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# Dairy Consumption and Metabolic Health

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**Abstract:** Milk and dairy foods are naturally rich sources of a wide range of nutrients, and when consumed according to recommended intakes contribute essential nutrients across all stages of the life cycle. Since then, seminal studies recommendations with respect to intake of saturated fat have been consistent and clear; limit total fat intake to 30% or less total dietary energy, with a specific recommendation for intake of saturated fat to less than 10% of total dietary energy. However, recent work has re-opened the debate on intake of saturated fat in particular, with suggestions that recommended intakes be considered not at a total fat intake within the diet, but at a food specific level. A large body of evidence exists examining the impact of dairy consumption on markers of metabolic health, both at a total dairy intake and also at a food level, with mixed findings to date, but suggests that the impact of saturated fat intake on health differs both across food groups and even between foods within the same food group such as dairy.

Milk and dairy foods contain a range of nutrients and bioactive components in different levels, housed within very different food structures. The interaction of the overall food structure and the nutrients describes the concept of the 'food matrix effect' which has been well documented for dairy foods. Studies show that nutrients from different dairy food sources can have different effects on health and for this reason, they should be considered individually rather than grouped as a single food category in epidemiological research. This review examines the current evidence from randomised controlled trials and meta-analyses, with respect to dairy, milk, yoghurt and cheese on aspects of metabolic health, and summarises some of the potential mechanisms for these findings.

**Keywords:** Dairy, Health, Matrix, Metabolism, Nutrient, Composition, Saturated Fats

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## 1. Importance of dairy in a balanced diet

Milk and dairy foods are naturally rich sources of a wide range of nutrients such as proteins, fats, oligosaccharides and micronutrients including vitamins A, D, E and K and Ca, Mg, P and Zn [1], Figure 1. Milk proteins are of high biological value, not only because they contain essential amino acids but also because of their high digestibility and bioavailability. Approximately 82% of milk protein is casein and the remaining 18% is serum, or whey protein for cow's milk [2]. Fat, mainly in the form of triacylglycerols (98%), is present in milk as globules which are surrounded by a membrane (or milk fat globule membrane (MFGM)). This component of milk fat has been suggested to elicit favourable lipid and low-density lipoprotein (LDL) cholesterol response to dairy consumption [3], and will be discussed later. With respect to micronutrients, milk is considered a major source of calcium in the diet [4]. As well as being a rich source of this nutrient, the bioavailability of calcium from dairy sources has also been shown to be higher compared to other dietary sources [5,6]. Considering the rich nutritional composition and bioavailability of nutrients in dairy products, it is not surprising that modelling of dietary intake data has indicated that without consuming dairy products in the diet, less than half of the calcium requirements would be met [7],

for example. Another study noted that nutrients from dairy foods are difficult to replace and modelled removal and replacement with available alternatives resulted in lower amounts of several nutrients including protein, phosphorus, riboflavin, zinc and vitamin B12 [8].

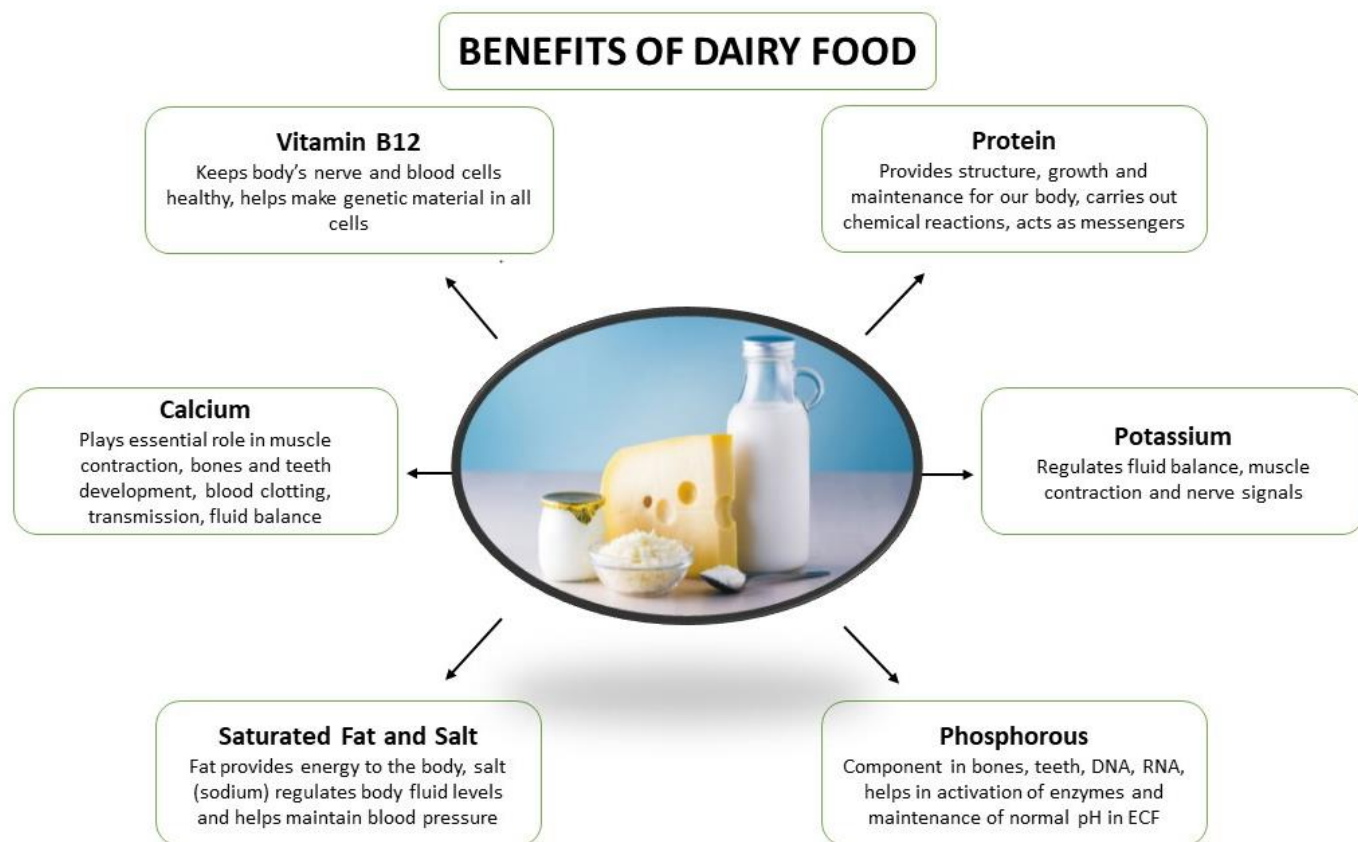


Figure 1 – Nutrient content and associated health benefits of dairy consumption

When consumed according to recommended intakes of national guidelines, milk and dairy products contribute essential nutrients across all stages of the life cycle [1]. For example, milk and dairy products are an important part of a young child's diet as they are a good source of energy and protein, and contain a wide range of vitamins and minerals, especially calcium, that young children need for healthy bones and teeth [9]. In Europe, it is reported that milk contributes proportionally more to the diets of young children than to adults [10]. Data from cross-sectional studies [11] and intervention studies [8,12] have reported the positive effect of milk consumption in childhood and adolescence on bone mineral content and bone mineral density. In addition, some research studies have indicated that the consumption of milk and milk product during adolescence is associated with neutral or reduced risk of adiposity [13,14]. During pregnancy, dairy products can be an important means of providing adequate calcium and other key nutrients in the diet [15]. Evidence from prospective cohort studies suggests that moderate milk consumption compared to none or low intakes during pregnancy, is positively associated with fetal growth and infant birth weight in healthy, Western populations [15]. Finally, several studies point to the benefits of milk and dairy products in diets of the elderly, and highlight that in combination with physical activity, can improve muscle mass and function resulting in a lower risk of sarcopenia and vertebral fractures [5,16].

