*Special Article*

# Yogurt, cultured fermented milk, and health: a systematic review

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*Consumption of yogurt and other fermented products is associated with improved health outcomes. Although dairy consumption is included in most dietary guidelines, there have been few specific recommendations for yogurt and cultured dairy products. A qualitative systematic review was conducted to determine the effect of consumption of fermented milk products on gastrointestinal and cardiovascular health, cancer risk, weight management, diabetes and metabolic health, and bone density using PRISMA guidelines. English language papers in PubMed were searched, with no date restrictions. In total, 1057 abstracts were screened, of which 602 were excluded owing to lack of appropriate controls, potential biases, and experimental design issues. The remaining 455 papers were independently reviewed by both authors and 108 studies were included in the final review. The authors met regularly to concur, through consensus, on relevance, methods, findings, quality, and conclusions. The included studies were published between 1979 and 2017. From the 108 included studies, 76 reported a favorable outcome of fermented milks on health and 67 of these were considered to be positive or neutral quality according to the Academy of Nutrition and Dietetics' Quality Criteria Checklist. Of the 32 remaining studies, the study outcomes were either not significant (28) or unfavorable (4), and most studies (18) were of neutral quality. A causal relationship exists between lactose digestion and tolerance and yogurt consumption, and consistent associations exist between fermented milk consumption and reduced risk of breast and colorectal cancer and type 2 diabetes, improved weight maintenance, and improved cardiovascular, bone, and gastrointestinal health. Further, an association exists between prostate cancer occurrence and dairy product consumption in general, with no difference between fermented and unfermented products. This article argues that yogurt and other fermented milk products provide favorable health outcomes beyond the milk from which these products are made and that consumption of these products should be encouraged as part of national dietary guidelines.*
***Systematic review registration:*** *PROSPERO registration no. CRD42017068953.*

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## INTRODUCTION

Fermented dairy foods and beverages were among the first "processed" food products consumed by humans and have been utilized for centuries as a method of food preservation.[1] Today, fermented foods are generally defined as "foods or beverages manufactured through controlled microbial growth and enzymatic conversion of major and minor food components."[1] Fermented (or cultured) milks, in particular, are made by the addition of suitable bacteria to usually heat-treated animal milk, followed by incubation to reduce the pH, with or without coagulation pretreatment. The most common examples of fermented milks are yogurt, cultured cream and buttermilk, and kefir, although many variations of these products exist based on historical practices, geography, and type of milk. Nonetheless, yogurt is generally defined as a cultured milk product made using *Streptococcus thermophilus* and *Lactobacillus delbrueckii* subsp *bulgaricus*.[2] In most regions, the microbes must be alive and abundant (containing at least $10^7$ cfu/g). Again, depending on region, additional microbes that belong to the genera *Lactobacillus* and *Bifidobacterium* are also added to provide health benefits, and these so-called probiotic or bio-yogurts now account for much of the yogurt market.[3]

Decades of research suggests that consumption of fermented foods, especially fermented milk products, is associated with improved health outcomes. Although milk and dairy products are included in nearly every national dietary guideline, only a few of these specifically recommend fermented foods.[4–6] Recently, several researchers have proposed that sufficient evidence now exists to consider yogurt and other fermented dairy products that contain live bacteria when developing dietary strategies for improving health.[6–9]

The human gastrointestinal (GI) tract is colonized by a diverse and complex population of more than a trillion microbes. The gut microbiota performs many critical functions, including protecting the host against potential pathogens, extracting nutrients from dietary constituents, and modulating digestive and immune homeostasis.[10] Although it is well established that the adult human microbiome is relatively stable,[11,12] antibiotics, diet, disease, hygiene, and other factors can disturb the composition and function of this ecosystem.[13] Both the microbes associated with the manufacture of fermented foods, as well as microbes added as probiotics, may influence not only the gut microbiota but also other physiological functions. Some of the microbes found in fermented dairy foods have been shown to survive digestion, and reach the distal GI tract.[1,14–16] However, survival of the 2 species used in the manufacture of yogurt beyond the proximal GI tract is less clear.[17–19]

Lactic acid bacteria are the major microbes used in yogurt and dairy fermentations, although a diverse range of other organisms are used in other fermentation processes. Among the lactic acid bacteria, *Lactobacillus*, *Streptococcus*, *Lactococcus*, and *Leuconostoc* are most frequently found in fermented dairy foods, either as starter cultures or as naturally occurring members of the raw material. However, some fermented foods, especially yogurt and other fermented milk products, may also contain added probiotic species of *Bifidobacterium* and *Lactobacillus*. Probiotics are currently defined "as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host."[20]

The role of fermented milk products on human health has been the subject of extensive research, including epidemiological, observational, and clinical studies. The purpose of the present study was to perform a systematic review of the published literature to evaluate the effect of fermented milk consumption on specific critical health outcomes, including GI health and disease, cardiovascular health and disease, cancer risk, weight management, diabetes and metabolic health, and bone density.

## METHODS

### Eligibility criteria

The protocol for this systematic review was registered with PROSPERO (registration no. CRD42017068953). A systematic computerized search was performed and optimized using the PubMed database to identify studies published from its inception to 2017. The search strategy was limited to articles written in English language only. The search terms included "yogurt," "kefir," and "other fermented milks" as the subjects of interest, as well as search terms related to aligned health outcomes, including, but not limited to, "digestive health," "obesity," "cardiovascular disease," and "bone density." Included were all interventional and observational studies conducted among children aged over 2 years and adults without age restriction that reported one or more health outcomes associated with yogurt or fermented milk consumption. These health outcomes included GI and cardiovascular health, cancer risk, weight management, diabetes and metabolic health, and bone density. No restrictions were placed upon the geographic location of studies or the date of publication. Systematic or narrative reviews, conference or dissertation abstracts, and general information articles were excluded. Study selection was completed using the steps outlined in the Academy of Nutrition and Dietetics' *Evidence Analysis Manual*, which uses the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) model

