	Full-fat dairy	200 g/d inversely associated with stroke risk (RR: 0.96; 95% CI: 0.93, 0.99)
de Goede et al., 2016 (34)	Meta-analysis	Full-fat dairy, milk	200 g/d full-fat dairy inversely associated with stroke (RR: 0.96; 95% CI: 0.93, 0.99); 200 g/d full-fat milk marginally positively associated with stroke risk (RR: 1.04; 95% CI: 1.02, 1.06)
Bechthold et al., 2017 (48)	Meta-analysis	Full-fat dairy	No difference in incident stroke risk for low- and full-fat dairy food intake
Chen et al., 2017 (37)	Meta-analysis	Cheese	Inverse association between cheese intake and stroke (high vs low intake—RR: 0.90; 95% CI: 0.84, 0.97)
Drouin-Chartier et al., 2016 (25)	Systematic review	Total dairy	High- to moderate-quality evidence for neutral associations between full-fat dairy, milk, and yogurt consumption and stroke risk

[1] CHD, coronary heart disease; CVD, cardiovascular disease; T2D, type 2 diabetes.

Recently, Dehghan et al. (44) examined the association between total dairy and specific types of dairy foods with mortality and major adverse cardiovascular events [defined as nonfatal myocardial infarction, stroke, or heart failure (HF)] in 136,384 individuals from the Prospective Urban Rural Epidemiology (PURE) Study, a multinational cohort study of individuals aged 35–70 y from 21 countries in 5 continents. Dairy foods were defined as milk, yogurt, and cheese and further grouped into whole-fat and low-fat dairy categories. Higher intake of total dairy (defined as >2 servings/d) was associated with a lower risk of the composite of mortality and major cardiovascular events (HR: 0.84; 95% CI: 0.75, 0.94; $P = 0.0004$), total mortality (HR: 0.83; 95% CI: 0.72, 0.96; $P = 0.0052$), cardiovascular mortality (HR: 0.77; 95% CI: 0.58, 1.01; $P = 0.029$), major cardiovascular disease (HR: 0.78; 95% CI: 0.67, 0.90; $P = 0.0001$), and stroke (HR: 0.66; 95% CI: 0.53, 0.82; $P = 0.0003$) compared with no intake. Analysis of whole-fat dairy intake produced similar results, showing inverse associations between higher intake (>2 servings/d vs no intake) and the composite outcome (HR: 0.86; 95% CI: 0.77, 0.97; $P = 0.009$) and major cardiovascular events (HR: 0.81; 95% CI: 0.77, 0.93; $P = 0.001$). The authors further examined the association among individuals who consumed only whole-fat dairy and those who reported consumption of both whole-fat and low-fat dairy foods. In both groups, higher dairy consumption (comparing >2 servings/d with <0.5 servings/d) was inversely associated with the total mortality and major CVD. To address potential residual confounding from differences in socioeconomic status as well as the amount and type of dairy foods consumed across world regions, the authors conducted an exploratory subgroup analysis to examine whether the associations of dairy intake with the outcomes of interest were similar in each region. The results remained consistent across regions with notably different lifestyles, leading the authors to conclude that confounders that vary by region were unlikely to explain the observed results (44).

The findings of this study are supported by a growing body of observational evidence showing inverse or neutral relations between total and full-fat dairy intakes and cardiometabolic outcomes. Soedamah-Muthu and de Goede (22) recently updated their meta-analyses of observational cohort studies on dairy intake and risk of T2D, CHD, and stroke (23, 34, 39). The addition of 4 cohort studies (published between April 2015 and July 2018) to the 22 studies included in the meta-analysis of dairy and diabetes risk by Gijsbers et al. (39) produced findings similar to the original analysis. In the updated analysis, a nearly linear inverse association was observed for total dairy and T2D risk per 200 g/d (RR: 0.97; 95% CI: 0.95, 1.00; $P < 0.001$), while yogurt consumption showed a significant nonlinear inverse association with incident diabetes (RR: 0.86 at 80 g/d compared with 0 g/d; 95% CI: 0.83, 0.90; $P < 0.001$). Consistent with the original meta-analysis by Gijsbers et al., no statistically significant associations were found for full-fat dairy, milk, or cheese and T2D risk (22). The original meta-analysis of 13 studies that reported separate results for high-fat dairy intake showed no significant association with T2D risk (RR: 0.98 per 200 g/d; 95% CI: 0.93, 1.04; $P = 0.52$). The authors found significant heterogeneity ($I^2 = 52\%$, $P = 0.016$), although publication bias was not detected. Additionally, the definition of high-fat dairy differed between the studies, with some including butter, cream, sour cream, and dairy desserts in addition to full-fat milk, yogurt, and cheese. There was no association between full-fat milk (RR per 200 g/d: 0.99; 95% CI: 0.88, 1.11; $P = 0.85$) or cheese (RR per 10 g/d: 1.00; 95% CI: 0.99, 1.02) and risk of T2D (39).

In the updated meta-analyses for total dairy and milk in relation to CHD risk, 4 studies were added for a total of 15 cohort studies. Consistent with previous findings, neither total dairy nor milk was associated with incident CHD ($RR_{Total\ Dairy}$: 1.00; 95% CI: 0.98, 1.03; RR_{Milk}: 1.01; 95% CI: 0.97, 1.04) (22, 23). A 2016 meta-analysis by de Goede et al. (34) showed that an increment of 200 g of daily milk intake was associated with a 7% lower risk of stroke (RR: 0.93; 95% CI: 0.88, 0.98; $P = 0.004$). Based on a limited number of studies, they also found that 200 g full-fat milk intake/d was positively associated with increased stroke risk (RR: 1.04; 95% CI: 1.02, 1.06; $P = 0.001$; $n = 4$ studies) whereas 200 g full-fat total dairy/d showed an inverse association of similar magnitude (RR: 0.96; 95% CI: 0.93, 0.99; $P = 0.02$; $n = 6$ studies). In the updated analyses, an increment of 200 g of daily milk intake was associated with an 8% lower risk of stroke (RR: 0.92; 95% CI: 0.88, 0.97), whereas results for full-fat dairy were consistent with previous findings (RR: 0.96; 95% CI: 0.93, 0.99) (22).