Current consumption patterns of dairy are in a period of considerable change, with reported decreases in dairy consumption in countries who had traditionally consumed large quantities, potentially due to increased intake of 'dairy-free' alternative products [17] and reported increases in some global regions, where dairy was not commonly consumed [18]. These changes are reported to

be due to several factors, but are predominantly driven by consumer perception of the health effects of dairy consumption, and the environmental impact of dairy production [19]. A particular nutrient of concern, when considering intake of dairy, is fat, principally saturated fat. Whilst dairy has been shown to contribute beneficially to the diet, dairy foods also contribute significantly to saturated fat intakes. For example, in the 2011–2014 National Health and Nutrition Examination Survey (NHANES), dairy foods contributed 26% of saturated fat and 14.2% of total fat to the diets of US adults [20,21]. Similarly, Feeney *et al.*, found that within the Irish diet, dairy foods contributed 12.8% of total fat to the diet, and 19.8% of the saturated fat [22]. For this reason, many healthy eating guidelines recommend 3-5 portions of dairy daily, with consumption of “low/reduced-fat dairy” when possible [23,24]. However, research investigating the importance of the food source of saturated fatty acids (SFA) suggests that although SFAs from meat and processed-meat are associated with detrimental health effects [25], SFA intake from dairy sources may be associated with either neutral [26] or beneficial effects on health [27,28]. Much work in this area is underway, which is summarised below.

## 2. Dairy fat and health - changing perspectives

Since the seminal Seven Countries Study and other subsequent studies [29, 30], recommendations with respect to intake of saturated fat have been consistent and clear; limit total fat intake to 30% or less total dietary energy, with a specific recommendation for intake of saturated fat to less than 10% of total dietary energy [31-33]. However, recent work, particularly by DeSouza re-opened the debate on intake of saturated fat in particular [34]. In a large review and meta-analysis, de Souza *et al.*, examined associations between intake of total fat, saturated fat and trans unsaturated fat with all-cause mortality and differing morbidities. The authors concluded that, contrary to previous evidence, saturated fat intake was not associated with all-cause mortality, CVD mortality, total CHD, ischemic stroke or type 2 diabetes [34]. Drouin-Chartier *et al.* in 2016 also examined the impact of dairy consumption and dairy fat on cardiometabolic disease risk factors, and also reported that 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 [35]. Similarly, Alexander *et al.*, (2016) completed a meta-analysis of prospective studies and the intake of dairy products and CVD risk. These authors more cautiously concluded that although for some individual dairy products the risk estimates below 1.0 were observed, additional data are needed to more comprehensively examine potential dose–response patterns [36].

Dehghan *et al.*, (2018) specifically examined the associations between total dairy and specific types of dairy products with mortality and major cardiovascular disease. Dietary intakes of dairy products for 136,384 individuals were recorded using country-specific validated food frequency questionnaires and associations with mortality or major cardiovascular events were examined [37]. The authors reported that a higher intake of total dairy (>2 servings per day compared with no intake) was associated with a lower risk of the composite of mortality or major cardiovascular events, total mortality non-cardiovascular mortality, cardiovascular mortality, major cardiovascular disease, and stroke. No significant association with myocardial infarction was observed. Higher intake (>1 serving vs no intake) of milk and yogurt was associated with lower risk of the composite outcome, whereas cheese intake was not. Butter intake was low and was not significantly associated with clinical outcomes. The authors concluded that dairy consumption was associated with lower risk of mortality and major cardiovascular disease events in a diverse multinational cohort [37].

More recently Cavero-Redondo *et al.*, (2019) also examined the association between dairy product consumption and all-cause mortality risk, and concluded that dairy product consumption was not

associated with risk of all-cause mortality, but also concluded that there was no reduction in risk, with relative risks reported ranging from 0.96 to 1.01 per 200 g/d of dairy product consumption (including total, high-fat, low-fat, and fermented dairy products), from 0.99 to 1.01 per 200–244 g/d of milk consumption, and from 0.99 to 1.03 per 10–50 g/d of cheese consumption [38]. Finally, also in 2019, Fontecha and colleagues [39] specifically examined evidence regarding the influence of dairy product consumption on the risk of major cardiovascular-related outcomes and how various doses of different dairy products affected such responses. In this overview of 12 meta-analyses involving RCTs as well as the updated meta-analyses of RCTs, increasing consumption of dairy products did not result in significant changes of known risk biomarkers such as systolic and diastolic blood pressure and total cholesterol and LDL cholesterol. They concluded that consumption of total dairy products (either regular or low fat content), did not adversely affect the risk of CVD [39].

Despite these more recent findings, the most recent review of published literature by the UK Scientific Advisory Committee on Nutrition (SACN), concluded that there is a significant body of evidence demonstrating a relationship between intake of saturated fats and CVD and CHD events, but not CVD and CHD mortality [40] and noted that, irrespective of the lack of evidence for an effect on mortality, non-fatal CVD and CHD events have a serious adverse impact on health and quality of life, and that existing public health recommendations for saturated fat to be <10% total energy dietary energy intake were still valid [40]. This mirrors recommendations in other countries and regions of the world [31-33]. However, some criticisms on the continued support for such recommendations note that such policies are based on evidence from total dietary saturated fat intake, and may have not considered the source of fat, whereby the food source, or matrix may in fact have a differing influence on metabolism and subsequently, health [41,42]. In addition, different food sources contain different types and amounts of SFA, and the continued promotion of an overall <10% total dietary energy recommendation may be perceived to overlook this [41,42]. Further, by focusing on SFA content alone, foods that are nutrient dense but also high in SFA may be excluded from the diet and inadvertently result in a reduced intake of important micronutrients [42]. For this reason, many are advocating for food-based guidelines rather than nutrient-based advice. As such, evidence may need to be considered at a food item level within the dairy food group, rather than together. In light of a reported shift in recent dairy consumption [43], where instances of decreased dairy consumption may be potentially explained by an increase in dairy free alternatives due to the perceived impact of dairy on health [17], it is important to consider some of the recent evidence at both a total dairy level and for individual dairy products cheese, milk and yogurt, and the further discuss potential mechanisms influencing the metabolic response to consumption.

Considering total dairy consumption initially, characteristics of fifteen published RCTs that studied the effects of overall dairy consumption on markers of metabolic health and CVD risk on variable age groups are included in Table 1. RCTs included in the table were either parallel or crossover trials and the participant's age ranged from 20-75 years. Duration of interventions varied widely from 4-8 weeks in some to 12-24 weeks in the others, with a washout period included in some of the trials. Most of the interventions were based on consumption of different dairy products such as milk, cheese or butter. Zemel *et al.*, (2010) compared the effects of consumption of soy-based smoothie to a dairy-based smoothie and observed suppressed inflammatory and stress markers for the latter [44]. Groups that consumed low-fat or non-fat dairy diet showed decreased levels of TC and LDL cholesterol as compared to the diet containing conventional levels of fat. Most recently, Vasilopoulou *et al.*, (2020) examined the impact of modified dairy fat consumption, through the provision of products with modified MUFA content in adults at moderate CVD risk – the RESET study. The authors concluded that consumption of a high-fat diet containing modified dairy products with reduced saturated fatty acids, and enriched mono unsaturated fatty acids showed beneficial effects on fasting LDL cholesterol and endothelial function compared with conventional dairy products [45]. Finally, although not an



intervention study, Drouin-Chartier (2019), recently examined dairy intake and risk of diabetes, and reported positive impacts for yoghurt and reduced fat milk, but a negative association for cheese [46].

