CARDIOVASCULAR DISEASE (JHY WU, SECTION EDITOR)



# Effect of Yogurt Consumption on Metabolic Syndrome Risk Factors: a Narrative Review

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Accepted: 20 December 2020 / Published online: 6 January 2021

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#### Abstract

**Purpose of Review** Metabolic syndrome (MetS) comprises risk factors such as obesity, hypertriglyceridemia, hypertension, and hyperglycemia. Here we described the outcome of various yogurt consumption, either conventional, low-fat, high-fat, Greek, or enriched with nutrients or probiotics: (1) on the parameters of MetS risk factors and (2) on the mechanisms of action of the MetS risk factors.

**Recent Finding** The majority (25 studies) of clinical trials and meta-analyses of clinical trials reported a beneficial effect of yogurt consumption in the prevention of MetS risk. Yogurt components, such as calcium, vitamin D, proteins, and probiotics, were associated with the multiple beneficial effects on the prevention of MetS.

**Summary** In general, yogurt consumption may be promoted within healthy dietary patterns to prevent MetS. More studies are needed to determine what type of yogurt has the greatest benefits for specific MetS risk factor prevention.

Keywords Metabolic syndrome · Yogurt · Hyperglycemia · Obesity · Hypertension · Hypertriglyceridemia

# Introduction

The cardiometabolic syndrome, also more recently known as the metabolic syndrome (MetS), is associated with the dysfunction of lipid and carbohydrate metabolism, adipose tissue homeostasis, and the control of blood pressure, which lead to an increase in the risk of cardiovascular disease (CVD) [1]. It is estimated that approximately a quarter of the world's population has MetS [2]. Individuals with MetS are at a higher risk of chronic diseases such as CVD [3], cancer [4], type 2 diabetes (T2D) [5], and liver disorders [6]. Specifically, MetS is defined as a cluster of clinical and anthropometric abnormalities when three or more of the five following components are met: waist circumference ( $\geq$  102 cm men,  $\geq$  88 cm women), low high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL for men and < 50 mg/dL for women, hypertriglyceridemia ( $\geq$  150 mg/dL), hypertension ( $\geq$  130 mmHg systolic,  $\geq$  85 mmHg diastolic) and hyperglycemia (fasting glucose  $\geq$  100 mg/dL). Furthermore, metabolically triggered inflammation may be considered one of the MetS components through the deterioration of lipids, glucose, and energy regulation [7]. Risk factors associated with the MetS include genetic background, low physical activity, and poor dietary habits [8]. Overall, the prevalence of the MetS will not be decreased until efforts are made to modify different aspects of lifestyle, especially dietary intake and physical activity.

Recently, several meta-analysis of observational studies [9–12] demonstrated that the increase of one serving of dairy consumption may reduce the risk of MetS. Specifically, a meta-analysis of cohort [13] studies suggested that yogurt consumption, specifically low-fat and probiotics, was inversely associated with the risk of MetS and CVD. The current literature describes the effects of various types of yogurt on MetS. First, conventional (also known as plain or regular) yogurt is produced when milk is heated to denature the proteins and fermented by lactic acid-producing bacteria, such as Lactobacillus delbrueckii bulgaricus and Streptococcus thermophilus. Secondly, conventional yogurt can be non-fat (< 0.5% of total calorie), low-fat (0.5-2% of total calorie), and whole-fat (>2% of total calorie) [14]. Moreover, one of the most popular yogurts is Greek yogurt, which contains higher protein (24 g/one serving compared to 13 g/one serving in

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conventional yogurt) and less carbohydrate (10 g/one serving compared to 17 g/one serving in conventional yogurt) [15]. Yogurt may also be enriched with micronutrients, including vitamins (B<sub>6</sub>, B<sub>12</sub>, D) and minerals (calcium, zinc), to improve the nutritional value. Furthermore, the addition of live bacteria strains (*Bifidobacterium lactis* or *Lactobacillus casei*, *acidophilus*, *reuter*) to a conventional yogurt produces probiotic yogurt which promotes healthy immune and digestion systems [16]. Currently, the USA is considered a region with the highest consumption of yogurt [15]. Specifically, 6% and 13% of the population in the USA and Europe consumed the recommended dose of yogurt which comprises three servings of dairy/day preferably fat-free or low-fat milk or yogurt, respectively (1 serving yogurt equals to 226 g) [17].