Search terms and strategy:
1. ((((((((((((((((((((((((((((((((((((((((((((((((((((((((yoghurt[ti] OR yogurt[ti]) OR yogurt*[Title/Abstract]) OR yoghurt*[Title/Abstract]) OR fermented milk[Title/Abstract]) OR cultured milk[Title/Abstract]) OR yogurt[MeSH Terms]) OR kefir[MeSH Terms]) OR "Fermented milk"[Title/Abstract]) OR acidophilus milk[Title/Abstract]) OR yogurt) OR yoghurt) OR fermented milk) OR kefir[Title/Abstract]))
2. AND
a. (((((((((((((((((((((((((diabetes) OR diabetes mellitus[MeSH Terms]) OR diabet*[tiab] OR ''type 2 diabetes mellitus''[tiab]) OR diabetes mellitus[tiab]) OR ''type 2 diabetes''[tiab]) OR Diabetes Mellitus, Type 2[MeSH] OR diabet*) OR prediabetic state[MeSH Terms]) OR prediabet*) OR hyperglycemia[MeSH Terms]) OR ''fasting blood glucose''[tiab] OR blood glucose[MeSH Terms]) OR blood glucose[tiab]) OR glucose intolerance) OR insulin resistance[MeSH Terms]) OR Metabolic Syndrome[tiab]) OR metabolic syndrome X[MeSH Terms]]) OR ((lipid) AND profile)))[tiab] OR ((glycemic) AND control))[tiab] OR glycemia[tiab]))
b. OR ((((((((((((((((((((((((((digestive system[MeSH Terms]) OR digestive system diseases[MeSH Terms]) OR gastrointestinal motility[MeSH Terms]) OR gastrointestinal tract[MeSH Terms]) OR constipation[MeSH Terms]) OR constipation[Title/Abstract]) OR diarrhoea[Title/Abstract]) OR diarrhea[Title/Abstract]) OR diarrhea[MeSH Terms]) OR gastrointestinal microbiome[MeSH Terms]) OR gastrointestinal disease[MeSH Terms]) OR pouchitis[MeSH Terms]) OR helicobacter pylori infection[MeSH Terms]) OR lactose intolerance[MeSH Terms]) OR lactose digestion[Title/Abstract]) OR clostridium difficile infection[MeSH Terms]) OR "transit"[Title/Abstract]) OR "bowel habit"[Title/Abstract]) OR "urgency"[Title/Abstract]) OR "stool quantity") OR "stool frequency"[Title/Abstract]) OR "stool consistency") OR "digestive symptom"[Title/Abstract]) OR "flatus"[Title/Abstract]) OR "bloating"[Title/Abstract]) OR "visceral hypersensitivity") OR "gas evacuation"[Title/Abstract]) OR "abdominal distension"[Title/Abstract]) OR flatulence[MeSH Terms]) OR IBS[Title/Abstract]) OR irritable bowel syndrome[MeSH Terms]))
c. OR ((((((((((((((((((((((((((((("body size"[Title/Abstract]) OR body size[MeSH Terms]) OR growth[Title/Abstract]) OR obesity[Title/Abstract]) OR obese[Title/Abstract]) OR obesity[MeSH Terms]) OR overweight[Title/Abstract]) OR overnutrition[Title/Abstract]) OR adiposity[Title/Abstract]) OR adiposity[MeSH Terms]) OR "body weight"[Title/Abstract]) OR body weight[MeSH Terms]) OR "body-weight related"[Title/Abstract]) OR "weight gain"[Title/Abstract]) OR weight gain[MeSH Terms]) OR "weight loss"[Title/Abstract]) OR "weight-loss"[Title/Abstract]) OR "weight-gain"[Title/Abstract]) OR (Body Weights and Measures[MeSH Major Topic])) OR "Body Composition"[MeSH Terms]) OR "body fat"[Title/Abstract]) OR adipos*[Title/Abstract]) OR weight[Title]) OR "Anthropometry"[Mesh:noexp]) OR "body mass index"[Title/Abstract]) OR BMI[Title/Abstract]) OR "weight status"[Title/Abstract]) OR adipose tissue[MeSH Terms]) OR "healthy weight"[Title/Abstract]) OR waist circumference[MeSH Terms]) OR "body fat mass"[Title/Abstract]) OR body weight changes[MeSH Terms]) OR "waist circumference"[Title/Abstract]) OR ideal body weight[MeSH Terms]))
d. OR ((((((((((((((cardiovascular diseases[MeSH Major Topic]) OR heart[Title/Abstract]) OR cardiac[Title/Abstract]) OR coronary[Title/Abstract]) OR hypertension[MeSH Major Topic]) OR hypertens*[Title/Abstract]) OR blood pressure[MeSH Terms]) OR "blood pressure"[Title/Abstract]) OR "metabolic syndrome"[Title/Abstract]) OR cerebrovascular[Title/Abstract]) OR metabolic syndrome x[MeSH Major Topic]) OR hypercholesterolemia[MeSH Terms]) OR dyslipidemias[MeSH Terms]) OR cholesterol, ldl[MeSH Terms]) OR Cholesterol, blood[MeSH Terms]) OR lipoproteins, hdl[MeSH Terms]) OR lipoproteins, ldl[MeSH Terms]))
e. OR ((((((("Colorectal Neoplasms"[MeSH Terms]) OR "polyps"[MeSH Terms]) OR "lung neoplasms"[MeSH Terms]) OR "Prostatic Neoplasms"[MeSH Terms]) OR "Breast Neoplasms"[MeSH Terms]) OR (cancer[tiab] OR cancers[tiab] OR cancerous[tiab] OR neoplasm*[tiab] OR carcinogen*[tiab] OR "Carcinogens"[Mesh] OR tumor[tiab] OR tumors[tiab] OR tumour*[tiab] OR carcinoma*[tiab] OR adenocarcinoma*[tiab] OR sarcoma*[tiab] OR metastasis[tiab] OR metastases[tiab] OR polyp*[ti]) AND (colonic*[tiab] OR colon[tiab] OR colorect*[tiab] OR rectal OR rectum OR breast*[tiab] OR mammary[tiab] OR prostate*[tiab] OR prostatic[tiab] OR lung[tiab])))

*Figure 1* **Search terms and strategy.**

f.   OR (((((((((((("Bone Density"[MeSH Terms]) OR "Fractures, Bone"[MeSH Terms]) OR "Bone Diseases"[MeSH Terms]) OR osteoporosis[Title/Abstract]) OR bone[Title/Abstract]) OR fracture*[Title/Abstract]) OR "bone density"[Title/Abstract]) OR (bone[ti] OR bones[ti]) AND health*[ti])) OR bone health*[Title/Abstract]) OR "Bone Demineralization, Pathologic"[MeSH Terms]) OR bone mineral*[Title/Abstract] OR bone demineral*[Title/Abstract])))))))

3.   AND (((((((((((((((((((((trial[tiab]) OR longitudinal[Title/Abstract]) OR retrospective[Title/Abstract]) OR prospective[Title/Abstract]) OR Prospective Studies[MeSH] OR cross-sectional studies[MeSH Terms]) OR observational study[ptyp]) OR observational[Title/Abstract]) OR controlled[Title/Abstract]) OR Cohort Studies[MeSH Terms]) OR case-control[Title/Abstract]) OR cohort[Title/Abstract]) OR follow-up studies[MeSH Terms]) OR Follow-up[Title/Abstract]) OR Support of Research[Publication Type]) OR Study Characteristics[Publication Type]) OR placebo-controlled[tiab] OR Randomized Controlled Trial[Publication Type]) OR "crosssectional"[All Fields] OR "cross-sectional"[All Fields] OR Epidemiologic Studies[MeSH]) OR Clinical Trial[Publication Type]))))))

NOT (((((((in vitro[tiab]) OR in vitro techniques[MeSH])) NOT (((in vivo[tiab]) OR humans[tiab]) OR humans[MeSH])) OR (((((((comment[Publication Type]) OR news[Publication Type]) OR review[Publication Type]) OR letter[Publication Type]) OR systematic review[Publication Type]) OR case reports[Publication Type])

*Figure 1* **(Continued)**

([Figure S1](); *please see the Supporting Information online*). The eligibility criteria are described in [Table 1](), using the PICOS (population, intervention, comparison, outcome, and study design) format as well as the search terms described in [Figure 1](). Restrictions were placed on age to exclude studies that exclusively evaluated children aged under 2 years. The outcomes were based on the systematic review protocols of the Nutrition Evidence Library, which has historically been used in the United States to develop the Dietary Guidelines for Americans. Only peer-reviewed published journals were considered. Randomized controlled trials, randomized crossover trials, cohort studies, case-control studies, and cross-sectional studies were eligible for inclusion if a fermented milk product was the dietary component under study.