Focusing specifically on cheese, several published randomised controlled trials (RCT) have demonstrated a beneficial effect of cheese consumption on markers of metabolic health and CVD risk, summarised in Table 1 [27,47-53]. Brassard *et al.*, (2017) compared the impact of consuming equal amounts of SFAs from cheese and butter on cardiometabolic risk factors [53]. In this multicentre, crossover, randomized controlled trial, participants were assigned to a randomised sequence of 5 isoenergetic diets of 4-week duration (separated by 4-week washout periods). The diets were rich in SFAs from either cheese or butter, or a monounsaturated fatty acid (MUFA)-rich diet, a polyunsaturated fatty acid (PUFA)-rich diet and a low-fat, high-carbohydrate diet. The authors reported that serum HDL-cholesterol concentrations were similar after the cheese and butter diets but were significantly higher in comparison to response after the carbohydrate diet. Comparing cheese and butter, LDL-cholesterol concentrations after the cheese diet were lower than after the butter diet but were higher than after all of the other diets. Some variation in response was noted. Research conducted within UCD previously has both supported and added to the existing evidence. A 6-wk randomized parallel intervention involving 164 volunteers who received ~40 g of dairy fat/d, in 1 of 4 treatments: 120 g full fat Irish cheddar cheese (group A), 120g reduced fat Irish cheddar cheese + butter (21 g) (group B); butter (49 g), calcium caseinate powder (30 g), and Ca supplement (CaCO<sub>3</sub>) (500 mg) (group C) or 120 g full fat Irish cheddar cheese, for 6 weeks following completion of a 6-wk "run-in" period, where this group excluded all dietary cheese before commencing the intervention (group D). This study found that a stepwise-matrix effect was observed between the groups for total cholesterol (TC) ( $P = 0.033$ ) and LDL cholesterol ( $P = 0.026$ ), with significantly lower post-intervention TC and LDL cholesterol when all of the fat was contained within the cheese matrix (Group A), compared with Group C when it was not. These findings suggest that dairy fat, when eaten in the form of cheese, appears to differently affect blood lipids compared with the same constituents eaten in different matrices, with significantly lower total cholesterol observed when all nutrients are consumed within a cheese matrix. However, there is a need to further understand this research in the context of both public health and industry needs [54]. Other groups have also looked at post-prandial response to cheese consumption, as the post prandial response to lipid consumption is considered an independent indicator of CVD risk [55]. Hansson *et al.*, 2019 examining post-prandial response to sour cream, whipped cream, cheese and butter, noted that sour cream resulted in a larger post prandial triacylglycerol (TAG) area under the curve (AUC), compared to whipped cream, butter and cheese ( $P = 0.05$ ). Intake of sour cream also induced a larger HDL cholesterol AUC compared to cheese. Intake of cheese induced a 124% larger insulin AUC compared to butter. Hansson *et al.*, concluded that high-fat meals containing similar amount of fat from different dairy products induce different postprandial effects on serum TAGs, HDL cholesterol, and insulin in healthy adults [56]. Drouin-Chartier (2017) reported minor differences in post circulating TAG concentrations, in a post prandial RCT where participants ingested 33 g fat from a firm cheese (young cheddar), a soft cream cheese (cream cheese), or butter (control) incorporated into standardized macronutrient matched meals. They conclude that the study demonstrates that the cheese matrix modulates the impact of dairy fat on postprandial lipemia in healthy subjects [55].

Characteristics of seven recently published RCTs that studied the effects of milk consumption on markers of metabolic health and CVD risk are described in Table 2. RCTs included in the table were either parallel or crossover trials and the participant's age ranged from 20-85 years. Duration of interventions ranged from 4-16 weeks with a washout period included in some of the studies. Gardner *et al.*, (2007) compared the effects of soy-based drinks to dairy milk consumption on metabolic health markers, and found that LDL was significantly lower after consuming soy milk compared to dairy

milk, but no significant differences between groups were observed for HDL, triacylglycerols, insulin, or glucose [56]. In 2016, Lee *et al.*, examined the impact of increased milk consumption (400ml per day) compared to normal intake on markers of metabolic health, and found no significant differences in body mass index, blood pressure or lipid profile. Hidaka *et al.*, compared intakes of full fat versus non-fat milk intakes and showed lower plasma triglyceride and phospholipid levels in the no fat group [57].

Table 3 presents a summary of RCTs that specifically studied the effects of yogurt consumption on markers of metabolic health and CVD risk. Most of these studies focused specifically on the microbial content of yogurts, where consumption of probiotic yogurt or modified-bacterial-strain containing yogurts or comparisons between commonly available varieties of yogurts such as non-fat yogurt, natural yogurt and heated yogurt were examined. In general, when compared to participants on a controlled diet (diet with zero consumption of fermented products), the participants who consumed probiotic or conventional yogurt showed significant decrease in TC and LDL cholesterol.

Table 1. Randomised controlled trials (RCT) demonstrating an effect of overall dairy consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
Vasilopoulou <i>et al.</i> , 2020 [45]	UK	Crossover	n= 54 (31 male; 23 female), with risk of CVD	25 – 70	2 arm: <b>A)</b> MUFA-modified dairy- 340g UHT milk, 45g Cheese 25.1g butter. <b>B)</b> Control- 340g UHT milk, 45g Cheese 25.1g butter.	Two 12 week periods separated by an 8 week washout period	No significant change from baseline in serum TC between diets. Group <b>A</b> had a significant beneficial effect in terms of attenuation of the rise of the LDL. No changes in HDL between diets. The LDL:HDL ratio decreased significantly after <b>group A</b> , and increased after the control. No significant differences were observed for indexes of insulin sensitivity/resistance. Fasting plasma nitrite concentrations increased after the modified diet, yet decreased after the control.
Markey <i>et al.</i> , 2017 [58]	UK	Crossover	n= 54 (31 male; 23 female), with risk of CVD	25 – 70	2 arm: <b>A)</b> MUFA-modified dairy- 340g UHT milk, 45g Cheese 25.1g butter. <b>B)</b> Control- 340g UHT milk, 45g Cheese 25.1g butter.	Two 12 week periods, separated by an 8 week washout period	Group <b>A</b> showed a smaller increase in SFA and greater increase in MUFA intake when compared with the control.
Rosqvist <i>et al.</i> , 2015 [3]	Sweden	Parallel	n= 57 (gender split not stated), overweight or obese	20 – 70	2 arm: <b>A)</b> milk-fat globule membrane (MFGM) group- 100mL whipping cream (40%fat)/d, 100mL fat-free milk (0.1% fat)/d, and 1 scone/d (baked with wheat flour, water, sodium chloride, and baking powder). <b>B)</b> 100mL fat-free milk (0.1% fat)/d and 1 scone/d	8 weeks	Control diet increased TC, LDL, apolipoprotein B:apolipoprotein A-I ratio and non-HDL plasma lipids, whereas the MFGM diet did not. HDL, triglyceride, sitosterol, lathosterol, campesterol, and proprotein convertase subtilisin/kexin type 9 concentrations and fatty acid compositions did not differ between groups.

