

Dynamics of Dairy Product Consumption, Confounding Factors, and Their Influence on the Risk of Type 2 Diabetes

Abstract

It has long been debated whether or not dairy consumption increases the risk of type 2 diabetes (T2D). This link has been assessed by a large number of case-control studies, prospective cohort studies, systematic reviews, and meta-analyses. The majority of their studies demonstrated an inverse relationship between the risk of T2D and dairy consumption. It is yet unclear how dairy products specifically contribute to metabolic diseases like type 2 diabetes. However, a surprising number of studies have indicated either no association or a positive correlation between the development of type 2 diabetes and certain dairy products. The objective of this narrative review is to collate research findings from diverse geographical contexts, exploring the impact of dairy product consumption on the incidence and risk of Type 2 diabetes (T2D). This review includes studies that addressed this research issue and were released between the years 2000 and 2023. This will help the public draw logical inferences and validate the body of recent research. To shed light on this matter, the writers conduct a comprehensive search of electronic scientific databases such as PubMed, Scopus, and Web of Science. Thus, this review emphasizes the connection between the usage of different dairy products and the risk of T2D. After controlling for confounding variables, this review indicates that the relationship between the incidence of type 2 diabetes and consumption of dairy products is context-dependent. In conclusion, not all dairy products help to prevent type 2 diabetes. There is no association between most other dairy products and T2D, while in some cases benefits of yogurt and other low-fat dairy products have been reported.

Keywords: *Confounders, dairy consumption, dietary impact, milkfat, nutrition*

Introduction

As per Disease Control and Prevention (CDC) in 2023, nearly 39 million people worldwide are suffering from diabetes, wherein only 30 million have been diagnosed, and a budding population of nearly 98 million have prediabetes.^[1] While diet and exercise are considered key constituents to prevent and manage diabetes, the awareness of the right type and time of diet and exercise is still haywire. Healthcare practitioners around the world have inconsistent opinions on diet and physical activity plans, making it an intuitive practice at patients' end. High-fat fermented dairy, whole cheese, and high-fat cheese were linked to a decreased incidence of prediabetes in the Hoorn trials (6.4 years of follow-up).^[2] However, total dairy and other dairy products did not appear to be linked to pre-diabetes. Conversely, high-fat milk and yogurt consumption were strongly linked to a decreased risk of prediabetes in

the Rotterdam investigations (11.4 years of follow-up), but low-fat dairy products and low-fat milk consumption were linked to a higher risk of prediabetes.^[3]

By prevailing ideology, the substantial presence of calcium, magnesium, vitamin D, and whey proteins within dairy products has prompted theoretical considerations regarding their potential efficacy in reducing adiposity and insulin resistance. Consequently, hypotheses have emerged positing their protective role against the development of Type 2 diabetes.^[4]

The relatively recent studies that were focused on diet intake and their impact on patients or prospects have shown some similarly mixed results. While fats have a reputation for having an ill effect on patients' health, some studies have shown that milk products with fat content have been reducing the risk of type 2 diabetes and are managing the levels in patients, while some have shown ill or no effect. As per the International Dairy Federation,

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the world's per capita consumption of dairy products rose dramatically between 2006 and 2019. Dairy products are seeing considerable growth in markets in Asia, Africa, and Latin America.^[5]

The studies have been conducted in different geographies and different audience types, which can potentially be the cause of inconsistency in results. Meta-analysis of a large number of cohort studies deduced that dairy products such as cheese, high-fat milk, yogurt, etc., which were evaluated with suspicion are now being associated with diet constituents for lowering the risk.^[6]

Researchers have deduced some plausible rationale for this positive impact of high milkfat on diabetes such as improvement in insulin sensitivity, reduced risk of weight mismanagement, and reduction in fat-cell lipid accumulation.^[1] While referring to the consumption of dairy fat as beneficial might not always be the case, especially when the patients are suffering from co-morbidities including obesity, cardiovascular diseases, or hypertension, the statement is more effective for prediabetes patients. In the case of diabetic patients' low-fat content is also effective.^[7]

This paradigm change may raise questions about the complex relationship between dairy consumption and prediabetes and provide fresh insights into dietary advice for people passing through the perils of metabolic health. The two main treatment choices for people with type 2 diabetes worldwide are diet modification and weight loss. However, there remains a great deal of disagreement about the optimal dietary guidelines and prescribed diets for better glycemic control. Consequently, it is very valuable to find reasonably priced and simple dietary changes for the management and prevention of persistent and metabolic conditions.^[8] In light of this, the goal of this thorough narrative review, which was founded on cohort studies, is to compile information regarding the relationships between the risk of type 2 diabetes and various forms of dairy product use, including fermented dairy, low-fat, high-fat, and total dairy. In this study, we examine the available data to investigate the complex connection between the consumption of dairy and its effects on the incidence of T2D.