A systematic review and dose-response meta-analysis published in 2017 by Bechthold et al. (48) including 13 prospective studies on dairy and CHD, 12 on stroke, and 3 on HF found no associations between dairy intake and risk of CHD (RR: 0.99; 95% CI: 0.92, 1.07), stroke (RR: 0.96; 95% CI: 0.90, 1.01), or HF (RR: 1.00; 95% CI: 0.90, 1.10) in the analyses comparing the highest with the lowest categories of dairy intake. Comparing low-fat and high-fat dairy foods, no significant differences were observed for incident CHD and stroke. Yu and Hu (27) and Drouin-Chartier et al. (25) also recently published systematic reviews of meta-analyses on the evidence regarding the association between dairy food intakes and cardiometabolic health. Yu and Hu concluded that most meta-analyses report a null or weak inverse association between dairy intake and CVD and related intermediate outcomes, with some evidence to suggest that dairy consumption is inversely associated with incident stroke and yogurt consumption associated with a lower risk of T2D (27). The authors also included a discussion of substitution analyses based on prospective cohort studies that suggest that replacing dairy fat with plant-based or polyunsaturated

fat is associated with a lower risk of CVD, although a number of other studies have found no association between dairy fat and CVD risk, suggesting that the substitution benefit is attributable to favorable effects of plant-based or polyunsaturated fats rather than an adverse effect of dairy fat (21).

The extensive systematic review by Drouin-Chartier et al. (25) summarizing meta-analyses of prospective population studies associating dairy consumption with CVD, coronary artery disease, stroke, hypertension (HTN), metabolic syndrome, and T2D found either favorable or neutral associations between the consumption of various forms of dairy foods and cardiometabolic clinical outcomes. The authors concluded there is no evidence that the consumption of any form of dairy food is detrimentally associated with the risk of any cardiovascular-related clinical outcome. They also concluded there is high-quality evidence supporting inverse associations between total dairy intake and hypertension risk and yogurt intake and the risk of T2D. They further concluded there is high- to moderate-quality evidence for neutral associations between the consumption of total dairy, cheese, and yogurt and CVD risk; the consumption of regular- and high-fat dairy, milk, and yogurt and stroke risk; the consumption of regular- and high-fat dairy, cheese, yogurt, and fermented dairy and hypertension risk; and the consumption of regular- and high-fat dairy, milk, and fermented dairy and T2D risk (25).

Authors of several earlier reviews and meta-analyses of observational evidence also suggested that the evidence base does not support the hypothesis that full-fat dairy foods contribute to cardiometabolic disease risk, and underscore the need for more research to elucidate the relation between full-fat dairy consumption and cardiometabolic health (32, 33, 45, 46). In 2014, Visioli and Strata (45) concluded that a large majority of published studies indicate that dairy consumption does not increase cardiovascular risk and there is evidence to suggest a benefit of dairy consumption on cardiovascular health (45). In an earlier meta-analysis of 11 prospective studies by Kratz et al. (32), the authors also reported a modest inverse association between the intake of full-fat dairy foods and cardiometabolic disease risk.

Milk, yogurt, and cheese intake and cardiometabolic risk

In addition to these comprehensive reviews on total dairy intake and cardiometabolic disease, several investigators have also conducted meta-analyses of specific dairy foods and cardiometabolic outcomes (Table 1). A dose-response meta-analysis by Mullie et al. (35) examined the associations between milk intake and CHD and stroke. The summary RR (SRR) of fatal and nonfatal CHD associated with the consumption of 200 mL milk/d was 1.01 (95% CI: 0.98, 1.05) and the SRR of fatal and nonfatal stroke was 0.91 (95% CI: 0.82, 1.02). Only 3 of 21 studies included in the analyses reported separate results for full-fat milk and cardiometabolic outcomes, with inconsistent findings. Hu et al. (49) found an increased risk of CHD (RR: 1.67; 95% CI: 1.14, 1.90) with ≥2 glasses of full-fat milk/d versus never, and Larsson et al. (50) showed a positive association between whole-milk intake and risk of intracerebral hemorrhage (highest vs lowest quintile RR: 1.41; 95% CI: 1.02, 1.96) and between yogurt intake and subarachnoid hemorrhage (RR: 1.83; 95% CI: 1.20, 2.80) in Finnish male smokers aged 50–69 y. However, in the analysis of the Netherlands Cohort Study by Goldbohm et al. (51), consumption of fermented full-fat milk (mainly full-fat yogurt) was inversely associated with all-cause mortality (per 100 mL/d—RR_{men}: 0.91; 95% CI: 0.86, 0.97; RR_{women}: 0.92; 95% CI: 0.85, 1.00), whereas fermented and nonfermented low-fat milk was not. The authors found no association between full-fat or low-fat milk and cardiovascular mortality in this cohort.

Chen et al. (37) recently published a meta-analysis of 15 prospective studies examining the association between cheese intake and CVD risk. The SRR for high versus low cheese consumption was 0.90 (95% CI: 0.82, 0.99) for total CVD ($n = 7$), 0.86 (95% CI: 0.77, 0.96) for CHD ($n = 8$), and 0.90 (95% CI: 0.84, 0.97) for stroke ($n = 7$), respectively, with evidence of nonlinear inverse relations between cheese consumption and risks of total CVD (P-nonlinearity < 0.001) and stroke (P-nonlinearity $= 0.015$), with the largest risk reductions observed with consumption of ∼40 g/d.

In a meta-analysis of 9 cohort studies, Wu and Sun (47) in 2017 found that the highest category of yogurt consumption, compared with the lowest, was not related to the risk of incident CHD (RR: 1.04; 95% CI: 0.95, 1.15) or stroke (RR: 1.02; 95% CI: 0.92, 1.13). A secondary analysis showed a suggestive trend for dose-response, with higher yogurt consumption (≥200 g/d) associated with a lower risk of incident CVD (RR: 0.92; 95% CI: 0.85, 1.00) compared with consumption of <200 g/d (RR: 1.06; 95% CI: 0.98, 1.15; P-difference = 0.09) (47). The relationship between yogurt consumption and T2D risk has also been extensively studied, with a large body of evidence supporting a potentially beneficial role (52). In the most up-to-date meta-analysis, yogurt consumption of 80–125 g/d was associated with a 14% lower risk of T2D compared with no consumption (22).