					(baked with wheat flour, water, butter oil (98.7% fat), sodium chloride, baking powder, and milk protein isolate).		
<b>Benatar et al., 2013 [59]</b>	New Zealand	Parallel	n= 180 (54 male; 126 female), healthy volunteers	>18	2 arm: <b>A)</b> Increased dairy- an extra two to three servings per day, and to change to high-fat milk and dairy solids. <b>B)</b> Habitual dairy intake remains unchanged <b>C)</b> Decreased dairy were asked to eliminate all possible sources of dairy.	1 month	No significant change in LDL or HDL, triglycerides, systolic or diastolic BP, C-reactive protein, glucose or insulin across groups. There was a small increase in weight in group <b>A</b> .
<b>Nestel et al., 2013 [60]</b>	Australia	Crossover	n= 12 (gender not specified) overweight or obese	40 – 70	3 arm: <b>A)</b> Low-fat dairy, 1% fat milk (400ml/d) and, 1% fat yogurt (200g/d). <b>B)</b> Full fat dairy (fermented), cheddar cheese (85g/d) and full-cream yogurt (three servings, 600g/d). <b>C)</b> Full fat dairy (non-fermented), butter (30g/d) and cream (70ml/d) and small amounts of ice-cream.	Two 3-week periods, for group <b>B + C</b> . Group <b>A</b> was consumed twice, between and at the end of the full-fat dairy dietary periods, for a duration of 2 weeks.	Lowest LDL and HDL concentrations were observed in group <b>A</b> , but plasma TAG concentrations did not differ significantly across the groups. Concentrations of plasma sphingomyelin and IL-6 were significantly higher after the non-fermented dairy diet (group <b>C</b> ) than the low-fat dairy diet
<b>Crichton et al., 2012 [61]</b>	Australia	Crossover	n= 61 (18 male; 43 female), overweight or obese	18 – 75	2 arm: <b>A)</b> 4 servings of reduced fat dairy/d, 1 serving = 250mL milk, 175-200g yogurt, and 190g custard. <b>B)</b> control- 1 serving of dairy/d, reflecting habitual intake.	Two 6 month periods, no washout period	No significant changes in resting metabolic rate or total energy expenditure, systolic and diastolic BP, fasting blood glucose, TC, HDL or LDL, triglycerides or <i>hs</i> -CRP. Also no differences between groups for WC, body weight and fat mass.



<b>Palacios et al., 2011 [62]</b>	Puerto Rico	Parallel	n= 25 (5 male; 20 female), obese	22 – 50	3 arm: <b>A</b> ) 4 servings of dairy/d (low-fat milk, low-fat cheese, and low-fat yogurt), with a dairy calcium intake goal of 1200–1300 mg/d. <b>B</b> ) calcium supplement (600 mg/d, calcium carbonate). <b>C</b> ) control- habitual diet with placebo tablet.	21 weeks	No significant group effects were observed for anthropometric measurements or serum lipids such as TC, HDL, LDL and TAG levels. Although TAG levels decreased by 18% in group <b>A</b> (high dairy).
<b>Stancliffe et al., 2011 [63]</b>	USA	Parallel	n= 40 (19 male; 21 female), overweight or obese with metabolic syndrome	37.0 ± 9.9	2 arm: <b>A</b> ) low-dairy diet- 0.5 servings/d and provided with a 3 servings/d of non-dairy foods i.e. low sodium luncheon meats, soy-based luncheon meat substitutes, packaged fruit cups, granola bars, and peanut butter crackers <b>B</b> ) adequate dairy diet- 3.5 servings/d, of which 2/3 servings were milk and/or yogurt.	12 weeks	Group <b>A</b> decreased malondialdehyde and oxidized LDL. Inflammatory markers were suppressed with intake of AD, with decreases in TNF- $\alpha$ ; decreases in IL-6 and monocyte chemoattractant protein 1 and an increase in adiponectin. Group <b>B</b> exerted no effect on oxidative or inflammatory markers. Group <b>A</b> significantly reduced waist circumference and trunk fat but group <b>B</b> exerted no effects.
<b>van Meijl and Mensink, 2010 [64]</b>	Netherlands	Crossover	n= 35 (10 male; 25 female), overweight or obese	18 – 70	2 arm: <b>A</b> ) 500ml low-fat milk and 150g low-fat yogurt per day <b>B</b> ) control- 600ml fruit juice and 43g fruit biscuits per day	Two 8 week periods separated by a 2 week washout period	Plasma concentrations of TNF- $\alpha$ decreased, and soluble TNF- $\alpha$ receptor-1 increased after low-fat dairy consumption compared to the control. s-TNFR-2 also increased. Low-fat dairy consumption had no effect on IL-6, monocyte chemoattractant protein-1, intracellular adhesion molecule-1 and vascular cell adhesion molecule-1 concentrations. Lipid profiles were not analysed.

<b>Zemel et al., 2010 [44]</b>	USA	Crossover	n= 20 (14 male; 6 female), overweight or obese	31.0 ± 10.3	2 arm: <b>A)</b> Dairy smoothie, 3 times/d, with non-fat dry milk as the protein source, and contained 350mg calcium per smoothie <b>B)</b> Soy smoothie, 3 times/d, with soy protein isolate as the protein source and 50 mg calcium per smoothie.	Two 4 week periods separated by a 4 week washout period	Group <b>A</b> resulted in significant suppression of oxidative stress and lower inflammatory markers; tumor necrosis factor- $\alpha$ ; IL-6; monocyte chemoattractant protein-1 and increased adiponectin. Group <b>B</b> exerted no significant effects. Lipid profiles were not analysed.
<b>Wennergren et al., 2009 [65]</b>	Norway	Parallel	n= 121 (41 male; 80 female)	30 – 65	2 arm: <b>A)</b> Milk group, 3–5 portions of dairy/d. Portion= 200 g milk, 200–250g yogurt or sour milk, 75g cream or crème fraiche, 15–40g cheese, 3–10g butter or butter containing spreads, 50 mL cottage cheese, and ice cream occasionally. <b>B)</b> Control- habitual daily diet.	6 months	No significant differences between changes in body weight or body composition, BP, markers of inflammation, endothelial function, adiponectin, or oxidative stress in group <b>A</b> and <b>B</b> . There was a modest unfavourable increase in serum TC concentrations in the group <b>A</b> .
<b>van Meijl and Mensink, 2009</b>	Netherlands	Crossover	n= 35 (10 males; 25 females), overweight or obese	18 – 70	2 arm: <b>A)</b> 500ml low-fat milk and 150g low-fat yogurt per day <b>B)</b> control- 600ml fruit juice and 43g fruit biscuits per day	Two 8 week periods separated by a 2 week washout period	In group <b>A</b> , systolic BP significantly decreased compared with the control, but diastolic BP did not reach significance. Decreases in HDL and apo A-1 concentrations were also observed in group <b>A</b> . Serum TC, LDL, apo B, TAG, non-esterified fatty acids, glucose, insulin, C-reactive protein and plasminogen activator inhibitor-1 remained unchanged.
<b>Tricon et al., 2006 [66]</b>	UK	Crossover	n= 32 males, healthy volunteers	34 – 60	2 arm: <b>A)</b> 500mL UHT full-fat milk, 12.5g butter, and 36.3 g cheese per day, naturally enriched with CLA. <b>B)</b> Control, 500mL UHT full-fat milk, 12.5g	two 6 week periods, separated by 7 week washout period	Diet <b>A</b> did not significantly affect body weight, inflammatory markers, insulin, glucose, TAG, or TC, LDL, and HDL cholesterol but resulted in a small increase in the LDL:HDL ratio. The modified dairy