The title, abstract, and keywords of identified records were initially screened for the health outcomes of interest. Only human studies using fermented milk products were included. Clinical trials with nonbovine milk, milk that had not undergone fermentation, and acidified milk as the test product were excluded. Clinical trials with milk and acidified milk used as the comparator/control were included. Full texts were obtained for all relevant studies.

Data were extracted and entered into a data extraction form, which included population characteristics and follow-up period, dietary assessment and endpoints, summary of results, and outcomes.

The quality of the studies, which reflected risk of bias, was assessed independently by both authors using the Quality Criteria Checklist in the Nutrition Evidence Library of the Academy of Nutrition and Dietetics, based on the Agency for Healthcare Research and Quality domains for research studies.[21] The latter is used by the Academy of Nutrition and Dietetics when conducting systematic reviews for its Evidence Analysis Library. The Quality Criteria Checklist was used to assess the methodological quality of individual studies using 10 criteria. These criteria were designed specifically to assess the validity of the research design, and included the following questions: (1) Is there a clearly specified research question? (2) Was the selection of subjects free from bias? (3) Were study groups comparable? (4) Was the method of handling withdrawals described? (5) Was blinding used to prevent bias? (6) Was the intervention described in detail? (7) Were outcomes clearly defined and the measures valid and reliable? (8) Was the statistical analysis appropriate for the study design and outcome? (9) Were conclusions supported by results? (10) Is a bias due to the study's funding or sponsorship unlikely? These criteria are derived from the quality constructs and domains identified by the Agency for Healthcare Research and Quality report on Systems to Rate the Strength of Scientific Evidence. Based on meeting the criteria cited in the Quality Criteria Checklist for each area, studies were designated as positive, neutral, or negative quality. If the answers to validity questions 2, 3, 6, and 7 were rated with a "Yes" by both authors/reviewers, along with at least one additional "Yes", then the study was rated as "positive quality." If the answers to validity questions 2, 3, 6, and 7 were rated as "No" by both authors/reviewers, then the study was rated as "neutral quality." If most (6 or more) of the answers to the questions were rated "No," the report was designated as a "negative quality" study. Any discrepancies between the 2 reviewers were resolved by discussion. A third reviewer was not necessary to resolve discrepancies. The results of the search process are described below.

*Table 1* **PICOS criteria for inclusion and exclusion of studies**

| Parameter | Criterion |
|---|---|
| Participants | Children over the age of 2 y and adults ≥18 y |
| Intervention | Yogurt, kefir, fermented milks |
| Comparator | Milk (unfermented) or acidified milks (defined as unfermented milk to which acid has been added) |
| Outcome | Major health outcomes, including gastrointestinal and cardiovascular health, cancer risk, weight management, diabetes and metabolic health, and bone density |
| Study design | Only peer-reviewed published journals were considered. Randomized controlled trials, randomized crossover trials, cohort studies, case-control studies, and cross-sectional studies were eligible for inclusion if a fermented milk product was the dietary component under study. |

## RESULTS

The search criteria returned a total of 1057 citations. After abstract review and full-text review, 108 studies (Figure 2) were included in the final review, as follows: 31 randomized controlled trials (RCTs), 15 randomized crossover trials (RCOTs), 6 case-control (CC) studies, 16 cross-sectional (CS) studies, 1 nonrandomized controlled trial, and 39 cohort studies. Of the 108 studies, 76 showed a favorable outcome of fermented milk products on health. Twenty-eight studies showed no significant effect on health (depending on whether the study was an RCT, epidemiological, or observational). A neutral outcome or no significant effect on health was not a negative effect. Rather, intervention caused no response. In 4 studies, unfavorable outcomes (associations with disease) were reported; these were cohort studies.

Thirty-eight of the 108 included studies were rated as positive quality according to the Quality Criteria Checklist, and 24 of those 38 positive-quality studies reported a favorable outcome of fermented milk products on health. Fourteen of the 38 positive-quality studies reported no significant effect. None of the positive-quality studies reported an unfavorable outcome of fermented milk products on health. Of the remaining 70 studies, 67 were rated as neutral quality, and 14 reported a favorable outcome. Below we present the specific results for each of the health outcomes reviewed.

### GI health and disease

Included were 26 studies evaluating the impact of yogurt and cultured fermented milk on GI health and disease[22–47]; 16 were RCTs,[22–27,29,32,35,37,39,42–44,46,47] 8 were RCOTs,[30,31,33,34,36,38,40,41] 1 was a nonrandomized controlled trial,[45] and 1 was a CS study.[28] Twenty[22–24,27–36,38–41,45–47] of the 26 studies showed a favorable outcome for GI health with yogurt or fermented milk consumption, and 6 studies[25,26,37,42–44] showed no effect. Based on the quality criteria (see Methods section), 19 studies[23–26,30–38,40,42–44,46,47] of the 26 studies were considered positive quality (see

summary in Table 2). Among these, 11 studies[23–26,32,35,37,42–44,46] evaluated GI symptoms including bloating, gas and abdominal discomfort, diarrhea, and constipation following consumption of fermented milk products. Another 7 studies[30,31,33,34,36,38,40] measured lactose digestion and tolerance, and 1 study[47] measured colonic permeability. Yogurt was the fermented product evaluated in 19[22–26,29,31–33,36–44,46] of the 26 studies, whereas 7 studies[27,28,30,34,35,45,47] evaluated kefir or other cultured milk products.

### Lactose digestion and tolerance

Seven positive-quality RCTs demonstrated that yogurt or kefir with live, active cultures significantly enhanced lactose digestion and reduced symptoms of intolerance in lactose maldigesters.[30,31,33,34,36,38,40] Studies included subjects ranging in age from 7 months to 53 years and compared consumption of yogurt with consumption of low-fat or whole milk, acidophilus milk, buttermilk, or lactose in water. Consumption of yogurt improved lactose digestion, as indicated by a reduction in breath hydrogen, and improved tolerance as measured by self-reported symptoms. Hertzler and Clancy[30] fed yogurts and kefir to lactose maldigesters, and both products improved lactose digestion and reduced symptoms of intolerance compared with milk. Kolars et al[31] fed yogurt, lactose-free milk, and milk to maldigesters and showed that yogurt improved lactose digestion and tolerance. They also reported the presence of active microbial beta-galactosidase in the intestinal contents of subjects.