Yogurt consumption provides several daily intakes of vitamin D; potassium; magnesium; calcium; iron; phosphorus; zinc; vitamin C; vitamins  $B_2$ ,  $B_6$ , and  $B_{12}$ ; carbohydrates; proteins; and fibers [18]. Compared to the same weight of milk, yogurt contains 50% higher potassium, magnesium, and calcium as well as approximately 30% (conventional yogurt) and 60% (Greek yogurt) more proteins [19].

Given the increasing amount of evidence on the beneficial role of yogurt consumption for optimum health, targeting specific yogurt intake may represent an additional key strategy to decrease MetS risk factors. The objective of the present study is to review the scientific evidence, including meta-analyses of clinical studies and clinical trials: (1) to examine the association between yogurt consumption (all types of yogurts, including conventional, low-fat, high-fat, Greek, enriched with nutrients or probiotics) and MetS components including body weight, lipid profile, blood pressure, glucose homeostasis, and inflammation; (2) to examine the mechanisms to explain the association between consumption of yogurt and MetS, to support intake for yogurt to decrease the risk of MetS.

## Search Strategy and Selection Criteria

PubMed was searched for meta-analysis and clinical studies and have been conducted in human during the last 5 years (2015–2020). Search terms are as follows: "metabolic syndrome," "body mass index" (BMI), "bodyweight," "obesity," "waist circumference," "hypertriglyceridemia," "high-density lipoprotein," "blood pressure," "hyperglycemia," "dyslipidemia," "fasting glucose," and "inflammation" in combination with yogurt intake either conventional, regular, plain, probiotic, non-fat, low-fat, high-fat, whole-fat, Greek yogurt, and enriched yogurt.

## **Yogurt Consumption and Body Weight**

Systematic reviews of cohort studies (between 6 to 22 cohort studies were included, and the median for follow-up duration

was between 9 months and 23 years) have established the beneficial role of conventional and low-fat yogurt to reduce body weight, weight gain, BMI, body fat, and waist circumference among the healthy population [20–22] and elderly adults at high risk of CVD [23]. However, a meta-analysis of cross-sectional studies reported not enough evidence to explain the protective role of conventional yogurt on body weight among both adults and children [24]. Yet, a meta-analysis of nine randomized clinical trials with yogurt fortified with vitamin D (400–2000 IU) demonstrated decreased body weight and waist circumference in adults with or without prediabetes, diabetes, or MetS [25].

Recently, five clinical studies were available in the literature which examined the relationship between vogurt consumption and body weight management [26-30]. Table 1 summarizes meta-analysis of clinical trials and clinical studies on yogurt consumption and MetS published between 2015 and 2020. Of these studies, two studies reported an inverse association between yogurt consumption and risk of being overweight [26, 27], whereas three studies found no association [28–30]. Specifically, the consumption of an enriched yogurt (two servings/day) by whey protein, calcium, vitamin D, and prebiotic fiber [27] or yogurt enriched with vitamins  $(B_1, B_5, and B_6)$  [26], was related to the reduction in body weight, BMI, body fat mass, and waist circumference in subjects with MetS and T2D. Oppositely, no difference in body weight variation was observed among diabetic postmenopausal women after consumption of yogurt enriched with calcium  $(\geq 1200 \text{ mg Ca/day in milk or yogurt})$  compared with consumption of conventional yogurt and baseline body weight, respectively [28]. Similarly, the consumption of yogurt enriched with calcium (1200 mg/day compared to 600 mg/ day) did not impact body weight over 1 year among healthy obese girls (13–14 years) [29]. Furthermore, no weight loss was found after consumption of low-fat yogurt (200 g twice/ day) or probiotic yogurt (200 g twice/day) (enriched with Lactobacillus acidophilus and Bifidobacteria Bifidobacterium lactis) during a 3-month intervention among overweight and obese women [30].