					butter, and 28g cheese per day.		products changed LDL fatty acid composition but had no significant effect on LDL particle size or the susceptibility of LDL to oxidation.
<b>Zemel et al., 2005 [67]</b>	America	Parallel	<b>Study 1.</b> n= 34 (11 male; 23 female), <b>Study 2.</b> n= 29 (4 male; 25 female), obese	26 – 55	<b>Study 1. A)</b> Dairy group-3 servings of dairy/d, at least one serving to be milk <b>B)</b> control- low dairy, 0-1 servings of low-fat dairy/d. <b>Study 2. A)</b> Dairy group- 3 servings of dairy/d, at least one serving to be milk and a 500-kcal/d deficit <b>B)</b> control- low dairy, 0-1 servings of low-fat dairy/d and 500kcal/d deficit diet.	24 weeks (both studies)	<b>Study 1.</b> Body weight remained stable for both groups. Group <b>A</b> resulted in decreases in total body fat, trunk fat, insulin, and BP and an increase in lean mass and no significant changes in the control group. <b>Study 2.</b> Both diets produced significant weight and fat loss. Weight and fat loss within group <b>A</b> were 2-fold higher, and loss of lean body mass significantly reduced compared with the control. There were no effects on circulating lipids in either group.
<b>Tholstrup et al., 2004 [48]</b>	Denmark	Crossover	n= 14 males, healthy volunteers	20 – 31	3 arms: <b>A)</b> 1.5L of whole milk/10 MJ (54 g of fat and 1779 mg calcium per 10 MJ). <b>B)</b> 64 g of butter/10 MJ (54 g of fat and 10 mg calcium per 10 MJ) <b>C)</b> 205 g of hard cheese, “Samsø”, 45% fat of dry weight, i.e. 26% fat/10 MJ (1989 mg calcium/10 MJ).	Three 3 week periods separated by a 4 week washout period	Fasting LDL concentrations were significantly higher after butter than cheese diet, with a borderline significant difference in TC after the experimental periods. Postprandial glucose showed a higher response after cheese diet compared to milk diet. No differences were found between groups for HDL, VLDL, apo A-1 and apo B concentrations.

**Table 2.** Randomised controlled trials (RCT) demonstrating an effect of cheese consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
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**Table 2.** Randomised controlled trials (RCT) demonstrating an effect of cheese consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
Feeney <i>et al.</i> , 2018 [27]	Ireland	Parallel	n= 164 (75 male; 89 female), BMI >25kg/m <sup>2</sup>	> 50	4 arm: <b>A)</b> 120g full-fat cheddar cheese (FFCC). <b>B)</b> 120g reduced-fat Irish cheddar cheese + butter (21g) (RFC+B). <b>C)</b> Butter (49 g), calcium caseinate powder (30 g), Ca supplement (BCC). <b>D)</b> 120 g full-fat Irish cheddar cheese (as per “a” but with 6 week run in period)	6 weeks	There was a significant difference in total cholesterol (TC) and LDL between groups. Group <b>A</b> had significantly lower TC and LDL compared with other groups. No differences were observed for HDL cholesterol, anthropometry, fasting glucose or insulin.
Limongi <i>et al.</i> , 2018 [68]	Italy	Crossover	n= 58 (16 male; 42 female), healthy volunteers	> 60	2 arm: <b>A)</b> 90 g/d of CLA enriched Pecorino cheese. <b>B)</b> Control, 90 g/d of Pecorino cheese	Two 2 month periods, separated by 1 month washout period	No significant differences found in relation to LDL between diet <b>A + B</b> . Participants consuming enriched cheese had a lower increase in glycaemia compared to control but did not display an increase in lipid levels.

**Table 2.** Randomised controlled trials (RCT) demonstrating an effect of cheese consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
Brassard <i>et al.</i> , 2017 [53]	Canada	Crossover	n= 92 (43 male; 49 female), abdominally obese	18 – 65	5 arm: <b>A)</b> 90g/2500kcal cheese (type not specified). <b>B)</b> 49g/2500kcal butter. <b>C)</b> MUFA rich diet <b>D)</b> PUFA rich diet. <b>E)</b> High CHO, low-fat diet. The SFA content was matched in diets <b>A + B</b> .	Five 4 week periods, separated by 4 week washout periods	No changes were evident in HDL after cheese consumption. LDL was lower in group <b>A</b> compared with group <b>B</b> , but higher than groups <b>C</b> , <b>D</b> and <b>E</b> . No significant differences were found in inflammation markers, blood pressure, and insulin-glucose homeostasis.
Raziani <i>et al.</i> , 2016 [69]	Denmark	Parallel	n= 139 (47 male; 92 female), risk of metabolic syndrome	18 – 70	3 arm: <b>A)</b> 40g equal parts regular-fat Danbo and cheddar cheese (REG), <b>B)</b> 40g reduced-fat Danbo and cheddar cheese (RED), <b>C)</b> noncheese, carbohydrate control (CHO40g/d)- 90g bread, 25g jam.	12 weeks	No differences were evident on lipid profile between groups. In addition, Insulin, glucose, and triacylglycerol concentrations as well as blood pressure and waist circumference did not differ.

**Table 2.** Randomised controlled trials (RCT) demonstrating an effect of cheese consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
Thorning <i>et al.</i> , 2015 [70]	Denmark	Crossover	n= 14 female, overweight, post-menopausal	45 – 68	3 arm: <b>A)</b> 96 – 120g of equal parts Dando and cheddar cheese per 8 – 10MJ diet. <b>B)</b> 164 g per 10-MJ diet of high fat meat <b>C)</b> non-dairy, low-fat control (CHO)- fruit (84 g), white bread, pasta and rice (58 g), marmalade (20g), ands cake, sweetened biscuits, and chocolate (13 g) per 10-MJ diet.	Three 2 week periods, separated by 2 week washout periods	Group <b>A</b> caused higher levels of circulating HDL levels and apo A-I concentrations, and a lower apoB:apo A-I ratio compared to group <b>C</b> . Faecal fat excretion was also higher in group <b>A</b> . TC and LDL was similar across all groups.
Nilsen <i>et al.</i> , 2015 [71]	Norway	Parallel	n= 153 (73 male; 80 female), normotensive and hypertensive	> 18	3 arm: <b>A)</b> 50g/d Gamalost. <b>B)</b> 80g/d Norvegia. <b>C)</b> Control- Limited intake of Gamalost and Norvegia.	8 weeks	There were no changes in MetS factors between the intervention groups and control. Significant reductions were noted for TC in those with MetS in group <b>B</b> . Those in group <b>A</b> with high TC also showed significant decreases compared with control.



**Table 2.** Randomised controlled trials (RCT) demonstrating an effect of cheese consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
Soerensen <i>et al.</i> , 2014 [72]	Denmark	Crossover	n= 15 males, healthy volunteers	18 – 50	3 arm: <b>A)</b> 500mg Ca/d- non-dairy control. <b>B)</b> 670mL semi-skimmed milk per 10 MJ. <b>C)</b> 120g semi hard cheese per 10 MJ (45 % fat).	Three 2 week periods, separated by 2 week washout period	Significantly lower increases in TC and LDL were found in the group <b>A + B</b> compared with control. Faecal fat excretion also increased group <b>A + B</b> compared with control. No changes were found in blood pressure, high-density lipoprotein cholesterol, triglycerides, and lipid ratios.
Hjerpsted <i>et al.</i> , 2011 [49]	Denmark	Crossover	n= 49 (28 male; 21 female), healthy volunteers	22 – 69	Test food amounts were dependent on participants' energy levels. 2 arm: <b>A)</b> 143g/d (based on medium energy level) hard cheese "Samsø" (27 g fat/100 g) <b>B)</b> 47g/d (based on medium energy level) salted butter.	Two 6 week periods, separated by 2 week washout period	Group <b>A</b> had significantly lower serum total, LDL, and HDL cholesterol, and increased glucose concentrations compared with group <b>B</b> . Faecal fat excretion did not differ between groups.