Biomarkers of dairy fat intake and cardiometabolic risk

To further inform this topic, several groups of researchers have recently summarized evidence relating specific biomarkers of dairy fat intake to clinical cardiometabolic outcomes (53–55). Although not entirely specific to dairy foods, several circulating odd-chain SFAs (OCFAs), pentadecanoic acid (15:0), heptadecanoic acid (17:0), as well as *trans*-palmitoleic acid (*t*16:1n–7) are biomarkers

that correlate strongly with dairy fat intake (56–58). A meta-analysis of 16 prospective cohort studies by Imamura et al. (53) demonstrated an inverse association between higher circulating and adipose tissue concentrations of pentadecanoic acid, heptadecanoic acid, and *trans*-palmitoleic acid and incident T2D. Fatty acid concentrations were measured from ≥1 lipid compartment, including erythrocyte phospholipids, plasma phospholipids, plasma cholesteryl esters, plasma triglycerides, total plasma, or adipose tissue and expressed as a percentage of total fatty acids in each lipid fraction. From the fully adjusted multivariable analyses, HRs (95% CIs) for incident T2D per cohort-specific 10th to 90th percentile range were 0.80 (0.73, 0.87) for pentadecanoic acid, 0.65 (0.59, 0.72) for heptadecanoic acid, 0.82 (0.70, 0.96) for *trans*-palmitoleic acid, and 0.71 (0.63, 0.79) for the sum of all 3 biomarkers (53). An earlier review by Risérus and Marklund (55) similarly showed an inverse association between OCFA biomarkers and T2D risk, while results from studies examining OCFAs and cardiovascular outcomes were inconsistent, with the majority of studies showing an inverse or neutral association. For example, the authors identified several observational studies that have shown inverse associations between plasma phospholipid pentadecanoic acid, heptadecanoic acid, and the sum of pentadecanoic acid and heptadecanoic acid and incident CVD (including CHD, stroke, and HF) and others that have shown no associations of plasma or erythrocyte OCFAs with CVD risk. Only 1 study included in the review reported a positive association between plasma but not erythrocyte pentadecanoic acid and risk of ischemic heart disease (59). Further, *trans*-palmitoleic acid measured in erythrocytes was linked to lower cardiovascular mortality in the Ludwigshafen Risk and Cardiovascular Health Study (60), yet plasma *trans*-palmitoleic acid was not associated with incident CVD or CHD in the Multi-Ethnic Study of Atherosclerosis (61). Adipose tissue OCFAs have similarly been shown to have both inverse and neutral associations with CVD-related outcomes (55). In 2018, Liang et al. (54) conducted a systematic review and meta-analysis of 13 prospective cohort studies of the relation between biomarkers of dairy fat and CVD risk, including CHD, stroke, HF, and CVD mortality and concluded that high-fat dairy exposure is not associated with increased risk of CVD. The pooled RRs of the risk of CVD for the top third versus bottom third for pentadecanoic acid, heptadecanoic acid, and *trans*-palmitoleic acid concentrations were 0.94 (95% CI: 0.77, 1.15), 0.82 (95% CI: 0.68, 0.99), and 0.82 (95% CI: 0.67, 1.02), respectively. Subgroup analysis indicated that there were no associations between the concentration of pentadecanoic acid with CHD and stroke, but there was an inverse relation with HF (RR: 0.72; 95% CI: 0.55, 0.95). No associations were observed between circulating heptadecanoic acid and *trans*-palmitoleic acid concentrations and subtypes of CVD, except for 1 study that reported an inverse relation between heptadecanoic acid and incident HF.

Recently, de Oliveira Otto et al. (62) investigated the prospective association of serial measures of plasma pentadecanoic acid, heptadecanoic acid, and *trans*-palmitoleic acid with total mortality, cause-specific mortality, and CVD risk in adults aged ≥65 y from the Cardiovascular Health Study (CHS). Unlike many previous studies that were limited by a single measure of these biomarkers, circulating fatty acid concentrations were measured serially at baseline and at study years 6 and 13 in the CHS. Circulating heptadecanoic acid was associated with 23% lower CVD mortality when comparing individuals in the highest with the lowest quintile of heptadecanoic acid (HR: 0.77; 95% CI: 0.61, 0.98). This association was especially strong for stroke, with a 42% lower risk of stroke mortality when comparing extreme quintiles (HR: 0.58; 95% CI: 0.35, 0.97). There were no significant associations of pentadecanoic acid, heptadecanoic acid, or *trans*-palmitoleic acid with total incident CVD, CHD, or stroke.

In summary, the current prospective observational evidence base supports a neutral or modest inverse association between full-fat dairy consumption and cardiometabolic disease outcomes, although the interpretation of these results must acknowledge several limitations. Substantial observed and unexplained heterogeneity was reported in a number of analyses (22) and dairy itself is a heterogeneous exposure that includes multiple products with unique food matrices. Further, there are no established definitions of total, low-fat, or full-fat dairy in research, resulting in inconsistent dairy food categorization across studies. Considering the findings from prospective observational studies, additional research is needed to better characterize and compare the impacts of low-fat with full-fat dairy on cardiometabolic disease risk to inform dietary recommendations.

Full-fat dairy intake and biomarkers of cardiometabolic risk

Although intervention trials studying dairy intake and cardiometabolic clinical outcomes are lacking, the observational body of evidence is supported by additional evidence from RCTs investigating the effects of dairy food consumption on markers of cardiometabolic health, including insulin sensitivity, lipoproteins, blood pressure, inflammatory markers, and adiposity. The available evidence from RCTs indicates neutral and, in some cases, beneficial effects of dairy, regardless of the fat content, on several markers of cardiometabolic health (summarized in **Table 2**).

Dyslipidemia.