Method

This narrative has been built by assessing global online research articles from Google Scholar, Science Direct, PubMed, and three health organizations (CDC, NHS, WHO) publications, with keywords Dairy products OR Milk OR Lactose AND Diabetes AND Prediabetes. Any other related facts or statistics have been sourced from authentic articles. The instrument used to qualify the articles for review was the CASP Cohort Study Checklist.^[9] Broad parameters for selection were - cohort studies; inclusion of adult population, aged 18 and above; consumption of dairy

products (including whole low-fat dairy, high-fat fermented dairy, milk, yogurt, cream, cheese, etc.) as the exposure of interest; confounding variables taken into account when evaluating the impact; the impact on T2D as the outcome; and quantitative estimates and their 95% confidence intervals reported. Remarks, letters, and editorials were not included. When several publications used the same data, the research study with the biggest sample size and/or the most thorough report was selected. Here in this manuscript was considered for discussion [Figure 1].

Patterns of studies and the impact

We assessed studies conducted in different geographies to infer the patterns in impact. The instruments used for assessment in all studies included a Food-frequency Questionnaire (FFQ) and the biomarker output was inferred primarily through Fasting Plasma Glucose (FPS), along with HbA1C or 2-h glucose levels (2hPG).

The study in Australia validated the results obtained from Hoorn trials, inferring that high-fat dairy consumption can be attributed to lowering the risk of T2D, especially in prediabetes patients. A 12-year-long follow-up study on more than 11,000 patients (of which ~ 50% were lactose tolerant), starting from 1999 to 2012, inferred these results. The population age was over 25 years old, so it does not include the younger population; however, the impact of milk-fat consumption was skewed towards positive for the wider population irrespective of age. The dairy products whose consumption was assessed included (and was not limited to) full fat, skimmed milk, yogurt, flavored milk, cheese, butter, and ice cream. The range of consumption varied from none to 3 cups per day. For the 15% population suffering from prediabetes, the higher intake of milk fat was linked with lowered risk. The average consumption of

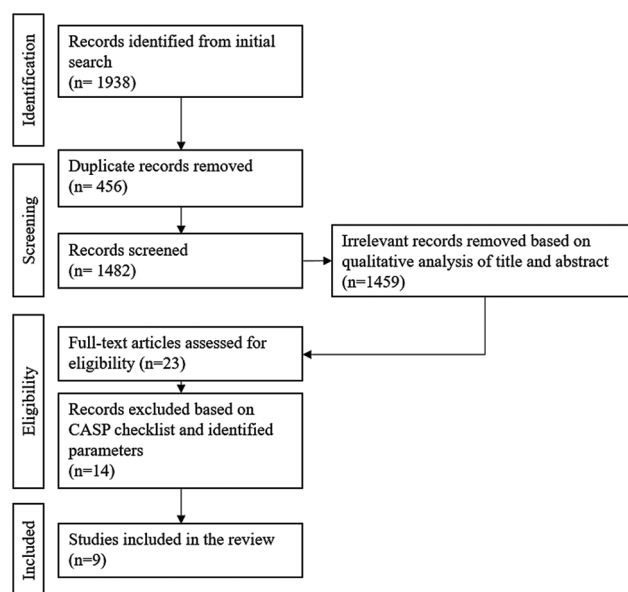


Figure 1: Literature search: Flow diagram

fat was 2.4 servings per day, of which nearly 60% was low fat and the remaining was high fat.^[10] The study leveraged different models adjusted for confounding factors, which included age, sex, energy intake, educational attainment, smoking status, physical activity, alcohol consumption, and a family history of diabetes - in one model, a lower risk of prediabetes was substantially correlated with a larger diet of total dairy; while in model two, consuming more fermented dairy products was linked to a decreased risk of prediabetes. When examined on a continuous scale in fully adjusted models, a larger consumption of high-fat dairy products (44.4% of total dairy consumption) was substantially related to a lower risk of diabetes. The fully adjusted model has a relative risk (RR servings/d: 0.92; 95% CI: 0.85, 1.00; P $\frac{1}{4}$ 0.04), which was similar to Hoorn's study with the relative risk of (RR 0.83, 95% CI 0.69–0.99, P trend = 0.04) for high fat fermented dairy.^[11] While there are prospective cohort studies that have shown the incidence of prediabetes through dairy product consumption, these results were not validated by this APAC study. The previous study with the same population sample, which had a 5-year follow-up, did not conclude anything substantial related to high-fat milk product consumption and the metabolic disorder. There was some evidence of lower incidences of diabetes through low dairy fat consumption but not at a robust level. There was no correlation found between the probabilities of diabetes occurrence and full-fat milk, yogurt, or cheese, but there was with low-fat milk.^[2]