**Table 2.** Randomised controlled trials (RCT) demonstrating an effect of cheese consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
Intorre <i>et al.</i> , 2011 [73]	Italy	Crossover	n= 30 (11 male; 19 female), healthy volunteers	20 – 40	2 arm: <b>A</b> ) 150g of hard cheese per week (milk from cows fed a grass and maize silage based diet with 5% of linseed oil added). <b>B</b> ) Control, 150g of hard cheese per week (from normal cow milk)	Two 4 week periods, separated by 4 week washout	The blood lipid profile did not change after diet <b>A</b> . Although it led to higher levels of vitamin C and E and stearic acid in blood, while myristic acid and oxidized LDL concentrations were significantly lower.
Pintus <i>et al.</i> , 2013 [74]	Italy	Crossover	n= 42 (19 male; 23 female), mildly hypercholesterolaemic	30 – 60	2 arm: <b>A</b> ) Control, 90g/d sheep cheese <b>B</b> ) 90g/d sheep cheese, naturally enriched with CLA	Two 3 week periods, separated by 6 week washout	The findings confirmed an association between anandamide and adiposity. Diet <b>B</b> significantly increased the plasma levels of fatty acid hydrocyperoxidases and LDL decreased. However, no changes were detected in levels of inflammatory markers.

**Table 2.** Randomised controlled trials (RCT) demonstrating an effect of cheese consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
Sofi <i>et al.</i> , 2010 [75]	Italy	Crossover	n= 10 (4 male; 6 female) healthy volunteers	30 – 65	2 arm: <b>A</b> ) 200g/week (3 times a week) of pecorino cheese, naturally rich in CLA. <b>B</b> ) 200g/week (3 times a week) of placebo cheese- control	Two 10 week periods, separated by 10 week washout period	Consumption of cheese naturally rich in CLA determined a significant reduction in some inflammatory parameters as well as some haemorheological, appearing to cause favourable biochemical changes of atherosclerotic markers, albeit limited. No significant effects on lipid profile were evident.
Nestel <i>et al.</i> , 2005 [51]	Australia	Crossover	n= 19 (14 male; 5 female), overweight and mildly hypercholesterolaemic	56.3 ± 7.8	2 arm: <b>A</b> ) 120g/d mature cheddar (40g fat). <b>B</b> ) Similar amount of butter fat to group <b>A</b> , from pre-weighed portions of butter and one butter-rich muffin.	Two 4 week periods, separated by 2 week washout period	Lipid values did not differ significantly between the group <b>A</b> and run-in periods, but TC and LDL were significantly higher with group <b>B</b> . Group <b>B</b> (butter) also raised total and LDL cholesterol significantly. This was not evident for cheese.

**Table 2.** Randomised controlled trials (RCT) demonstrating an effect of cheese consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
Biong <i>et al.</i> , 2004 [76]	Norway	Crossover	n= 22 (9 male; 13 female), healthy volunteers	21–54	3 arm: <b>A</b> ) 150g/d (per 8MJ diet) Jarlsberg 'Swiss-type' cheese. <b>B</b> ) 52g/d (per 8MJ diet) butter + casein (as calcium caseinate). <b>C</b> ) 52g/d (per 8MJ diet) butter + egg-white.	Three 3 week periods, separated by 1 week washout periods	TC was significantly lower after diet <b>A</b> compared to diet <b>B</b> . While LDL was lower after diet <b>A</b> , this was not statistically significant. There were also no significant differences in HDL-cholesterol, triacylglycerols, apo A-I, apo B or lipoprotein (a), haemostatic variables and homocysteine between groups.
Karvonen <i>et al.</i> , 2002 [77]	Finland	Crossover	n= 31 (17male; 14 female), hyperlipidaemic	25 – 65	2 arm: <b>A</b> ) 65g/d low-fat rapeseed oil-based cheese (11g fat, of which 1g was SFA) <b>B</b> ) 65g/d hard cheese (15g fat, of which 10g was SFA).	Two 4 week periods, washout period not specified	Serum TC and LDL concentration was lower in group <b>A</b> , 2 and 4 weeks after use of rapeseed oil-based cheese compared to group <b>B</b> (control).

Table 3. Randomised controlled trials (RCT) demonstrating an effect of milk consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
Lee <i>et al.</i> , 2016 [57]	Korea	Parallel	n= 58 (29 male; 29 female), overweight and obese with metabolic syndrome	35 – 65	2 arm: <b>A)</b> 400mL per day (200mL twice daily) of low-fat milk. <b>B)</b> control- maintain habitual diet.	6 weeks	No significant differences in BMI, BP, lipid profile and adiponectin levels, as well as levels of inflammatory markers, oxidative stress markers and atherogenic markers were found between groups.
Hidaka <i>et al.</i> , 2012 [78]	Japan	Parallel	n= 14 (8 male; 6 female), healthy volunteers	28.6 ± 6.0	2 arm: <b>A)</b> 500mL/d whole milk <b>B)</b> 500mL/d non-fat milk.	4 weeks	Group <b>B</b> showed lowering of plasma triglyceride (TG), phospholipid levels, TG level in HDL and increased plasma apolipoprotein (apo) C-III level. TG/cholesterol ratios in HDL and LDL significantly also decreased in group <b>B</b> . Whole milk consumption showed increases in plasma levels of apoC-III and apoE. C.

<b>Rosado <i>et al.</i>, 2011 [79]</b>	Mexico	Parallel	n= 139 females, obese	25 – 45	3 arm: <b>A)</b> 250 mL of low-fat milk, 3 times per day, and an energy-restricted diet (500 kcal/day). <b>B)</b> 250 mL low-fat milk with added micronutrients, 3 times per day, an energy-restricted diet (500 kcal/day). <b>C)</b> control- an energy-restricted diet (500 kcal/day) with no intake of milk.	16 weeks	Group <b>B</b> lost significantly more weight compared with group <b>A</b> + <b>C</b> . BMI and body fat changes were also significantly greater in the group <b>B</b> compared with group <b>A</b> + <b>C</b> . No differences were found between groups in glucose level, blood lipid profile, C-reactive protein level, or blood pressure.
<b>Venkat ramana <i>n et al.</i>, 2010 [80]</b>	Canada	Crossover	n= 18 (11 male; 7 female) moderately overweight and borderline hyperlipidaemic	30 – 60	3 arm: <b>A)</b> 1000mL/d milk naturally enriched CLA. <b>B)</b> 1000mL/d milk enriched with synthetic CLA. <b>C)</b> control- 1000mL/d untreated milk 1000mL/d of milk.	Three 8 week periods separated by 4 week washout periods	Group <b>A</b> + <b>B</b> failed to alter plasma TC, LDL, HDL, or triacylglycerol concentrations; body weight; or fat composition compared with the control group. CLA consumption did not significantly affect plasma ALT, TBIL, CRP, or TNF-a concentrations.
<b>Faghih <i>et al.</i>, 2009 [81]</b>	Iran	Parallel	n= 100 females, premenopausal and overweight or obese	20 – 50	4 arm: <b>A)</b> control- 500 kcal/d deficit (500 - 600mg/d dietary calcium). <b>B)</b> Calcium supplemented diet identical to control diet (800 mg/d of calcium carbonate). <b>C)</b> 220 ml servings of low fat milk (1.5%) and 500 kcal/d deficit. <b>D)</b> 3 servings of calcium fortified soy milk and 500 kcal/d deficit.	8 weeks	Body weight, BMI, waist circumference (WC), waist-to-hip ratio (WHR), body fat mass and percent body fat decreased significantly across all groups. The changes in WC and WHR were significantly higher in groups <b>C</b> and <b>D</b> compared to controls. Reductions in weight and BMI were significantly greater in the group <b>C</b> compared



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to controls. Lipid profiles were not analysed.