Full-fat dairy's effect on plasma LDL cholesterol concentrations has long been an area of concern due to its high saturated fat content, a driving factor in the promotion

TABLE 2 Prospective observational and experimental evidence for associations between intake of full-fat dairy foods and cardiometabolic risk factors[1]

Study (reference)	Study design	Dairy types (or intervention)	Results
Dyslipidemia			
Mitri et al., 2017 (63)	Meta-analysis of RCTs	Total dairy (4 of 9 studies used high-fat dairy)	Dairy intake ≥3 servings/d associated with a small increase in LDL cholesterol; no effect on HDL cholesterol or TGs compared with low intake
Benatar et al., 2013 (64)	Meta-analysis of RCTs	High-fat dairy (full-fat milk, cheese, butter, cream, and ice cream)	No impact on LDL- or HDL-cholesterol concentrations
Drouin-Chartier et al., 2016 (24)	Systematic review of RCTs	Total dairy	No effect of increasing total dairy intake on LDL- and HDL-cholesterol or TG concentrations
Engel et al., 2018 (65)	Randomized crossover trial	0.5 L/d full-fat milk (3.5% fat) vs skimmed milk (0.1% fat)	HDL-cholesterol concentrations increased with full-fat milk intervention; no difference between total and LDL-cholesterol, TG, insulin, or glucose concentrations
Chiu et al., 2016 (66)	Randomized crossover trial	Full-fat dairy DASH diet, low-fat dairy DASH diet, control	Decreased plasma TGs and VLDL-cholesterol concentrations and increased LDL peak particle diameter compared with low-fat DASH; no increases in LDL or non–HDL cholesterol compared with control diet
Brassard et al., 2017 (67)	Meta-analysis of RCTs	Yogurt	Fermented yogurt products produced a 4% decrease in total cholesterol and 5% decrease in LDL cholesterol
de Goede et al., 2015 (68)	Meta-analysis of RCTs	Cheese and butter	Cheese intake reduced LDL cholesterol (−0.22 mmol/L; 95% CI: −0.29, −0.14) and HDL cholesterol (−0.05; 95% CI: −0.09, −0.02) and had no effect on TGs compared with butter intake
Blood pressure			
Benatar et al., 2013 (64)	Meta-analysis of RCTs	Total and full-fat dairy	No effect of total or full-fat dairy intake on systolic or diastolic blood pressure
Drouin-Chartier et al., 2016 (24)	Review of RCTs	Total dairy	Mixed results with studies showing a favorable or null effect
Alonso et al., 2009 (69)	Randomized crossover trial	Full-fat and low-fat dairy	No difference in blood pressure after 8 wk of consuming full-fat or low-fat dairy as part of an ad libitum diet ($P > 0.6$)
Chiu et al., 2016 (66)	Randomized crossover trial	Full-fat dairy DASH diet, low-fat dairy DASH diet, control	Full-fat and low-fat dairy reduced blood pressure to a similar extent relative to the control diet
Schwingshackl et al., 2017 (70)	Dose-response meta-analysis of prospective studies	Total dairy, full-fat dairy	Inverse association between an increase in total dairy of 200 g/d and risk of HTN (RR: 0.95; 95% CI: 0.94, 0.97); no difference between low- and full-fat dairy foods
Soedamah-Muthu et al., 2012 (71)	Meta-analysis of prospective studies	Full-fat dairy	Pooled RR (95% CI) of HTN per 200 g/d full-fat dairy: 0.99 (0.95, 1.03)
Glucose metabolism			
Benatar et al., 2013 (64)	Meta-analysis of RCTs	Total and full-fat dairy	Nonsignificant improvement in insulin sensitivity (HOMA-IR: −0.94; 95% CI: −1.93, 0.04) with a high dairy diet, consistent with stratification by dairy fat content
Drouin-Chartier et al., 2016 (24)	Review of RCTs	Total dairy	Inconsistent results from short-term trials; favorable changes in glucose and insulin homeostasis with prolonged exposure to dairy
Morio et al., 2016 (43)	Review of observational and intervention studies	Full-fat dairy	No effect of full-fat dairy intake on insulin sensitivity
Obesity			
Benatar et al., 2013 (64)	Meta-analysis of RCTs	Full-fat dairy	Modest increase in weight with increases in both low-fat (0.82 kg; 95% CI: 0.35, 1.28) and full-fat dairy intake (0.41; 95% CI: 0.04, 0.79); no change in waist circumference with either intervention
Schwingshackl et al., 2016 (72)	Meta-analysis of prospective observational studies	Full-fat dairy	Significant reduction in adiposity with higher consumption of full-fat dairy foods
Santiago et al., 2016 (73)	Prospective observational analysis of the PREDIMED study	Whole-milk yogurt	Increased probability of abdominal obesity reversion and average 0.23-cm decrease in waist circumference in the highest vs lowest quintile of intake
Kratz et al., 2013 (32)	Systematic review of observational studies	Full-fat dairy	Inverse association between full-fat dairy intake and measures of adiposity over time

[1] DASH, Dietary Approaches to Stop Hypertension; HTN, hypertension; PREDIMED, Prevention with Mediterranean Diet; RCT, randomized controlled trial; TG, triglyceride.

of low-fat dairy foods for cardiometabolic health (8, 74, 75). However, evidence from RCTs has not consistently shown a detrimental effect of full-fat dairy intake on LDL-cholesterol concentration, and instead suggests little or no effect of increased dairy consumption, irrespective of fat content and product type (24, 63). For example, a 3-wk randomized crossover study by Engel et al. (65) published in 2018 compared the effects of 0.5 L of full-fat milk/d (3.5% fat) with skimmed milk (0.1% fat) as part of a habitual diet on fasting serum lipids, insulin, and plasma glucose in 17 healthy subjects. The results showed no difference between total and LDL cholesterol, triacylglycerol, insulin, or glucose concentrations after the full-fat milk and skimmed-milk interventions. HDL-cholesterol concentrations were significantly ($P = 0.04$) higher after the full-fat milk intervention (1.69 ± 1.10 mmol/L) than after the skimmed-milk intervention (1.63 ± 1.10 mmol/L). Chiu et al. (66) recently conducted a 3-period randomized crossover trial in 36 free-living healthy adults to test the effect of substituting full-fat for low-fat dairy foods in the Dietary Approaches to Stop Hypertension (DASH) diet on blood pressure and plasma lipids and lipoproteins wherein all food was provided for subjects throughout each study condition. Dietary interventions each lasted 3 wk and were separated by 2-wk washout periods. Compared with the control diet [standard American diet, as previously described (76)], blood pressure was similarly reduced with the DASH and full-fat DASH diets ($P < 0.017$). There were no significant increases in LDL cholesterol or non–HDL cholesterol (the sum of LDL and VLDL cholesterol) concentrations during the full-fat DASH diet compared with the control diet. The full-fat DASH diet significantly reduced plasma triglyceride ($P < 0.017$) and VLDL cholesterol ($P < 0.017$) concentrations and increased LDL peak particle diameter ($P < 0.001$) compared with the standard DASH diet (66). Previous studies have shown that total saturated fat consumption increases both serum LDL-cholesterol concentration and LDL particle size (77). Unlike small and medium-sized LDL particles, large particles show a weaker association with ASCVD risk (17).