Martini et al[33] compared lactose digestion and tolerance after feeding flavored and frozen yogurts, ice cream, and ice milks. Lactose digestion was improved significantly only with fresh yogurt, which was also the only product that did not cause GI symptoms among the subjects. Martini et al[34] compared yogurts made with different strains of *L delbrueckii* subsp *bulgaricus* and *S thermophilus* along with milk fermented with single strains of *L delbrueckii* subsp *bulgaricus*, *S thermophilus*, *Lactobacillus acidophilus*, and *Bifidobacterium bifidus*. The improvement in lactose digestion varied. The milk fermented with *B bifidus* only marginally
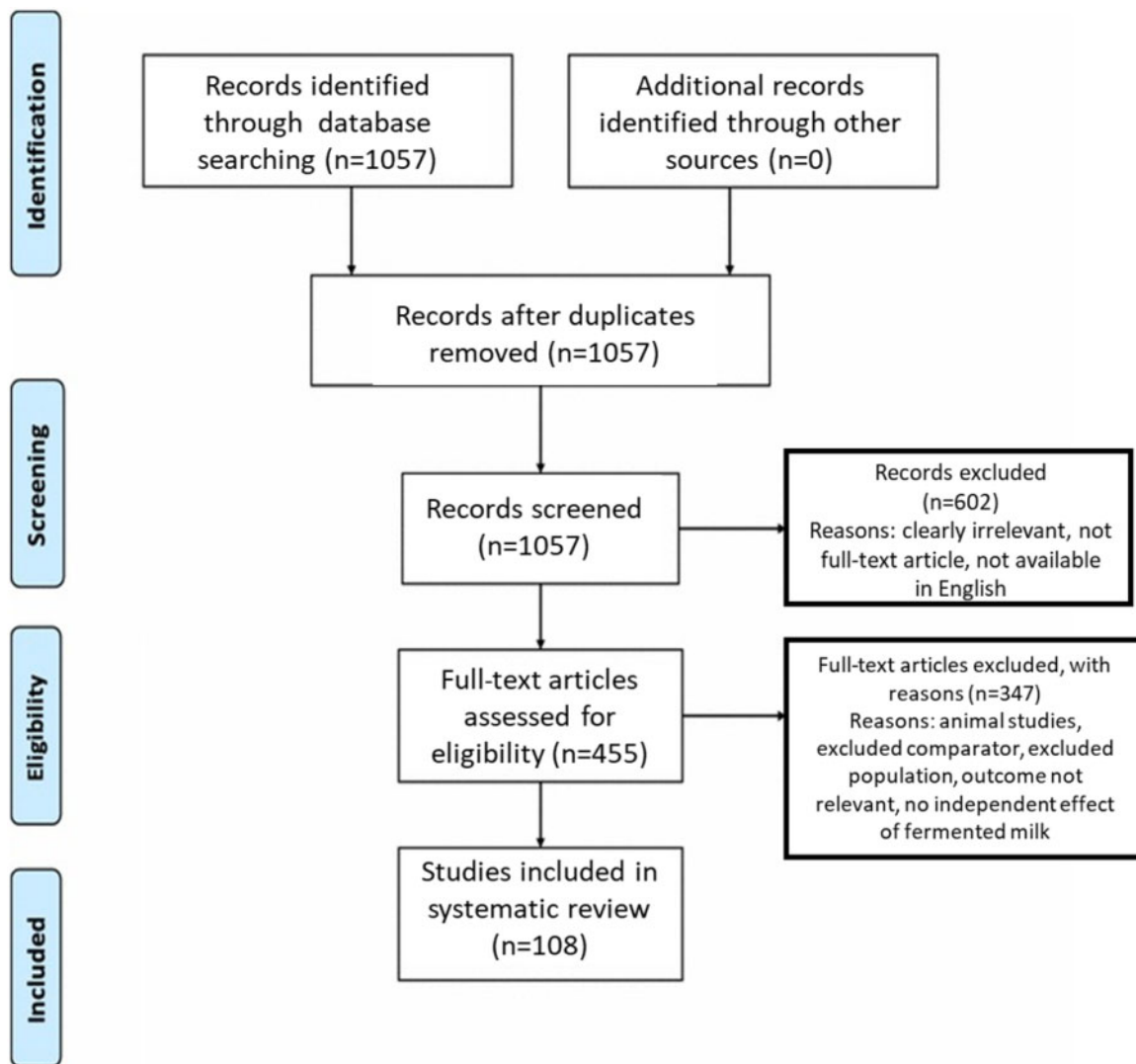
*Figure 2* **Flow diagram of the literature search process.**

improved lactose digestion, whereas milk fermented with *S thermophilus* and *L delbrueckii subsp bulgaricus* (ie, yogurt bacteria) resulted in significant improvements. Onwulata et al[36] found that yogurt was better tolerated than milk treated with commercial lactase. However, pasteurization of yogurt eliminated the enhanced digestion of lactose.[40] Rosado et al[38] fed both lactose-containing and lactose-hydrolyzed yogurt to maldigesters and reported both similarly improved lactose digestion. Finally, Savaiano et al[40] compared lactose digestion from yogurt, pasteurized yogurt, sweet (nonfermented) acidophilus milk (homogenized, pasteurized milk inoculated with *L. acidophilus* NCFM strain), and cultured milk (buttermilk). Only fresh yogurt significantly improved lactose digestion and tolerance. In one neutral-quality study, Shermak et al[41] also demonstrated improved lactose digestion from, and tolerance to, yogurt.

**Diarrhea and constipation**

Ten studies evaluated the effects of fermented milk products on diarrhea and/or constipation.[22,24–28,35,44–46] Included were 6 positive-quality studies,[24–26,35,44,46] 3 neutral-quality studies,[22,27,45] and one negative-quality study.[28] In one of the positive-quality studies, Boudraa et al[24] reported improvement in outcomes associated with diarrhea, while in another positive-quality study Yang et al[46] reported improvement in constipation outcomes following consumption of fermented milk. A third study by Nagata et al[35] reported improvements in both. Three positive-quality studies – conducted by Boudraa et al,[25] Conway et al,[26] and Tabbers et al[44] – reported no improvement relative to milk controls.

Among the neutral- and negative-quality studies, Agarwal et al,[22] de Vrese et al,[27] Glibowski and Turczyn,[28] and Van den Nieuwboer et al[45] all reported

Table 2 **Summary of studies**

| Area studied | Total no. of studies | Study types | No. of positive-quality studies | No. of neutral-quality studies | No. of negative-quality studies | Fermented products studied | Comparators | No. of studies with favorable outcome | No. of studies with no significant effect | No. of studies with unfavorable outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| Gastrointestinal health and disease | 26 | RCT=16 RCOT=8 CS=1 NRCT=1 | 19 | 6 | 1 | Yogurt, fermented milk, fermented milk drinks, pasteurized yogurt, probiotic yogurt, kefir | Dahi, ultra-heated yogurt, non-fermented dairy product, milk, pasteurized yogurt, acidified milk, yogurt, lactose water, ice cream, ice milk, frozen yogurt, hydrolyzed lactose milk, lactase tablet, fermented/cultured milk | 20 | 6 | 0 |
| Cardiovascular health and disease | 28 | RCT=7 RCOT=5 CC=1 CS=4 CH=11 | 8 | 19 | 1 | Yogurt, probiotic yogurt, fermented milk, probiotic fermented milk with added biopeptides | Chemically fermented dairy, pasteurized yogurt, 2% butterfat milk, probiotic cheese, probiotic yogurt, nonfermented dairy product, 2% milk, nonfat milk, low-fat yogurt, no milk, no yogurt | 16 | 11 | 1 |
| Weight | 22 | RCT=5 CS=8 CH=9 | 7 | 15 | 0 | Yogurt, kefir | Milk, chemically fermented milk, isoenergetic sucrose beverage, low-dairy calcium diet | 19 | 3 | 0 |
| Cancer | 17 | RCT=1 CC=5 CH=11 | 1 | 16 | 0 | Yogurt, fermented milk | No yogurt | 9 | 5 | 3 |
| Diabetes | 9 | RCT=1 RCOT=2 CS=1 CH=5 | 2 | 5 | 1 | Yogurt, probiotic in fermented milk | Sweetened yogurt, skim milk, orange juice, no supplementation, nonfermented milk | 7 | 1 | 0 |
| Bone health | 7 | RCT=1 CS=3 CH=3 | 1 | 6 | 0 | Yogurt, laban | No yogurt | 5 | 2 | 0 |