<b>Gardner et al., 2007 [82]</b>	USA	Crossover	n= 28 (6 male; 22 female), hypercholesteraemic	30 – 65	3 arm: <b>3</b> 2oz/d whole soy bean drink <b>B</b> ) 28oz/d soy protein isolate drink <b>C</b> ) 18.5oz/d dairy milk. (all volumes were standardised to yield 25g protein/d.	Three 4 week periods, separated by 4 week washout periods	LDL was significantly lower after consuming soy milk in groups <b>A</b> + <b>B</b> compared to dairy milk (group <b>C</b> ). No significant differences between groups were observed for HDL, triacylglycerols, insulin, or glucose.
<b>Barr et al., 2000 [83]</b>	USA	Parallel	n= 200 (70 male; 130 female), healthy volunteers	55 – 85	2 arm: <b>A</b> ) three 8oz/d skimmed of 1% milk. <b>B</b> ) Maintain habitual diet and consuming <1.5 dairy servings per day.	12 weeks	Similar decreases in BP were apparent across both groups. TC, LDL and the ratio of TC:HDL remained unchanged. Triglyceride levels increased within the normal range in group <b>A</b> .

Table 4. Randomised controlled trials (RCT) demonstrating an effect of yogurt consumption on markers of metabolic health and CVD risk

Author	Country	Study Design	Population	Age (years)	Intervention	Duration	Main findings
<b>El Khoury et al., 2014 [84]</b>	Canada	Crossover	n= 20 males, BMI 20 – 24.9 kg/m <sup>2</sup>	20 – 30	5 arm: A) 250g non-fat yoghurt- plain. B) 250g non-fat yoghurt with honey-plain. C) 250g non-fat yoghurt strawberry flavoured. D) 250g skimmed milk. E) 250g Orange Juice.	Postprandial	Pre-meal glucose responses were dose-dependent to increasing protein and decreasing sugars in dairy. Protein:carbohydrate ratio correlated negatively with pre-meal glucose due to improved efficacy of insulin action. Compared with treatment E, blood glucose was lower after dairy snack treatments, contribution of dairy products to post-meal glucose was independent of their protein:carbohydrate ratio
<b>Shab-Bidar et al., 2011 [85]</b>	Iran	Parallel	n= 100 (43 male; 57 female), type 2 diabetes	29 – 67	2 arm: A) 250mL vitamin D3 fortified yoghurt drink, twice a day B) 250mL plain yoghurt fortified drink, twice a day.	12 weeks	Diet A showed significant improvement in fasting glucose, glycated haemoglobin (HbA1c), TAG, HDL cholesterol, endothelin-1, E-selectin and MMP-9 compared with the control (diet B).

<b>Sadrzadeh-Yeganeh et al., 2010 [86]</b>	Iran	Parallel	n= 90 females, healthy volunteers	19 – 49	3 arm: A) 300g/d probiotic yoghurt. B) 300g/d conventional yoghurt. C) Control, no consumption of fermented products	6 weeks	No significant difference in lipid profile within any group. No difference in TAG and LDL across the groups. There was a decrease in cholesterol in both group A + B compared with the control as well as a decrease in TC:HDL ratio. HDL increased in group A compared with the control.
<b>Ejtahed et al., 2010 [87]</b>	Iran	Parallel	n= 60 (23 male; 37 female), type 2 diabetes	30 – 60	2 arm: A) 300g/d probiotic yogurt. B) Control, 300g/d conventional yogurt	6 weeks	Diet A caused a decrease in TC and LDL compared with the control. No significant changes from baseline were shown in TAG and HDL in diet A. The TC:HDL ratio and LDL:HDL ratio as atherogenic indices significantly decreased in after diet A compared with the control.
<b>Ataie-Jafari et al., 2009 [88]</b>	Iran	Crossover	n=14 (4 male; 10 female), mild to moderate hypercholesteraemic	40 – 64	2 arm: A) 3 x 100 g/d probiotic yogurt, <i>Lactobacillus acidophilus</i> and <i>Bifidobacterium lactis</i> B) 3 x 100 g/day control yogurt. Both yogurts contain 2.5% fat.	two 6 week periods, separated by a 4 week washout period	Consumption of diet A caused a significant decrease in serum TC compared with the control. No differences were reported for remaining blood lipids examined between the two diets.

<b>Kiebling et al., 2002 [89]</b>	Germany	Crossover	n= 29 females, normo- and hypercholesterolaemic	19 – 56	2 arm: A) 300g/d control yogurt <i>streptococcus thermophilus</i> and <i>L. lactis</i> . B) 300g/d probiotic yoghurt enriched with <i>L. acidophilus</i> 145, <i>B. longum</i> 913 and 1% oligofructose.	6 weeks (all on control diet), followed by two 6 week periods, separated by 9 day washout periods.	Serum TC and LDL concentrations was not influenced by diet A. The HDL concentration increased significantly after diet A. The ratio of LDL:HDL cholesterol decreased. Long term consumption of 300g yoghurt increased HDL and lead to desired improvement of LDL:HDL ratio in both diets.
<b>Rizkalla et al., 2000 [90]</b>	France	Crossover	n= 24 males, healthy volunteers	20 – 60	2 arm: A) 500g/d fresh yoghurt w/ live bacterial cultures. B) 500g/d heated yoghurt	Two 15 day periods, separated by a 15 day washout period	No changes detected in fasting plasma glucose, insulin, fatty acid, TAG, or cholesterol concentrations in both groups. Plasma butyrate was higher and plasma propionate tended to be higher in subjects without lactose malabsorption after diet A than B. Subjects with lactose malabsorption increased propionate production after fresh yogurt consumption compared with baseline measures.

<b>Larson et al., 2000 [91]</b>	Denmark	Parallel	<i>n</i> = 70 (20 male; 50 female), healthy volunteers	18 – 55	5 arm: A) 450mL/d yoghurt fermented with two strains of <i>Streptococcus thermophilus</i> and two strains of <i>Lactobacillus acidophilus</i> . B) 450mL/d placebo yoghurt fermented with delta-acid-lactone. C) 450mL/d yoghurt fermented with two strains of <i>Streptococcus thermophilus</i> and one strain of <i>Lactobacillus rhamnosus</i> . D) 450mL/d yoghurt fermented with one strain of <i>Enterococcus faecium</i> and two strains of <i>Streptococcus thermophilus</i> . E) 2 placebo pills per day.	8 weeks	Comparing all 5 groups, no statistical effects on LDL were observed after consumption of diet D. After adjusting for small changes in body weight, LDL decreased by 8.4% and fibrinogen increased. This was significantly different from the control groups, B + E. After diets A + D, systolic blood pressure reduced significantly more compared to diet C.
<b>Anderson and Gilliland, 1999 [92]</b>	USA	Study 1: single-blind, parallel. Study 2: double-blind, crossover.	Study 1: <i>n</i> = 29 (9 male; 20 female). Study 2: <i>n</i> = 40 (18 male; 22 female), all hypercholesterolaemic	49 – 55	Study 1: 2 arm: A1) 200g/d fermented milk yogurt containing human <i>L. acidophilus</i> L1 B1) 200g/d fermented milk yogurt containing swine <i>L. acidophilus</i> strain ATCC 43121 Study 2: 2 arm: A2) 200g/d fermented milk yoghurt containing <i>L. acidophilus</i> L1 strain B)	Study 1: 3 weeks Study 2: Two 4 week periods with a 2 week washout period	Study 1: Diet A1 showed a significant 2.4% reduction in TC. LDL was lower after both treatment groups although not significant. HDL decreased significantly in both groups. Study 2: diet A2 reduced TC in the 1st treatment period but not in the 2nd. A combined analysis of the 2 treatment study interventions demonstrated a significant reduction

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200g/d fermented milk  
yogurt without these active  
bacteria. in TC.