A recent meta-analysis by Mitri et al. (63) of 9 RCTs examined the influence of increased dairy consumption on plasma lipoprotein lipid concentrations in adults. Of the studies included in the analysis, however, only 4 used high-fat dairy or did not set a limit on dairy fat content. High dairy consumption of ≥3 servings/d was associated with a small increase in LDL-cholesterol concentration (standard mean difference: 0.13 mmol/L; 95% CI: 0.00, 0.26 mmol/L; $P = 0.04$) but had no effect on HDL cholesterol or triglycerides compared with low dairy consumption. An earlier meta-analysis of 9 RCTs by Benatar et al. (64) showed no significant impact of increased total dairy, low-fat (products with <1% fat) dairy, or high-fat (full-fat milk, cheese, butter, cream, and ice cream) dairy consumption on LDL- or HDL-cholesterol concentrations. In a systematic review, Drouin-Chartier et al. (24) concluded that increasing total dairy consumption does not impact LDL-cholesterol, HDL-cholesterol, or triglyceride concentrations. However, the authors also noted that evidence for the impact of the substitution of high-fat for low-fat dairy on these blood lipids and lipoproteins is limited to a few very small RCTs and additional studies in this area are warranted, especially those considering the dairy food matrix.

The investigation of the effects of fermented dairy foods on cholesterol concentration suggests possible favorable effects. A meta-analysis of controlled, short-term intervention studies showed that yogurt products produced a 4% decrease in total cholesterol and a 5% decrease in LDL cholesterol (78). Cheese consumption has been hypothesized to increase cardiometabolic disease risk by raising cholesterol concentrations due to its high saturated fat content. Current evidence, however, does not generally support this relation and highlights the importance of considering the effect of the food matrix when studying dairy foods and cardiometabolic health. Recently, experimental evidence has demonstrated differential effects of butter and cheese on serum LDL-cholesterol concentrations, despite nearly identical fatty acid composition of the products consumed. Feeney et al. (79) tested the effect of 6-wk daily consumption of ∼40 g dairy fat, consumed within macronutrient-matched food matrices, on markers of metabolic health in overweight adults aged ≥50 y. In this parallel-arm study, participants ($n = 164$) were randomly assigned to 1 of 4 dietary interventions: 120 g full-fat Irish cheddar cheese (FFCC); 120 g reduced-fat Irish cheddar cheese plus butter (21 g); butter (49 g), calcium caseinate powder (30 g), and calcium supplement ($CaCO_3$) (500 mg); or 120 g FFCC with a 6-wk run-in period with no dietary cheese consumption. The interventions provided 489 ± 19 kcal/d and were matched as closely as possible for total energy, macronutrient content, and calcium. Participants were additionally instructed to limit intake of other dairy foods to 50 mL milk/d, but no other dietary restrictions were given. The authors observed a stepwise matrix effect for the changes in total cholesterol ($P < 0.033$) and LDL-cholesterol ($P < 0.026$) concentrations, with significantly lower postintervention total cholesterol (mean ± SD) (5.23 ± 0.88 mmol/L) and LDL-cholesterol (2.97 ± 0.67 mmol/ L) concentrations when all of the dairy fat was contained within the cheese matrix compared with butter (total cholesterol: 5.57 ± 0.86 mmol/L; LDL cholesterol: 3.43 ± 0.78 mmol/L).

Total and LDL cholesterol decreased postintervention for all groups. Measures of anthropometry, triglycerides, blood pressure, fasting glucose, and insulin did not differ between the groups pre- or postintervention. The authors concluded that dairy fat differentially affects blood lipids when consumed in the form of cheese compared with the same constituents consumed in different matrices (79). Additionally, in a multicenter, randomized, controlled, crossover trial, 92 men and women with abdominal obesity and low HDL cholesterol were randomly assigned to sequences of five 4-wk isocaloric diets separated by 4-wk washout periods. Two of the diets were rich in SFAs (12.4–12.6% of calories) from either cheese or butter, while the other 3 experimental diets were rich in MUFAs (SFAs: 5.8%; MUFAs: 19.6%),

PUFAs (SFAs: 5.8%; PUFAs: 11.5%), and carbohydrate (fat: 25%; SFAs: 5.8%). Compared with the butter diet, serum LDL-cholesterol concentrations were lower (−3.3%; $P < 0.05$), whereas triglyceride concentrations were higher (5.1%; $P < 0.05$) after the cheese diet. LDL-cholesterol concentrations were higher after both the cheese (+2.6%, +5.3%, +12.3%; $P < 0.05$ for all) and butter (+6.1%, +8.9%, +16.2%; $P < 0.05$ for all) diets than after carbohydrate, MUFA, and PUFA diets, respectively. The cheese diet also resulted in higher triglyceride concentrations (+10.0%; $P < 0.05$) compared with the effects of PUFAs, but not of MUFAs or carbohydrates (67). There were no significant differences in blood pressure, markers of inflammation, or indices of glucose-insulin homeostasis across the experimental diets.

A meta-analysis of 5 RCTs by de Goede et al. (68) also examined the effect of similar amounts of saturated fat intake from hard cheese and butter on blood lipids and lipoproteins. Compared with butter intake, cheese intake reduced LDL cholesterol by 6.5% (−0.22 mmol/L; 95% CI: −0.29, −0.14 mmol/L) and HDL cholesterol by 3.9% (−0.05 mmol/L; 95% CI: −0.09, −0.02 mmol/L) but had no effect on triglycerides. Such findings underscore the importance of considering the dairy food matrix and metabolic phenotype (e.g., presence of metabolic disturbances such as insulin resistance, glucose intolerance, and dyslipidemia) (80) when evaluating the impact of dairy foods on cardiometabolic health and establishing dietary guidelines. Overall, results from RCTs suggest minimal effects of full-fat dairy food consumption on the lipoprotein–lipid profile in either healthy or at-risk adults.