A few potential mechanisms of action of yogurt consumption on body weight management exist. Figure 1 summarizes the mechanisms of nutrients in yogurt on reducing the risk factors of MetS. Research suggests that the calcium contained in yogurt plays a role in the reduction of lipogenesis and an increase in lipolysis and fat oxidation through inhibition of the formation of 1,25-dihydroxyvitamin D [31]. Moreover, vitamin D regulates energy metabolism through appetitesuppression effect on the leptin hormone, decrease in adipose tissue inflammation, and controlling the expression of uncoupling protein 1 (UCP1) which plays a role in enhancing energy expenditure [32]. Furthermore, fortification of yogurt with either vitamins  $B_6$ ,  $B_9$ , or  $B_{12}$  may contribute to bodyweight management through modification of normal

Metabolic risk factors	Beneficial effect	Negative effect	No effect
Body weight	Enriched yogurt with vitamin D compared to control treatment without supplement ( <i>Gasparri C/2019</i> $(25)^*)^{\forall}$ Enriched yogurt with vitamins B <sub>1</sub> , B <sub>5</sub> , and B <sub>6</sub> compared conventional yogurt ( <i>Yanni AE/2019</i> $(26)$ ) Enriched yogurt with whey protein, calcium, vitamin D, and prebiotic fiber compared with low-fat plain yogurt ( <i>Mohammadi-Sartang M/2018</i> $(27)$ ) Probiotic yogurt (high calcium and protein) (Kashk) compared to yogurt (Kashk)-free diet ( <i>Razmposh E/2020</i> $(51)$ ) <sup>*</sup>	-	<ul> <li>Enriched low-fat yogurt with vitamin D compared conventional yogurt (<i>Jafari T/2016 (28)</i>)</li> <li>Enriched yogurt with calcium (1200 mg) compared to enriched yogurt with calcium (600 mg) (<i>Lappe JM/2017 (29)</i></li> <li>Low-fat and probiotic yogurt compared conventional yogurt (<i>Madjd A/2016 (30)</i>)</li> </ul>
Lipid profile	<ul> <li>Enriched yogurt with vitamin D compared to control treatment without supplement (<i>Gasparri C/2019 (25)*</i>)<sup>¥</sup></li> <li>Enriched yogurt with vitamin D compared to conventional yogurt (<i>Li Q/2016 (39)</i>)</li> <li>Probiotic yogurt compared to yogurt-free diet (<i>Dumas A-A/2017 (37)*</i>)</li> <li>Probiotic yogurt (<i>Streptococcus thermophiles, Lactobacillus acidophilus</i>) compared to probiotic yogurt (<i>L. lactis</i> 11/19-B1 and <i>Bifidobacterium lactis</i> BB-12 strains) (<i>Nishiyama K/2018 (40)</i>)</li> <li>Probiotic yogurt compared to conventional yogurt (<i>Pourrajab/2020 (38)*</i>)</li> <li>Probiotic yogurt compared with probiotic suplementation (capsules/powder) (<i>Companys J/2020 (36)*</i>)</li> <li>Probiotic yogurt (high calcium and protein) (Kashk) compared to yogurt (<i>Bashc)-free diet (Raymoosh E/2020 (51)*</i>)</li> </ul>	-	Probiotic yogurt compared to conventional yogurt ( <i>Lee Y/2017 (42</i> ))
Blood pressure	Conventional yogur compared to non-yogurt diet ( <i>Detopoulou</i> M/2020 (52)) Probletic yogurt (high calcium and protein) (Kashk) compared to	-	-
Glucose homeosta- sis	Frobiotic yogurt (high calcium and protein) (Kashk) compared to yogurt (Kashk)-free diet ( <i>Razmpoosh E/2020 (51)</i> ) <sup>¥</sup> Greek yogurt compared to non-dairy snack (oat bran-beverage) ( <i>Gheller BJ/2019 (70)</i> ) Greek yogurt compared to skim milk, whole milk, cheddar cheese ( <i>Vien S/2019 (71)</i> ) Greek yogurt combined with cheddar cheese compared to non-dairy dietary pattern ( <i>Turner KM/2015 (72)</i> ) Conventional yogurt compared to milk and sugar-sweetened	-	Conventional yogurt compared to oat bran-beverage ( <i>Lindström C/2015</i> (76)) Probiotic yogurt compared to conventional yogurt ( <i>Barengolts E/2019</i> (68)*)
Inflammation	products ( <i>Maki KC</i> /2015 (73)) Low-fat yogurt compared non-dairy beverages ( <i>Law M</i> /2017 (74)) Greek yogurt and 2% fat yogurt compared to conventional yogurt ( <i>Toshimitsu T</i> /2020 (75)) Enriched yogurt with vitamin D compared to control treatment without supplement ( <i>Gasparri C</i> /2019 (25)*) <sup>¥</sup> Probiotic yogurt compared to non-yogurt diet ( <i>Zhang Q</i> /2016 (67)*) Conventional yogurt compared to milk ( <i>Chen Y</i> /2019 (69)) Low-fat and high-fat products, as well as fermented products in all dairy products ( <i>Bordoni A</i> /2017 (87))* Low-fat yogurt compared to soy pudding ( <i>Pei R</i> /2018 (89)) Cow/s whole yogurt compared to ewe's whole milk ( <i>Redondo</i> <i>N</i> /2019 (90)) Probiotic yogurt compared to acidified milk ( <i>Burton KJ</i> /2018 (88)) Probiotic yogurt compared to conventional yogurt ( <i>Mousavi</i>	-	-