*Abbreviations*: CC, case-control (study); CH, cohort (study); CS, cross-sectional (study); NRCT, nonrandomized controlled trial; RCOT, randomized crossover trial; RCT, randomized controlled trial.

improved treatment or reduced incidence of diarrhea with fermented milks. Agarwal et al[22] fed milk fermented with *Lactobacillus casei* to patients in a clinical setting, comparing diarrheal outcomes with patients fed Indian dahi (curd) and ultra-heated yogurt. Diarrhea was significantly improved in the hospital, but not in the community setting with *L casei* milk, perhaps because of patient compliance. de Vrese et al[27] reported improved treatment of antibiotic-related diarrhea with fermented milk in patients with *Helicobacter pylori*, and Van den Nieuwboer et al[45] reported improved bowel habits (reduced frequency and severity of diarrhea and constipation) with a probiotic fermented milk among elderly patients in a nursing home. Finally, Glibowski and Turczyn[28] found an inverse correlation between fermented milk consumption and problems with bowel evacuation and diarrhea.

### Miscellaneous GI symptoms

In one neutral-quality study, Guyonnet et al[29] fed yogurt with added *Bifidobacterium lactis* to 371 adults with self-reported digestive symptoms and found improvement in symptoms compared with a nonfermented milk. Marteau et al[32] fed the same yogurt with added *B lactis* and a nonfermented control milk product to a similar population in a positive-quality study, reporting improvements in GI well-being and digestive symptoms when pooling data from the study by Guyonnet et al[29] with their own. Composite scores of digestive symptoms (combining the Bristol scale and the Food Benefits Assessment questionnaire), but not GI well-being, were improved in the Marteau et al[32] study population.

### Irritable bowel syndrome

Five positive-quality studies evaluated the potential for fermented milk products to improve symptoms in patients with irritable bowel syndrome (IBS).[23,37,42,43,47] Agrawal et al[23] fed a fermented *B bifidus* milk to IBS patients and reported reduced stomach distension and an acceleration of orocecal and colonic transit, as well as reduced symptoms, compared with a nonfermented milk product. Zeng et al[47] fed IBS patients a probiotic fermented milk containing *S thermophilus*, *L delbrueckii* subsp *bulgaricus*, *L acidophilus*, and *Bifidobacterium longum* and reported a reduction in colonic permeability and a favorable effect on mean global IBS scores as compared with an unfermented milk control in a 4-week study. In contrast, Roberts et al[37] reported no improvement in IBS symptoms with fermented probiotic milks. Simren et al[42] reported an initial favorable effect, which was matched by the control at 8 weeks. Similarly,

Sondergaard et al[43] reported improvement in IBS symptoms in both the fermented milk and control groups after 8 weeks.

### Cardiovascular health and disease

Twenty-eight included studies evaluated the impact of yogurt and fermented milk on cardiovascular health and disease.[48–75] Eight studies[49,52,58,60,66,69,72,73] were of positive quality, 19 studies[48,50,53–57,59,62–65,67,68,70,71,74,75] were neutral quality, and 1 study[51] was negative quality. Seven studies were RCTs,[49,50,60,61,69,72,73] 5 were RCOTs,[52–56,58,66] 11 were cohort studies,[50,54,55,59,62–64, 67,68,71,74] 1 was a CC study,[75] and 4 were CS studies.[48,53,65,70] The studies assessed the effect of fermented milk products on cardiovascular disease and cardiovascular markers, coronary heart disease risk factors, metabolic syndrome, risk of stroke, and heart health–related risk factors, including low-density lipoprotein (LDL) cholesterol, triglycerides, and blood pressure (BP). Twenty-one studies[48,50,51,53–57,59,62–70,72–74] evaluated yogurt as the fermented product used, and 7 studies[49,52,58,60,61,71,75] evaluated fermented milk, not classified as yogurt per United States and European standards. Of the 28 studies, 16 studies[49–51,53,54,56–62, 65,71,74,75] demonstrated a favorable outcome for yogurt and fermented milk on cardiovascular outcomes, and 11 studies[48,52,55,64,66–70,72,73] demonstrated no significant effect. One study, a well-controlled (>26 000 participants) large prospective cohort of high-risk Finnish male smokers,[63] reported an association between yogurt consumption and increased risk of subarachnoid hemorrhage, but not between yogurt consumption and cerebral infarction or intracerebral hemorrhage. However, no association was found for sour-milk consumption. The authors suggested that other factors in cream – in particular, conjugated linoleic acid – may have accounted for this result.

### Hypertension

Four positive-quality RCTs examined the effect of fermented milk products on hypertension and BP.[58,60,72,73] Inoue et al[58] fed either a placebo (n = 15) or milk fermented with *L casei* strain Shirota and *Lactococcus lactis* YIT 2027 (n = 20) to mildly hypertensive men and women in an RCT. These strains, in concert, were shown to produce aminobutyric acid at 10–12 mg/ 100 mL during the fermentation. Significant decreases were observed for diastolic BP and systolic BP within 2 or 4 weeks, respectively, and for mean BP at 4 weeks between baseline and treatment for subjects consuming the fermented milk product. All 3 measures remained lower throughout the 12-week intake period. For the

subjects consuming the fermented milk product, significant differences between treatment and placebo were observed in systolic BP after 4 and 12 weeks (13.4 ± 4.1 and 17.4 ± 4.3 mmHg, respectively).

Jauhiainen et al[60] conducted an RCT with hypertensive adults who consumed a fermented milk product containing bioactive peptides resulting from fermentation with *Lactobacillus helveticus* strain LBK-16H. Compared with the placebo group, subjects in the fermented milk group experienced significant decreases in systolic and diastolic BP (4.1 and 1.8 mmHg, respectively).

In another RCT, Usinger et al[72] fed milk fermented with an angiotensin-converting enzyme–inhibitory peptide-producing strain of *L. helveticus* to 94 prehypertensive and borderline hypertensive subjects. Daily consumption of either 150 mL or 300 mL of the fermented milk did not influence BP compared with the placebo. However, at the higher feeding level, within-group reductions in BP were observed. Thus, the authors concluded that consumption of 300 mL fermented milk containing bioactive peptides may have a modest effect on BP. In a companion study (Usinger et al),[73] angiotensin-converting enzyme–inhibitory activity in these subjects was measured; however, the fermented milk product did not reduce angiotensin-converting enzyme activity.