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### 3. The Dairy 'Matrix'

While dairy products are often considered together as a food category in nutritional epidemiology, they vary considerably in term of their content and structure and how these interact with other food components, which describes the 'dairy matrix' concept [93]. Across the range of commercially available dairy products, nutrient composition varies greatly (summarised in Figure 2), as does their overall matrix or structure, depending on the product type. For example, whole milk contains 3.6 % fat in a liquid oil-in-water emulsion with lactose and protein (both casein and whey) while cheeses mainly consist of casein proteins and fat, in a solid matrix, with only trace levels of lactose and whey [54]. Butter is an emulsion of water-in oil, and contains mostly fat and water, with no protein or carbohydrate, while (liquid) cream is also a water-in-oil emulsion, and contains low levels of protein (approx. 2 %)[54] and lactose (approx. 3%) (in 35% fat cream). The various processing steps that different products undergo from raw milk to final foodstuff, impact the level of the different nutrients, and the overall macro and microstructure of these foods. The nature of these differences may result in the different health outcomes associated with their consumption.

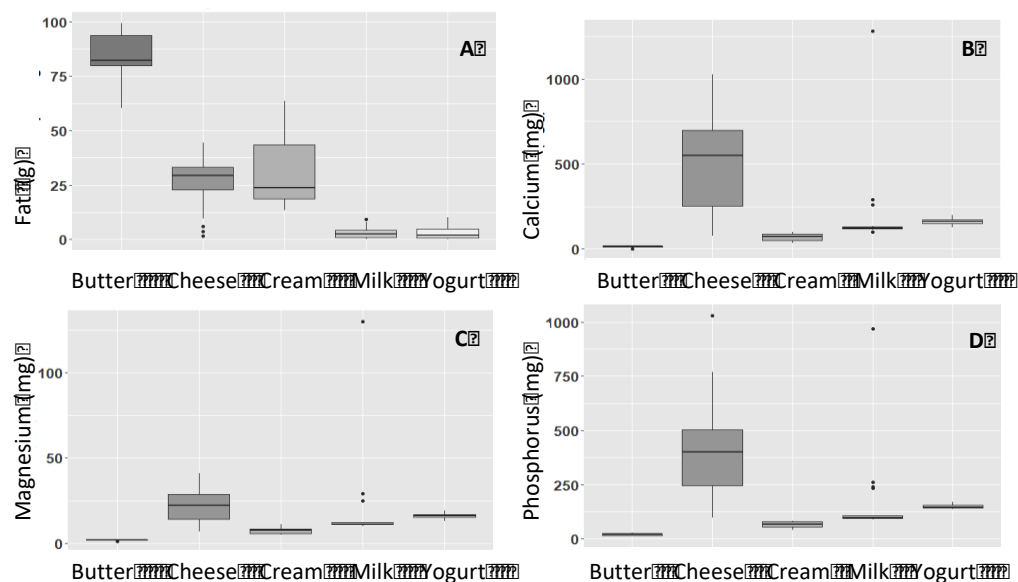


Figure 1. Boxplot showing average Fat and mineral content in dairy products per 100g.

Values from the Composition of Foods Integrated Dataset (CoFID). Nutrients shown are:

A) Total Fat (g), B) Calcium (mg), C) Magnesium (mg) and D) Phosphorus (mg), calculated from  $n=4$  butter,  $n=43$  cheese,  $n=8$  cream,  $n=20$  milk and  $n=4$  yogurt samples.

Cheese in particular is associated with lower levels of blood cholesterol than other dairy products and especially when compared to butter (see Table 2 for an overview of studies in this area). Cheese structures contain aggregated casein micelles [94] which may impact the ability of lipases to break down the fat contained within the matrix, compared to the same fat contained within other food matrices (e.g. milk and butter). The structure of cheese, including the degree of hardness and cohesiveness, can result in it being more physically resistant to digestion than other matrices [95] which affects the degree to which the fat can be digested and absorbed. There may be additional effects from the calcium contained within this matrix, reacting with the fatty acids to form insoluble calcium soaps [96], as well as the separate textural effects from calcium that increase the

cohesiveness [95] which may result in enhanced digestive resistance. This mechanism also appears to be supported by a higher faecal fat excretion following cheese consumption compared to other sources, in postprandial studies [72] although not fully confirmed [49]. In addition to the calcium content of cheese, the phosphorus content is also implicated in the reduction of fat digestibility, by affecting the ability of cheese constituents to form insoluble soaps during digestion (calcium phosphate). This is thought to further increase fat excretion via the adsorption of bile acids to the surface, and has been implicated in the reduction of LDL-c [54,97]. Both phosphorus and calcium are particularly concentrated in cheese compared to other dairy products [54].

Cheese is a fermented dairy product, and the fermentation process may also be one of the contributors to the cardiometabolic protective nature of cheese via a number of mechanisms. Lactic acid bacteria found in fermented dairy products can result in PAF-inhibitory lipid production [98,99]. Further, as cheeses ripen and age, shorter peptides are produced and in some cases there is a release of latent bioactives, as some of these peptides have specific bioactivity that is not apparent in the intact 'parent' protein [100,101]. In cheeses, anti-hypertensive peptides are produced during fermentation, including V-P-P and I-P-P, which are tripeptides that exert their effects via inhibition of the angiotension converting enzyme (ACE) pathway [102,103]. Some cheeses have also been found to have bioactivity related to glycaemic control [104], which may also contribute to the cardio-metabolic benefits from cheese consumption. The starter culture used in the cheesemaking process can have an additional impact on the inherent bioactivity produced during fermentation [105,106] as well as the overall gut microbiota following consumption. Finally, the form in which fat is contained in cheese compared to butter may also result in some of the differences observed between these two products. The polar lipids found in dairy products in general appear to have anti-inflammatory properties compared to other oxidised dietary lipids [107-109] and they are mostly contained in a bioactive envelope surrounding the fat, known as the Milk Fat Globule Membrane (MFGM) [110]. Cheese contains particularly high levels of polar sphingolipids that are not present in the same levels in butter, since the membrane is disrupted the churning process [54,111]. Studies suggest that polar lipids can impact blood lipid levels in the acute postprandial period, with lower lipaema (and insulin) observed following a liquid meal of palm fat when an MFGM-rich dairy fraction was added, compared to the same meal without this addition [112].

With research strongly suggestive of postprandial hyperlipidemia as an independent risk factor for CVD [113], this could be a further explanation for the growing list of studies showing a protective effect of cheese consumption on CVD risk [47,48] [27,49-53] despite the relatively high SFA content.

#### 4. Conclusions/Future Directions

This paper summarises the significant body of work that examines the link between dairy intake and CVD risk. Whilst the evidence is mixed for some dairy foods (milk), but stronger or more consistent for others (cheese / yogurt), this research supports the concept that the source of saturated fat intake has an important impact on cardiometabolic response to consumption. To date many of the studies have focused on traditional markers of cardiometabolic risk, particularly circulating lipid levels, which may not show subtle changes between products and/or further elucidate the cause/mechanisms for difference. Blood lipid profiles and particularly LDL-c concentrations, are established risk factors for CVD development [114]. It has been suggested that the use of traditional markers alone may limit the ability to predict health outcomes from the fat in dairy products, since many other components in dairy may have impact on CVD risk [115]. For this reason, studies are also examining novel biomarkers that include vascular function (Arterial stiffness, FMD) [45] and LDL-c particle size distribution [116].

While the link between dairy foods and metabolic health has been well-studied, research gaps still remain. Many of the RCTs completed are short-term studies with single products, and there is a need to consider combinations of foods in a dietary pattern. This has been considered by only a few studies to date [117]. The manner of the food consumption also needs to be considered, as dairy is often consumed in many forms (heated, melted) and as part of meals or recipes or in sweetened beverages. In addition, the amount of dairy product given in many of the randomised controlled trial studies to date are largely outside of recommended portion size intakes, as such, caution is required in interpreting and generalising findings.

In conclusion, dairy foods are diverse in their structure and their nutrient content, with different biological health outcomes. As such, treating them as a single food category may obscure the individual effects of these foods. As diets transition, there is an urgent need to understand the impact of different dairy foods, their preparation methods and how they are consumed, within the overall patterns of dietary intake in different cultural groups.

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