Blood pressure.

Evidence from intervention trials also suggests that blood pressure is not adversely impacted by full-fat dairy consumption, and in some cases, it may exert a beneficial effect. The meta-analysis of 7 studies by Benatar et al. (64) found no effect of total dairy intake on systolic or diastolic blood pressures and results were consistent when the studies were stratified by full-fat and low-fat dairy foods. As summarized by Drouin-Chartier et al. (24), several recent RCTs in hypertensive subjects have produced mixed results, with some showing a favorable effect of dairy intake on blood pressure and others showing a null effect. Two RCTs that specifically compared full-fat and low-fat dairy foods found no impact of dairy fat content on blood pressure outcomes (66, 69). In the crossover RCT in 45 normotensive subjects who consumed low-fat milk, full-fat milk, or yogurt as part of their regular diet for 8 wk there was no difference in the effect of low-fat or whole-fat dairy on blood pressure ($P > 0.60$) (69). In the RCT by Chiu et al. (66), described above, consumption of a high-fat (full-fat dairy) DASH diet reduced blood pressure to a similar extent compared with the control diet, as did the standard low-fat dairy DASH in healthy adults.

Prospective observational evidence also supports a neutral or beneficial relation between full-fat dairy consumption and the risk of elevated blood pressure or HTN. A recent systematic review and dose-response meta-analysis by Schwingshackl et al. (70) reported an inverse association between an increase in total dairy intake of 200 g/d and the risk of HTN (RR: 0.95; 95% CI: 0.94, 0.97), with no significant differences observed when comparing low- and high-fat dairy foods. These findings are consistent with results from a previous meta-analysis by Soedamah-Muthu et al. (71) of 9 prospective observational studies with pooled RRs (95% CIs) per 200 g/d of 0.97 (0.95, 0.99) for total dairy, 0.96 (0.94, 0.98) for milk, and 0.99 (0.95, 1.03) for full-fat dairy. Thus, experimental and observational evidence generally supports a neutral association between full-fat dairy intake and blood pressure, with some evidence to suggest a modest inverse association in individuals with HTN.

Insulin resistance/sensitivity.

Results from intervention studies on the impact of full-fat dairy consumption on insulin resistance have been mixed and remain inconclusive. A meta-analysis of 8 randomized studies by Benatar et al. (64) found that HOMA-IR was slightly, but nonsignificantly, improved with a high-dairy diet (−0.94; 95% CI: −1.93, 0.04 units; $P = 0.06$), and findings did not change with stratification by dairy fat content. Drouin-Chartier et al. (24) reported inconsistent results from short-term intervention studies but showed favorable changes in glucose and insulin homeostasis in RCTs with prolonged exposure to dairy. A more recent review by Morio et al. (43) in 2016 identified 3 intervention studies, the combined results from which indicate that increased full-fat dairy food consumption was not detrimental to insulin sensitivity. Additional research is warranted to clarify the findings of these studies and provide insight into potential underlying mechanistic pathways.

Vascular function and inflammation.

Evidence for the effect of full-fat dairy consumption on vascular function is sparse, yet it represents an important marker of cardiometabolic health that is directly affected by dietary habits (81). The systematic review by Drouin-Chartier et al. (24) provides evidence from a small number of studies suggesting that total dairy and milk intake have no effect on vascular function. For instance, Nestel et al. (82) carried out a small RCT examining the effect of dairy fat on surrogate biomarkers of vascular function in 13 overweight subjects. Each subject participated in 5 test meals consisting of low-fat milk (control) or 45 g fat from butter, cream, yogurt, or cheese over 3 wk. Between-group analysis showed that single high-fat dairy meals did not increase any of the circulating biomarkers related to inflammation or atherogenesis. Recently, McDonald et al. (83) published findings from a crossover RCT in 22 adults with prediabetes showing that milk, regardless of fat content, protects against postprandial hyperglycemia-mediated impairments in vascular endothelial function by limiting oxidative stress responses that reduce NO availability.

Low-grade systemic inflammation is also recognized as an important risk factor associated with the development and progression of cardiometabolic disease (84), and dietary

intake has been identified as a modulator of both acute and chronic inflammation (85). A meta-analysis of 6 RCTs by Benatar et al. (64) found no effect of high versus low dairy consumption on plasma C-reactive protein (CRP) concentrations. Further, the authors reported no difference between low- and high-fat dairy consumption on plasma CRP. These findings are consistent with those from a systematic review of 8 RCTs conducted in overweight or obese adults from which the authors concluded there is no adverse effect of dairy consumption on circulating inflammatory biomarkers (86). In the most recent review by Drouin-Chartier et al. (24), consumption of a combination of low- and high-fat dairy foods had no impact on inflammatory gene expression or serum inflammatory biomarker concentrations compared with low dairy intake in overweight or obese subjects.

Evidence from RCTs suggests that full-fat dairy foods do not have a detrimental effect compared with lower-fat dairy foods on cardiometabolic risk factors, and in some cases, a beneficial role has been shown. The number of RCTs supporting these conclusions, however, is limited. Further, study designs to maintain isocaloric conditions for lower-fat dairy interventions introduce a variety of macronutrient mixtures and, thereby, heterogeneity across studies. Well-controlled randomized dietary intervention studies in both healthy and high-risk individuals are needed to inform conclusions about the health benefits of full-fat dairy foods.