 Table 1
 Summary of studies (clinical trials and meta-analysis of clinical trials) with yogurt consumption and their effect risk factors of the metabolic syndrome (2015–2020)

\*Meta-analysis of clinical studies

<sup>¥</sup> Study with multiple beneficial effects



Fig. 1 Summary of the potential mechanisms of action of nutrients in yogurt on the prevention of cardiometabolic diseases. GLP-1, glucagonlike peptide 1; PYY, peptide YY; LPS, lipopolysaccgaride; PTH,

↓ Hyperglycemia ↓ Inflammation

energy-yielding metabolism and glucose regulation [33]. Next, appetite is controlled after higher protein content of yogurt through satiety and glucagon-like peptide 1 (GLP-1) and peptide YY (PYY) increase in the circulation [34]. Finally, probiotic (Bifidobacterium, Lactobacillus, Streptococcus) added in yogurt may play a role in the weight loss process by lowering appetite, increasing satiety, and promoting energy expenditure [35].

## **Yogurt Consumption and Lipid Profile**

A meta-analysis of nine cohort studies reported an intake of  $\geq$ 200-g/day vogurt (conventional low-fat/ high-fat, probiotic) was associated with a lower risk of CVD [13]. The metaanalysis analysis of nine randomized clinical trials as described above also reported the beneficial effect of yogurt fortified with vitamin D (400-2000 IU) to decrease total cholesterol (TC) and triglycerides (TGs) in adults with or without prediabetes, diabetes, or MetS [25]. Furthermore, three systematic reviews of clinical studies indicated that probiotic (such as Lactobacillus bulgaricus and Streptococcus thermophilus) products are associated with a decrease in TC and low-density lipoprotein (LDL) among obese or overweight adults or subjects diagnosed with MetS, T2D, or hypercholesterolemia [36–38].

In recent clinical studies, two studies reported a beneficial effect of yogurt consumption on serum lipid profile [39–41] while two studies found no association [42]. First, the intake of one servings per day of vitamin D3-supplemented yogurt (500 IU) reduced TC, LDL, and TGs levels compared with consumption of conventional yogurt during a 4-month

# $\downarrow$ risk of cardiometabolic diseases

parathyroid hormone; CHO,carbohydrate; NA, sodium; K, potassium; CA, calcium; ACE, angiotensin-converting enzyme activity; Mg, magnesium; MetS, metabolic syndrome

intervention among women with gestational diabetes [39]. Moreover, Nishiyama K et al. (2018) demonstrated that the LDL level decreased after consumption of a probiotic vogurt enriched with Bifidobacterium lactis compared to another enriched with Streptococcus thermophiles, Lactobacillus delbrueckii subspecies bulgaricus, and Lactobacillus acidophilus among adults with slightly elevated blood lipid or glucose levels [40]. In contrast, Lee Y et al. (2017) found no differences in TC, LDL, HDL, and TGs levels between before and after consumption of yogurt containing Bifidobacterium animalis (BB-12) among healthy overweight or obese adults [42]. Hutt P et al. (2015) also demonstrated no difference in LDL-C after 3-week daily consumption of probiotic yogurt (L. plantarum TENSIA) and conventional yogurt among healthy individuals; however, in both probiotic and conventional yogurt, the level of LDL decreased [41].