Neutral-quality studies evaluating the effect of fermented milk on BP generally showed a favorable effect.[61,74] In the Kawase et al[61] study, systolic BP was lowered significantly (by about 5 mmHg) after 8 weeks of consumption of fermented milk containing *L casei* and *S thermophilus*. Results from a cohort study of 2636 men and women aged 28–62 years (part of the Framingham Heart Study) showed that yogurt consumption for >15 years was associated with lower risk of hypertension.[74] After adjusting for demographic and lifestyle factors (including overall diet quality, total energy intake, metabolic factors, and medication use), consumption of one additional serving/wk of yogurt correlated with a 6% reduction in risk of developing incident hypertension. Masala et al[65] found an inverse association between yogurt consumption and systolic BP in a CS study of adults, aged 18–25 years. The authors concluded that the results support the beneficial effect of selected dairy products (milk and yogurt) but also cautioned that the effect could be interpreted as yogurt being an indicator of an overall 'health-conscious' attitude of the subjects. Hutt et al[57] investigated the effect of consuming a probiotic cheese or yogurt, compared with a control without the additional probiotic strain, on BP in healthy adults. The main effect of the consumption of probiotic cheese and yogurt was a modest, but statistically significant, decrease in diastolic BP, while consuming probiotic cheese was also linked to a significant reduction in systolic BP.

## Blood lipids

Three positive-quality studies evaluated the effect of fermented milk products on blood lipids.[49,66,69] In one RCT, Agerbaek et al[49] reported that milk fermented with *S thermophilus* and *Enterococcus faecium* lowered LDL 10% from baseline in 58 Danish adult men, all 44 years old. After 6 weeks of consuming a fermented milk product, total and LDL cholesterol were reduced as compared with placebo. Total cholesterol was reduced by 0.37 mmol/L vs 0.02 mmol/L for the chemically acidified milk used as the control ($P < 0.01$). Richelsen et al[69] fed of identical composition fermented milk and acidified milk control to 87 healthy adults – male and female, aged 50–70 years, with normal cholesterol levels. After 1 month, total and LDL cholesterol were significantly reduced in the fermented milk group compared with the control. Maximum reduction occurred at 3 months (LDL −0.32 mmol/L). Interestingly, however, the placebo group also showed a gradual reduction in LDL cholesterol over the 6-month duration of the study. Thus, although both groups showed a similar reduction in total and LDL cholesterol at the end of the study (6 mo), no statistically significant response for the intervention compared with the placebo was observed. Men and women responded similarly to the intervention. The authors concluded that milk may have a hypocholesterolemic effect but they did not provide an explanation for the more rapid response to fermented milk. Another positive-quality RCT was reported by Massey.[66] Female college students consumed 480 mL of 2% fat yogurt for 4 weeks, then no yogurt for 4 weeks, in a crossover trial. Yogurt consumption had no effect on total cholesterol, triglycerides, high-density lipoproteins, or distribution of lipoprotein fractions.

Several neutral-quality studies supported the finding that fermented milks are hypocholesterolemic. Kawase et al[61] conducted an RCT with 20 men aged 30–51 years with elevated total cholesterol and found that consuming 200 mL of fermented milk twice a day for 8 weeks resulted in an increase in high-density lipoproteins. Subjects in 2 RCTs by Hepner et al[56] of adults aged 21–55 years, who consumed either pasteurized or nonpasteurized yoghurt for 12 weeks, experienced reductions of 5% and 10% in total cholesterol, respectively. As both pasteurized and nonpasteurized yogurt resulted in lowering of serum cholesterol levels, it was suggested that a milk component may have contributed to the cholesterol-lowering effect. Kawase et al[61] conducted an RCT involving 20 men and women aged 30–

51 years and found that consuming fermented milk for 8 weeks resulted in a decrease in triglycerides.

Four studies found no significant association between cardiovascular risk factors and consumption of yogurt or fermented or sour milk.[64,66,72,73] Likewise, no consistent associations were found between intakes of total milk, low-fat milk, fermented milk products, cheese, or yogurt, and stroke incidence, stroke mortality, or coronary heart disease incidence or coronary heart disease mortality in a subset of subjects in the Rotterdam cohort study.[68]

Collectively, the published reports suggest that the hypertension-lowering effects of fermented milk products may depend on the specific bacteria used during fermentation. Additional positive-quality studies comparing the effects of specific strains on BP are needed. Several neutral-quality studies support the hypocholesterolemic effect of fermented milks.

## Cancer risk

Seventeen studies – 1 positive quality and 16 neutral quality – evaluated the effect of yogurt and cultured fermented milk on colorectal, breast, and prostate cancer risk or biomarkers.[76–92] Of these, 1 study[78] was an RCT, 11 were cohort studies,[76,79–85,87,91,92] and the remaining 5 were CC studies.[77,86,88–90] Yogurt was evaluated in 13[76,80,82–88] of the 17 studies and 4[81,89–92] evaluated fermented milk not classified as yogurt. The one positive-quality study was an RCT[78] in which the authors assessed cell-mediated immune function (lymphocyte proliferation assays) as a proxy for cancer protection. No differences were observed in immune function between young women (n = 13) who consumed 2 cups of yogurt per day for 3 months and young women who did not consume yogurt (n = 12). The authors related immune function measurements to risk of breast cancer. Nine studies[77,84–87,89–92] out of 17 showed a favorable outcome for yogurt and fermented milk on cancer outcomes, 5 studies[76,78–81] demonstrated no significant effect, and 3 studies[82,83,88] demonstrated an unfavorable outcome.

## Colorectal cancer

Seven neutral-quality studies assessed yogurt or buttermilk consumption and risk of colorectal cancer or colon cancer risk factors.[77,79,81,84,85,87,88] Using cohort data based on the European Prospective Investigation into Cancer and Nutrition (EPIC) study, Pala et al[85] reported that yogurt consumption was inversely associated with colorectal cancer risk, when comparing highest to lowest intakes based on a prospective study of 45 241 volunteers and 289 diagnosed cases of colorectal

cancer. Murphy et al[84] extended these findings using EPIC data and observed an inverse relationship between yogurt consumption and colon cancer occurrence, based on 477 122 volunteers and 4513 cases of colorectal cancer. This relationship was also true for milk in multivariable models but weakened to nonsignificant in linear models. Further, Kampman et al[81] found that yogurt and buttermilk separately exhibited a weak inverse relationship with colorectal cancer in highest vs lowest intake groups in a cohort study of more than 3000 elderly men and women. The authors concluded that intake of fermented dairy products was not significantly associated with colorectal cancer risk in this population. Similarly, in a cohort study, Dik et al[79] found no association between historical prediagnosis intake of yogurt (highest vs lowest quartiles) and diagnosed colon cancer, and colorectal cancer-specific or all-cause death, using EPIC data with 3859 cases of colorectal cancer.

Boutron et al[77] and Senesse et al[87] published CS studies that revealed an inverse association between large-adenoma diagnosis and yogurt consumption. In the Boutron study,[77] the association differed by sex. In men, only the highest level of intake was associated with a reduced risk, whereas in women a reduced risk was observed among those who consumed vs those who did not consume yogurt. In another CS report,[88] investigators found that consumption of labaneh, but not yogurt, was associated with an increased risk of colorectal cancer. Labaneh is a strained yogurt made from whole milk that contains 10% fat, and the authors suggested the saturated fat may account for the increased risk.