Dairy intake and anthropometry

The association between dairy intake and adiposity has been extensively studied in both RCTs and prospective observational cohorts, although few studies have specifically examined the effect of full-fat dairy foods on body weight and body composition. A recent meta-analysis of 37 RCTs by Geng et al. (87) provided evidence to support a beneficial effect of high dairy intake on body weight and body composition in the context of calorie restriction (target energy deficit ranging from 500 to 600 kcal/d) but no effect without calorie restriction. A significant reduction in body weight (−0.64 kg; 95% CI: −1.05, −0.24 kg), waist circumference (−2.18 cm; 95% CI: −4.30, −0.06 cm), and body fat (−0.56 kg; 95% CI: −0.95, −0.17 kg) was observed in the 16 RCTs with energy restriction as a component of the intervention. In the overall sample, high dairy intervention was associated with an increase in lean mass (0.37 kg; 95% CI: 0.11, 0.62 kg). These results are consistent with the findings of 2 previous meta-analyses showing an inverse association between dairy intake and body weight, waist circumference, and fat mass with calorie restriction (88, 89). Inferences from the findings of these studies about the effect of full-fat dairy on body weight and body composition are limited since the majority of dairy interventions used low-fat and fat-free dairy foods. A meta-analysis by Benatar et al. (64) in 2013, which did include a stratified analysis of low- and full-fat dairy foods, produced similar results independent of dairy fat content. Modest weight gain was observed in studies that increased low-fat (0.82 kg; 95% CI: 0.35, 1.28 kg; $P < 0.001$; $n = 8$ studies) and full-fat (0.41; 95% CI: 0.04, 0.79 kg; $P = 0.03$; $n = 10$ studies) dairy intake while waist circumference did not change with either type of dairy intervention. This analysis did not distinguish between the weight gain due to lean body mass and fat mass, so it is plausible that the small increase found in body weight without an increase in waist circumference was due to increases in fat-free body mass.

Prospective observational studies of the association between dairy intake and body weight have also produced mixed results, although, in general, suggest a beneficial role of full-fat dairy in relation to risk of overweight and obesity. In a meta-analysis of 22 longitudinal observational studies, Schwingshackl et al. (72) found that dairy consumption was not related to changes in body weight but was inversely associated with changes in waist circumference as well as the risk of overweight and abdominal obesity. The highest dairy intake category was associated with lower risks of abdominal obesity (OR: 0.85; 95% CI: 0.76, 0.95) and overweight (OR: 0.87; 95% CI: 0.76, 1.00) compared with the lowest intake category. A sensitivity analysis comparing low-fat versus full-fat dairy showed a significant reduction in adiposity only for higher consumption of full-fat dairy foods (72). In 2016, Santiago et al. (73) examined the association of yogurt consumption and obesity in a subset of 4545 participants from the Prevention with Mediterranean Diet (PREDIMED) Study. Whole-milk yogurt consumption was associated with an average decrease in waist circumference of 0.23 cm in the highest (52.5 g/d) compared with the lowest (1.7 g/d) quintile of consumption after adjustment for known confounding factors. Further, individuals with consumption of yogurt made from whole milk in the highest quintile of intake had a 43% increased probability of reversion of abdominal obesity over 4.9 y of follow up compared with those in the lowest quintile (OR: 1.43; 95% CI: 1.06, 1.93) (73).

Similarly, a systematic review by Kratz et al. (32) of observational studies examining the relation between dairy fat and high-fat dairy foods, obesity, and cardiometabolic disease reported that, in 11 of 16 studies with adiposity-related outcomes, high-fat dairy intake was inversely associated with measures of adiposity over time. To control for potential reverse causation, a separate analysis included only prospective studies that adjusted for baseline weight or BMI, and 4 of 6 studies reported inverse associations between dairy fat intake and obesity risk. None of the included studies reported a positive association between baseline consumption of dairy fat or high-fat dairy foods and measures of adiposity at baseline or over time (32). The current evidence base therefore does not support an increased risk of overweight and obesity with full-fat versus low-fat dairy consumption, further suggesting that the health effects of dairy foods cannot simply be ascribed to the caloric density or saturated fat content of the foods.

Considering calories in body-weight regulation.

Body weight is an established driver of many cardiometabolic risk factors, and more research is needed to understand how the consumption of full- and reduced-fat dairy versus low- and nonfat dairy foods may impact appetite regulation and

body weight. In addition to saturated fat and cholesterol contents, a driving force behind the recommendations to consume low- and nonfat dairy foods is the idea that dairy fat is a source of empty calories, since removing the fat from dairy does not alter its nutrient-rich composition of protein, calcium, vitamin D, magnesium, and potassium (8). Compared with low-fat (1%) and fat-free milk, full-fat milk provides ~44–63 additional calories per 237-mL serving (90). Replacing the recommended 3 servings of low- or nonfat dairy with full-fat milk, for example, would therefore contribute an additional 132–189 calories/d. In other words, adherence to the current dietary guidelines suggests that 132–180 calories would be spared each day if full-fat milk were replaced with low- or nonfat milk. The questions we considered are whether the extra energy from full-fat dairy are detrimental to cardiometabolic risk and if dairy fat may exert a functional benefit to promote satiety, limit metabolic excursions at subsequent meals, and replace other sources of empty calories (defined by the DGA Scientific Report as calories from solid fats and added sugars) (8) in the diet.

The answers to these questions are complex and, although a large body of observational and experimental evidence has examined the relation between dairy intake and adiposity, the association between dairy fat and cardiometabolic risk in the context of weight is highly nuanced. Evidence from RCTs has shown that dairy intake reduces body fat and preserves lean body mass in the context of calorie restriction. Additionally, prospective observational evidence suggests that dairy consumption, and specifically full-fat dairy, is inversely associated with weight gain over time and risk of overweight and obesity. Another challenge to addressing these questions is the lack of evidence related to the implementation of dietary recommendations by consumers and the resulting impact this has on food choices. In response to the recommendations to reduce fat intake in the original DGA published in the 1980s, the food industry developed thousands of new low-fat products in which fat was often replaced with a combination of sugars and processed starches to preserve palatability. Consequently, many people consumed more refined starches and added sugars. Such observations, however, do not fully explain how consumers will change their eating behaviors in response to dietary recommendations (30). For instance, currently available population data cannot reliably predict whether consumers are likely to replace the extra calories in full-fat dairy foods with energy-dense or nutrient-dense foods. To address this question, longitudinal studies with good measures of dietary intake and that give subjects non- or low-fat dairy and full-fat dairy foods to incorporate into their diets are needed.