A recent investigation showed that dairy nutrients, such as calcium, modulate lipid profile [43] (see Fig. 1). Specifically, high calcium intake is associated with the formation of calcium soap which contributes to the reduction in fat absorption together with fecal fat excretion, reduces TG content of postprandial chylomicrons, and leads to increased HDL/LDL ratio [44]. Furthermore, the high calcium intake is also associated with increase in fat oxidation and lipolysis together with suppression in lipogenesis [45]. In addition, the beneficial effect of serum vitamin D has been reported on the lipid profile, through upregulated lipoprotein lipase, reduced TGs, and increased HDL and apolipoprotein A1 contents [46]. Another study showed that probiotics have the ability to change the transcription of genes including fatty acid synthase, sterol regulatory element-binding protein-1, carnitine palmitoyl transferase II, and peroxisome proliferator-activated receptor- $\alpha$ , which are associated with decreased plasma TG levels [47]. Furthermore, probiotics play a role to increase the production of short-chain fatty acids (SCFAs) which are inhibited the production of fatty acids in the liver [48]. In addition, fatty acids in yogurt play a role in the endogenous synthesis of carnitine which is associated to decrease blood pressure (through interaction with nitric oxide pathways) and insulin resistance [49].

#### **Yogurt Consumption and Blood Pressure**

A meta-analysis of cohort studies indicated a beneficial effect of low-fat fluid dairy (milk and yogurt) [50] and yogurt consumption (200 g/day) [12] in controlling hypertension among subjects with elevated blood pressure.

Recently, two clinical studies demonstrated the beneficial effect of yogurt in the reduction of elevated blood pressure [51, 52]. Daily consumption of conventional yogurt compared to non-yogurt consumers for 8 weeks was associated to decreased systolic and diastolic blood pressure among healthy subjects [52]. Furthermore, consumption of 50-g/day probiotic condensed yogurt (Kashk) compared to a low-energy diet without Kashk during 8 weeks beneficially decreased the diastolic-systolic blood pressure, waist circumference, LDL, and TG among women who are overweight and obese [51]. Kashk is a traditional dairy product in the Middle East, which is considered one of the dairy products with the highest amount of calcium (2.4 g/100 g) and protein, compared to milk alone (300 mg/100 g), as well as high protein and enriched with probiotics [53].

Nutrients in yogurt may play a major role in the management of blood pressure (see Fig. 1). First, calcium in combination with other ions such as potassium and magnesium provides a balance to reduce vasoconstriction [54]. Secondly, potassium can reduce the blood pressure through endothelium-dependent vasodilatation, increase baroreceptor sensitivity and sodium/potassium ATPase activity [55], and decrease the vasoconstrictive sensitivity to angiotensin II [56]. Thirdly, magnesium is an important cofactor to stimulate prostaglandin E<sub>1</sub> production that is a vasodilator and platelet inhibitor [57]. In addition, magnesium also plays an important role in the regulation of intracellular calcium, sodium, and potassium levels [58]. Furthermore, vitamin D has a role in the regulation of blood pressure through the modification of the intracellular calcium level [59]. The fermented dairy tripeptides may play a role to decrease hypertension through an effect on vascular stiffness and vascular endothelial function [60]. Yogurt enriched with  $\beta$ -case in is associated with anti-hypertensive activity through the inhibition of angiotensin-converting enzyme activity (ACE), production of angiotensin II, and narrowing of blood vessels [61]. Furthermore, probiotic products exert anti-hypertensive effects by ACE inhibitory effect, with modulation blood pressure by Olfr78 and Gpr41 receptors [62], and bile acid deconjugation [63]. Overall, the blood pressure-lowering features of yogurt may be related to a reduction in renal sodium reabsorption, increasing the synthesis of nitric oxide to promote vasodilation and modify vascular resistance [64].