## Breast cancer

Three neutral-quality CC studies[86,89,90] and 3 cohort studies[76,91,92] examined associations between consumption of fermented milk products and breast cancer risk. In a CC study in the Netherlands with 133 incident breast cancer cases and 289 controls, van't Veer et al[89] found that yogurt and buttermilk consumption was associated with a decreased risk of breast cancer with an odds ratio of 0.63/g. However, milk consumption did not result in a similar correlation. In a later study, Van't Veer et al[90] expanded this cohort to 168 breast cancer cases and 548 controls, and observed that combining factors relating to low fat, high fiber, and high consumption of fermented milk products resulted in an odds ratio of 0.33. Ronco et al,[86] in a CC study involving 111 breast cancer diagnoses and 222 frequency-matched controls, found a significant inverse association between consumption of skim-milk yogurt/total yogurt and breast cancer in a dose-response pattern. In the Malmö Diet and Cancer cohort of 17 000 women, Wirfält et al[91] found consumption of fermented milk

products, including yogurt (<0.5%–7% fat), was associated with a decreased risk of breast cancer (hazard ratio = 0.89). In a follow-up study, Wirfalt et al[92] observed that consumption of milk fat contained within fermented milk products was also associated with a decreased risk of breast cancer. In contrast, in a cohort study involving 9039 females, Berkey et al[76] found the risk for benign breast disease in girls consuming 1+ cup/d of yogurt was below that of smaller-intake categories.

## Prostate cancer

Two neutral-quality cohort studies found association between yogurt consumption and increased risk of prostate cancer when comparing highest to lowest consumption.[82,83] As part of the French SU.VI.MAX (Supplementation en Vitamines et Minéraux Antioxydants) study, dietary intakes of 2776 men, 69 of whom were diagnosed with prostate cancer, were analyzed. The association between yogurt intake and increased prostate cancer risk was found to be similar to that between all dairy foods and prostate cancer. The authors attributed their findings to a relationship between calcium intake and prostate cancer risk. Kurahashi et al[83] evaluated prostate cancer risk among 43 435 Japanese men aged 45–64 years. During the 7.5-year duration of the study, 329 men were diagnosed with prostate cancer. The relative risk of diagnosis in the highest consumption quartile was 1.52 – similar to that for other milk products.

Additional positive-quality studies are needed to determine whether yogurt or its microbial components can influence the risk, development, or treatment of cancers. The evidence suggests a favorable relationship between fermented milk consumption and reduction of risk for breast and colon cancer. It appears that the risk for prostate cancer from fermented dairy foods may not be different than the risk from dairy foods in general, but again, further studies are needed.

## Weight and body composition

Twenty-two included studies examined the relationship between consumption of yogurt and cultured fermented milk and weight and body composition[70,93–113]; 5 were RCTs,[96,107,108,112,113] 9 were cohort studies,[94,100–102, 104,106,109–111] and 8 were CS studies.[70,81,93–95,97–99,105] Six studies[96,97,107,108,112,113] were positive quality and focused on body composition, weight loss, obesity, and muscle soreness. The remaining 16 studies[70,98–106,109–111] were neutral quality. In 21 of the 22 studies,[93–95,97–113] subjects were fed yogurt, and in the remaining study[96] they were fed kefir. Eighteen of the 22 studies[94–107,]

[109–111,113] reported a favorable outcome for weight control or positive body composition effect, and 4 studies[70,93,108,112] reported no effect.

The 6 positive-quality studies comprised 5 RCTs[96,107,108,112,113] and one CS study.[97] Three of the positive-quality RCTs evaluated body composition changes with yogurt consumption; in one trial subjects were fed bifidobacteria-fermented milk, while in another they were fed kefir. Fathi et al[96] observed improved body composition and greater weight loss with kefir or milk. In another study, Takahashi et al[107] fed a bifidobacteria-fermented milk to mildly overweight Japanese subjects. The control was an acidified milk control, matched for nutrient composition, skim-milk powder, and calories. Visceral fat was reduced with the fermented milk, and fecal bifidobacteria were increased, suggesting a microbiome effect. Body weight, BMI, and waist-to-hip ratio did not change. Thomas et al[108] evaluated yogurt, as compared with an isoenergetic sucrose beverage, on postexercise changes in body composition. No significant group differences were observed. Similarly, White et al[112] found no improvement in body composition with yogurt feeding during a resistance training program. Zemel et al[113] fed yogurt to obese subjects as part of a 2-arm dietary restriction protocol. The rate of fat loss increased, and lean mass was spared, with yogurt, vs a lower-calcium control matched for macronutrients and fiber. Finally, in a CS study of adolescent European and Australian populations, Huybrechts et al[97] found that a dietary pattern associated with greater incidence of overweight and obesity, as measured by BMI, was characterized, in part, by a low intake of yogurt.

There were 15 neutral-quality studies.[70,93–95,98–106,109,111] Of these, 13 demonstrated significant correlations or associations between yogurt consumption and less obesity, lower body weight, lower adiposity, or reduced weight gain over time in both CS and cohort studies.

In summary, of the 7 positive-quality studies, only one showed a weight-loss difference (Zemel et al 2005).[113] Five showed no difference in weight loss. One was correlative and one showed a change in visceral fat, suggesting a microbiome role of *Bifidobacterium animalis* subsp *lactis*.[107] Most of the neutral-quality studies showed correlations between yogurt consumption and weight control. Performing RCTs with a focus on weight control is particularly problematic, based on the likely long duration of the necessary intervention and multiple external variables that are difficult, if not impossible, to control. The available studies on fermented dairy foods and body weight demonstrated a strong

correlation between fermented milk consumption and weight control. Such effects could be modulated by changes in the microbiome as suggested by Takahashi et al.[107]

### Diabetes risk and metabolic syndrome

*Diabetes risk.* Nine studies evaluating the impact of yogurt and cultured fermented milk on diabetes risk were included in this review[114–122]; 1 study was an RCT,[117] 2 were RCOTs,[116,118] 1 was a CS study,[122] and 5 were cohort studies.[114,115,119–121] The studies assessed the impact of fermented milk products on type 2 diabetes (T2D) risk, glycemia, satiety, glucose metabolism, and insulin resistance. Seven studies[114–116,119–122] used yogurt as the fermented product being tested and the other 2 studies[117–118] used a fermented milk and a probiotic fermented milk. Of the 9 studies,[114–120,122] 8 reported a favorable outcome of yogurt or fermented milk on diabetes outcomes, and 1 study reported no consistent relationship between yogurt consumption and incident diabetes.[121]

The 2 positive-quality studies were conducted by Diaz-Lopez et al[115] and El Khoury et al.[116] The former was an RCOT (20 healthy males) with nonfat plain and sweetened yogurts and skim milk among the treatments.[116] The results showed improved efficacy of insulin action of yogurt and skim-milk treatments that was independent of their protein-to-carbohydrate ratios and physical form. In a CS study, Diaz-Lopez et al[115] followed 3454 nondiabetic elderly subjects in a Mediterranean population and reported an inverse relationship between T2D cases and total low-fat dairy and yogurt consumption. Three neutral-quality studies[114,119,120] reported a significant association between consumption of either yogurt or fermented milk and decreased risk of T2D, and 2 neutral-quality studies[121,122] reported an association between yogurt consumption, lower levels of glucose, lower levels of insulin, and less insulin resistance. One neutral-quality study reported a nonsignificant outcome on the effect on diabetes risk with consumption of fermented milk products, Soedamah-Muthu et al[121] evaluated the intake of fermented milk products in a subpopulation from the Whitehall II study and found it to be inversely associated with overall mortality, but not with diabetes. Overall, these studies indicate a significant correlation between fermented milk consumption and reduced risk for T2D.