In summary, the consumption of full-fat dairy foods is not associated with increased risk of obesity in children or adults in observational studies and no long-term RCTs of full-fat dairy consumption and body-weight change or incident overweight/obesity are available. Although epidemiological evidence does not support a relation between higher dietary fat intake and greater risk of obesity, theoretical concerns about the effect of full-fat dairy consumption on body-weight regulation remain. Animal studies show that higher fat intake is associated with increased weight gain and obesity (91–93). Energy density, which is associated with higher 24-h energy intake and weight gain (92), is higher for full-fat dairy foods. However, Americans currently consume less than the recommended 3 servings of dairy foods/d (8) and a recommendation of 3 servings of dairy without qualification to low-fat and fat-free versions might lead to increased total dairy consumption (94). An important, yet currently limited, area of research is the assessment of the interpretation and implementation of dietary recommendations by the general population. Such data could further inform how the specific language used in recommendations for dairy intake may impact dairy food consumption at the population level.

The role of low-fat versus full-fat dairy in personalized nutrition

The health status of the US adult population must be taken into consideration when formulating dietary guidelines intended for the general population. According to the latest CDC reports, 71.6% of US adults are overweight or obese (95) and an estimated 33.9% of US adults aged ≥18 y and 48.3% of adults aged ≥65 y are affected by prediabetes (2). On the other hand, research shows that there is a measurable preference for both lower-fat and full-fat dairy foods among individuals (96–98) and taste preferences, in addition to other factors such as health concerns, influence food choices (99–101).

Considering the complete dairy food matrix, it is clear that dairy foods of any fat content represent a more nutritionally complete choice than empty-calorie foods such as sugar-sweetened beverages and some packaged snack foods. Therefore, it is important to establish where nutrient-rich full- and reduced-fat dairy foods such as milk, yogurt, and cheese best fit in the context of overall healthy eating patterns. Individuals with elevated LDL cholesterol, particularly those with ASCVD, are recommended to consume a diet low in SFAs and dietary cholesterol (102), and thus, while the data do not clearly support an adverse effect of full-fat dairy foods on lipoprotein lipids, it may be reasonable to recommend low-fat and nonfat dairy foods for such individuals. This raises the question of whether national dietary guidelines can be compatible with the trend toward personalized nutrition and suggests that careful review and interpretation of the available evidence, with attention to the characteristics of the populations under study, is critical for developing accurate dietary recommendations.

Weight-loss responsiveness according to glycemic status

Weight-loss diets produce variable outcomes, ranging from major weight loss to almost no loss. Efforts to identify responders based on pretreatment biomarkers such as initial BMI, age, gender, or hormones have explained only a small percentage of the variability. However, novel insights suggest an interaction between diet composition and the individual

obese patient's glucose metabolism. The prescription of personalized diets may therefore offer much greater weight-loss success for individuals than the previous "one diet fits all" concept.

Recent evidence shows that the acute satiating effect of carbohydrates depends on glucose uptake in insulin-dependent tissue (brain, muscle, and liver) (103), whereas the satiating effect of fat and protein depends more on the release of gastrointestinal hormones with neurohumoral signaling to the brain (104). There is evidence that the "gluco-static concept" is an important regulator of satiation and determinant of spontaneous energy intake during meals. With increasing insulin resistance and failure to compensate with enhanced postprandial insulin secretion, the satiating effects of carbohydrates are attenuated due to reduced glucose uptake in the brain, and possibly in other tissues. Consequently, the satiating effect of carbohydrate is weakened in obese individuals with T2D or prediabetes with low insulin secretion.

Analyses of a number of both European and US RCTs suggest that low-fat, carbohydrate-rich diets may thus be more effective in normoglycemic obese individuals, whereas individuals with T2D lose more weight with carbohydrate-restricted diets rich in protein and fat (105). For example, a randomized energy-restricted diet comparison of a low-fat, high-carbohydrate versus a low-carbohydrate, higher-fat diet [Nutrient–Gene Interactions in Human Obesity (NUGENOB) trial]), found no difference in weight loss (7.5 kg in both arms). In a reanalysis, subjects with T2D lost 2.0 kg more with the low-carbohydrate, higher-fat diet than with the low-fat, high-carbohydrate diet, whereas normoglycemic individuals lost a mean of 0.4 kg more with the low-fat, high-carbohydrate diet (group difference: 2.5 kg) (105). The finding that fasting glucose (and insulin) can be used to personalize the optimal diet has been supported in reanalyses of a number of previously published RCTs (80, 103, 105–109), and we are now further awaiting results from large prospective RCTs. Such trials aim to elucidate the role of low-fat versus full-fat dairy in the optimal diets for different metabolic phenotypes.

Conclusions

In summary, the totality of evidence from meta-analyses of both observational studies and RCTs does not suggest harmful effects of full-fat dairy consumption on cardiometabolic disease outcomes and associated risk factors. Results from meta-analyses and prospective observational studies suggest that fermented dairy foods, such as full-fat yogurt and cheese, may be protective against CVD and T2D. Further, in RCTs, yogurt and cheese consumption generally does not exert detrimental effects on blood lipids and blood pressure as would be predicted by the sodium and saturated fat contents, which may be related to effects of the food matrices of these products. Thus, the current state of the evidence, although incomplete, lacks compelling support for the recommendation to consume only low-fat and fat-free dairy and avoid full- and reduced-fat dairy foods to support cardiometabolic health. Unlike foods with low nutrient density that may be selected for taste or convenience, dairy foods are nutrient rich and provide several nutrients of concern in the US diet, including calcium, vitamin D, and potassium.

The current evidence base is also limited by heterogeneity in results and the reliance on observational studies for all evidence regarding disease incidence endpoints, as residual confounding cannot be ruled out with this type of research. Additional experimental and observational studies are needed to establish a comprehensive understanding of the effect of full-fat dairy food consumption on cardiometabolic health. Future studies should focus on whole-dairy foods (milk, yogurt, and cheese) in the context of dietary patterns and consider metabolic phenotype, meal composition, and energy balance. A uniform definition of what constitutes high- and low-fat dairy should also be established for use in studies when dairy foods are grouped into categories by fat content. Studies to elucidate potential mechanisms linking full-fat dairy intake to indices of cardiometabolic health are also needed. There is a particular need for long-term RCTs of full-fat dairy consumption and body-weight change. Despite these caveats, the current evidence supports the view that the full-fat dairy foods milk, yogurt, and cheese are nutrient rich and may be consumed without producing adverse effects on the cardiometabolic risk marker profile.

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