#### Yogurt Consumption and Glucose Metabolism

A recent meta-analysis of 22 cohort studies showed the inverse association between conventional yogurt consumption (80 g/day) and the risk of T2D among healthy individuals [65]. Similarly, increasing the consumption of 100 g/day of low-fat or whole-fat yogurt was associated with a 16% reduction in the risk of hyperglycemia in the meta-analysis of nine observational studies [9]. Consistently, a meta-analysis of nine randomized clinical trials reported the beneficial effect of yogurt fortified with vitamin D (400-2000 IU) to decrease fasting glucose and insulin resistance (measured by HOMA-IR (homeostatic model assessment insulin resistance)) in subjects with or without prediabetes, diabetes, or MetS [25]. Furthermore, a review of six meta-analyses of observational studies were examined in which probiotic yogurt is inversely associated with the risk of T2D and glucose metabolism among healthy adults at high risk of CVD [66]. Correspondingly, a meta-analysis of seven randomized controlled trials reported the reduction in fasting plasma glucose and the risk of T2D after consumption of probiotic products among T2D subjects [67] (see Table 1). However, another meta-analysis of nine randomized controlled trials reported no differences in glucose control, fasting insulin, insulin resistance, and glycated hemoglobin A1c (HbA1c) before and after consumption of probiotic yogurt as well as the consumption the probiotic yogurt compared to the conventional yogurt among subjects with T2D and obesity [68].

Recently, seven clinical studies indicated the inverse relationship between yogurt consumption and insulin [69-73] as well as glucose [74] and HbA1c [75] levels (see Table 1). Furthermore, one study reported no association between yogurt intake and glycemic parameters [76]. First, among overweight individuals, the consumption of conventional yogurt (220 g/day) [69] and 0.5 servings/day (170 g/day) of low-fat yogurt combined with milk (474 g/day) were associated with a reduction in insulin resistance (measured by HOMA-IR) compared with consumption of milk and sugar-sweetened products, respectively [73]. Secondly, three randomized crossover trials reported the positive effect of Greek yogurt (198.9 g) [70, 71] or Greek yogurt (one serving and 175 g) combined with cheddar cheese and milk [74] compared with milk and non-dairy beverages on decreasing the postprandial glycemia among healthy children and adults. Thirdly, daily consumption of 112 g yogurt enriched with Lactobacillus plantarum compared to the baseline and consumption of conventional

yogurt during 12 weeks decreased HbA1c level in prediabetic adults [75]. Consistent with previous studies, higher insulin sensitivity (measured by MATSUDA index) was demonstrated after dietary patterns including 4–6 servings/day of dairy (200 g yogurt, 250 g milk, 160 g cheese) compared to the non-dairy dietary patterns among women with normal or impaired glucose tolerance [72]. Oppositely, one study reported no difference in insulin and postprandial glucose level between yogurt consumption (250 ml/day, during 4 breakfast meals) and oat bran beverages [76] in healthy overweight individuals.

Numerous possible mechanisms of yogurt consumption on glucose metabolism have been examined (see Fig. 1). The mineral components of yogurt including potassium, magnesium, and phosphorus may have a positive impact on carbohydrate metabolism through improving the renin-angiotensin system (second messenger in oxidative glucose metabolism) and a role in tyrosine-kinase activity in the insulin receptor [77, 78]. In addition, vitamin D-enriched yogurt may reduce the leptin/ghrelin ratio which is related to decrease fasting glucose [79]. Furthermore, Greek (high-protein) yogurt may have an insulinotropic effect to reduce both glucose serum level [80] and hepatic gluconeogenesis [81]. Research findings also showed that bioactive peptides, branched-chain amino acids, and different compositions of B-casein improved blood glucose homeostasis and postprandial insulin response [82]. Furthermore, trans-palmitoleic acid as one of the major dairy fat may improve pancreatic B cell survival, muscle insulin response, and insulin secretion [83]. In addition, recent studies indicated the role of inflammation in the progression of diabetes through activation of pro-inflammatory pathways such as in target cells of insulin [84]. Finally, it should be considered that added sugar to dairy products such as fruit yogurt or flavored yogurt may have an adverse effect on body weight and increased the risk of T2D [85].

#### **Yogurt Consumption and Inflammation**

Recently, a meta-analysis of 28 clinical trials indicated that daily consumption of probiotic yogurt (< 200 g/day) contributed to a decrease in C-reactive protein (CRP) among overweight participants [86]. Furthermore, a systematic review of 52 clinical studies reported beneficial anti-inflammatory (measured by inflammatory index) effect of low-fat and high-fat dairy products as well as fermented dairy (yogurt and cheese) among subjects with metabolic disorders [87].