*Metabolic syndrome.* Four neutral-quality studies specifically evaluated metabolic syndrome. As part of the PREDIMED (Prevención con Dieta Mediterránea) cohort study, Babio et al[50] found that among 1868 men and women aged 55–80 years, consumption of both low-fat and high-fat yogurt was associated with a decreased risk for metabolic syndrome (MetS). In a CS study using NHANES (National Health and Nutrition Examination Survey) data, Beydoun et al[53] showed a significant inverse relationship between yogurt consumption and MetS. As part of the Tehran Lipid and Glucose cohort study, Cheraghi et al[54] found that for every serving of yogurt consumed per day (equivalent to 200 g), the incidence of MetS decreased by 57% – a finding that was modest, but significant. One component of the 5 MetS criteria, central adiposity, was found to be significantly inversely associated with high yogurt consumption. Kim and Kim[62] reported that for a cohort of 5510 men and women aged 40–69 years, consumption of 4 or more servings of yogurt per week was associated with a decreased risk for MetS. Among a cohort of 664 men and women aged 18–55 years, Cormier et al[94] reported that yogurt consumption led to an improved cardiometabolic risk profile.

Overall, studies suggest yogurt consumption is strongly associated with risk reduction of metabolic syndrome and diabetes.

### Bone health

Seven included studies evaluated the impact of yogurt and cultured fermented milk on bone health[123–129]; 1 study was an RCT,[124] 3 were cohort studies,[125–127] and 3 were CS studies.[123,128,129] The studies assessed the effect of fermented milk products on growth, bone density, risk of dental caries, and risk of hip fracture. All of the studies evaluated yogurt consumption or yogurt feeding (and one of these used laban, a liquid-type yogurt). Five of the studies[123–125,128,129] reported a favorable outcome of yogurt consumption, and 2 studies[126,127] reported a neutral outcome.

Only one study, conducted by He et al,[124] was positive quality; the other 6 studies[123,125–129] were neutral quality. In the He et al[124] study, the diets of preschool children in Beijing suburbs were supplemented with 125 g/d of yogurt for 9 months (vs no supplementation). The treatment group reported improved nutrient intake, lower incidence of respiratory infections and diarrhea, greater height and weight gain, and greater bone mineral density.

In a CS study of an Iranian female adult population, AlQuaiz et al[123] found an increased risk for low bone mineral density among those who did not drink laban (yogurt drink). As part of the Framingham Offspring cohort study, Sahni et al[125] found an association between yogurt consumption and increased bone density. No other dairy groups showed an association. Greater intakes of milk and yogurt (>1 serving/wk) also

lowered risk for hip fracture by 20% in older adults, compared with those with a low intake of these dairy foods.[126] Further, as part of the Framingham original cohort study, Sahni et al[127] found less bone loss over a 4-year period among those taking vitamin D supplements, who were also medium-to-high consumers of a combination of milk, yogurt, and cheese.

Additionally, in a CS study by Uenishi and Nakamura,[128] after adjusting for exercise frequency, weight, gender, age, and area of residence, regression analyses indicated that milk and yogurt intake among a population of teenagers (aged 15–18 y) were independently associated with the osteo-sono assessment index, a standard measurement of bone mineral density, while cheese intake was not.

Overall, the studies confirm the positive effect of the high nutrient content of yogurt on bone health.

## DISCUSSION

Conclusions that may be drawn from this systematic review are that (1) a causal relationship exists between lactose digestion and tolerance and yogurt consumption, and (2) consistent associations exist between fermented milk consumption and reduced risk of breast and colorectal cancer, T2D, improved weight maintenance, and improved cardiovascular, bone, and GI health. Further, an association exists between prostate cancer and dairy product consumption in general, with no difference between fermented and unfermented products.

There exist several possible mechanisms for these findings. During fermentation, metabolic activity of microorganisms can alter the nutritive and bioactive properties of dairy products. Thus, health-promoting properties of fermented milk products may be due, in part, to the biosynthesis or release of bioactive compounds resulting from the fermentation process,[130] including bioactive peptides with antihypertensive, antimicrobial, antioxidative, and immune-modulatory activities.[131] Lactic acid bacteria may also produce bacteriocins, biogenic amines, and exopolysaccharides.[132,133] Conjugated linoleic acid, which has demonstrated anti-inflammatory, anti-atherogenic, and antioxidant properties, is naturally present in milk fat and may increase during fermentation.[1] The B vitamins folate, riboflavin, and B12 can be synthesized by fermentation-associated bacteria in dairy foods, thereby increasing the nutritive content and providing additional health benefits.[134–136]

The strongest evidence supporting the health benefits of fermented foods is for their ability to improve lactose digestion and tolerance. Multiple RCTs support this function and the physiological role of the beta-galactosidase enzyme produced by yogurt bacteria for in vivo hydrolysis of lactose during GI transit, resulting in improved lactose digestion and tolerance.

## LIMITATIONS

An important potential confounding factor in cohort and other correlation-based studies is that individuals with a propensity toward healthy diets may simply consume more fermented foods. Thus, it is critical that, when feasible, controlled and blinded studies be conducted with populations matched for age, gender, socioeconomic status, education, and other factors that may influence food consumption behavior. Although the limitations of observational studies are well known (including potential for bias and lack of causation),[137] they can still provide valuable suggestions for improving public health.[138–140]

Further, dairy foods contain high levels of several essential nutrients, including high-quality protein, calcium, potassium, phosphorus, and vitamins A, D, B12, riboflavin, and niacin. Hence, distinguishing the health benefits of fermented vs nonfermented milk products is often difficult. Many of the studies cited in this review used milk products as controls. Thus, these studies are able to distinguish the specific effect of fermentation. In contrast, other studies utilized nonmilk controls, cannot distinguish between nutrient content and fermentation factors influencing the results.

## CONCLUSION

In a review of dietary recommendation in 13 European Union member states, none mentioned yogurt as an alternative for people with lactose intolerance, despite an approved function claim in the European Union for live cultures in yogurt or fermented milk to aid with lactose digestion.[141] Further, only 5 European Union member states currently have national nutrition guidelines or recommendations that include yogurt with live bacteria.[142] Nonetheless, there appears to be emerging interest in including fermented foods as part of dietary guidelines.[4,16,133,142–144] While the US dietary guidelines, as well as national recommendations from other countries, recommend the consumption of yogurt for its nutrient content, specific comments on fermented milk products are rare. Evidence described in this review suggests such recommendations are warranted.

### Acknowledgments

## Supporting Information

The following Supporting Information is available through the online version of this article at the publisher's website.

*Appendix S1* **PRISMA checklist**

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