Four randomized controlled studies demonstrated the inverse association between yogurt consumption and inflammatory parameters [88–91]. First, the consumption of 339 g/day low-fat yogurt compared with 324-g/day pudding soy reduced the ratios of lipopolysaccharide-binding protein (LBP)-to-soluble form of CD14 (sCD14) molecule, interleukin-6 (IL-6) [89] as well as tumor necrosis factor- $\alpha$  (TNF)- $\alpha$ / soluble tumor necrosis factor receptor-type II (sTNFR-RII) level and

LBP/sCD14, which are related to improved inflammatory profile in obese and non-obese premenopausal women [91]. Secondly, the consumption of 800 g/day of probiotic yogurt compared to acidified milk for a 2-week intervention indicated a greater reduction in the up-regulation of aryl hydrocarbon receptor (AhR) gene (major role in the downregulation of inflammatory gene sets) among healthy young men [88]. Oppositely, no difference of inflammatory biomarkers including monocyte chemoattractant protein-1 (MCP-1) and intercellular adhesion molecule *1* (ICAM-1) was found after consumption of 250 g/day ewe's whole-milk yogurt (5.8% fat of total calories) and cow's whole-milk yogurt (2.8% fat of total calories) in with borderline-high plasma TC [90].

Intake of yogurt modulates the inflammatory and proinflammatory biomarkers through different mechanisms. For example, conventional yogurt plays a role in the increase of the expression of the RAR-related orphan receptor gamma (ROR $\gamma$  receptor) gene among obese and overweight individuals [92]. Specifically, ROR $\gamma$  receptor plays a role in the reduction of cell apoptosis and increasing the differentiation of T helper 17 cells as a pro-inflammatory factor [93]. Furthermore, consumption of conventional yogurt may be associated with a higher intestinal abundance of Akkermansia and serum lipid peroxidation (CRP and malondialdehyde) compared to non-consumers [94]. Furthermore, the intake of probiotic yogurt may increase the production of intestinal mucin and immunoglobulin secretion among obese and nonobese individuals [95]. Particularly, the mucus stimulates a signaling system which activates the immune system in response to the inflammation [96]. The higher ratio of the LBP-to-soluble form of CD14 (sCD14) is positively correlated with inflammation and endotoxin bioactivity [97]. In addition, palmitoleic acid as one of the major fatty acids in yogurt has an anti-inflammatory effect on lipopolysaccharidestimulated macrophages through a reduction in the nuclear factor kappa-light-chain-enhancer of activated B cells (NFKB) [98]. Moreover, natural killer (NK) cell activity, IL-12, and immunoglobulin (Ig) G1 are increased after consumption of probiotic yogurt (Lactobacillus paracasei spp. paracasei, Bifidobacterium animalis spp. Lactis, and heattreated Lactobacillus plantarum) which promotes the differentiation and function of T cells in immune systems [99].

# Conclusions

In sum, in the last 5 years, 31 studies including 8 metaanalyses of clinical trials and 23 clinical studies examined the effect of various yogurt consumption on MetS prevention. The results of these studies demonstrate 25 studies with the beneficial effects of yogurt intake on MetS risk factors. Furthermore, most recent studies investigate the potential of enriched yogurt (e.g., calcium, vitamin D, Greek, and probiotics) on MetS risk factors. More clinical studies are needed to confirm the additional beneficial effects of enriched yogurt compared to conventional yogurt consumption on risk factors of the MetS. The various yogurt nutrients, such as calcium, vitamin D, protein, and probiotics, are likely responsible for the beneficial effects on MetS risk factors. However, the individual and synergistic roles of these nutrients on MetS risk factors should be investigated in depth. Overall, yogurt consumption especially nutrient-rich yogurts such as vitamin D–enriched, Greek, and probiotic yogurts, as part of a healthy diet may play a role to prevent MetS risk factors.

**Funding** L.K. received a scholarship from CHU de Québec-Laval University Research Center and Fonds de recherche du Québec— Nature et technologies (FRQNT); I.R. hold a Junior 2 research Scholar from the Fonds de recherche du Québec—Santé (FRQ-S).

#### **Compliance with Ethical Standards**

**Conflict of Interest** The authors declare that they have no conflict of interest.

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