A study in the Netherlands with an emphasis on food network models reported indifference in the impact of dairy on diabetes.^[12] The study aimed to examine the correlations between incident prediabetes and dairy products, as well as the relationships between dairy consumption and dietary choices, metabolic risk factors, and lifestyle choices. One food's correlation with prediabetes is dependent upon its covariation with lifestyle choices or other foods that may have distinct health impacts.^[13,14] Nearly 74,000 Dutch participants were included. The study hypothesized that the idea of consuming dairy products is a component of metabolic risk factors and personal health practices. The average daily consumption of dairy products was 3.5 servings, with high-fat cheese (1.15 servings), low-fat milk (0.60 servings), and low-fat yogurt (0.18 servings) making up the majority of this intake. The study was adjusted for food network models to include the confounding effect of food associations on metabolic health. Coffee, bread, meat, and high-fat cheese had a positive correlation and a marginally positive correlation with low-fat milk. On the other hand, adverse associations between tea, coffee, and sugar-filled beverages were noted. Food groups like fruits, vegetables, seafood, legumes, tea, and nuts were thought to be good for health and there was a significant favorable correlation found between low-fat yogurt and fruit. When evaluated together the study

found no correlation between the risk of prediabetes and the consumption of cream, ice cream, fermented dairy products, and cheese, regardless of fat level. Regression analysis showed that consumption of plain and low-fat milk was linked to a higher incidence of prediabetes (RR: 1.18; 95% CI: 1.06, 1.31; P-trend $\frac{1}{4}$ 0.01), but high-fat yogurt was shown to have a strong but nonsignificant effect estimate on prediabetes (RR servings/day: 0.80; 95% CI: 0.64, 1.01), leading to non-tangible outcomes

A similar pattern in an EU-8 study was observed, which had a population of ~16,000. After adjusting for age, sex, BMI, diabetes risk factors, education, and dietary variables, the intake of total dairy products was not linked to diabetes (HR comparison of the highest and lowest quintile of dairy products: 1.01; 95% CI: 0.83, 1.34; P-trend = 0.92). A higher combined intake of fermented dairy products (cheese, yogurt, and thick fermented milk) was inversely associated with diabetes (HR: 0.88; 95% CI: 0.78, 0.99; P-trend = 0.02) in adjusted analyses that compared extreme quintiles. Of the dairy subtypes, cheese intake tended to have an inverse association with diabetes (HR: 0.88; 95% CI: 0.76, 1.02; P-trend = 0.01).^[2]

In emerging economies such as Iran, the study result was in sync with the majority of studies conducted globally, which suggested that increased intake of low-fat dairy is inversely linked to the incidence of T2D risk. In the study, the risk of type 2 diabetes was reduced in individuals who increased their intake of low-fat milk (OR = 0.59; 95% CI: 0.37 to 0.92) and low-fat yogurt (OR = 0.55; 95% CI: 0.33 to 0.93) compared to those who remained relatively stable in their consumption. ~600 prediabetic people were included in the study and had a 3-year duration. During the 3-year-long research, the consumption patterns of milk-based products were evaluated and their influence on diabetes.^[15] Samples were divided into 3 models, one that increased dairy consumption by 0.5 servings/day, one that kept it constant, and one that reduced consumption by 0.5 servings/day. The models were adjusted for confounding factors such as age, sex, physical activity, change in body mass index, family history of diabetes, and total energy intake. It was inferred that the participants who reduced their dairy consumption showed an increase in T2D incidence, vis-à-vis ones who kept it consistent or increased. Figuratively, an increase in total dairy and low-fat dairy consumption of 0.5 servings/d was linked to a 15% and 12% decreased risk of type 2 diabetes, respectively. In the following 3-year follow-up period, it was estimated that substituting 0.5 servings/day of high-fat dairy with 0.5 servings/day of low-fat dairy was linked with an 11% decreased risk of diabetes. T2D risk was found to be 27% lower when low-fat yogurt consumption was increased by 0.5 servings/day and high-fat yogurt consumption was decreased concurrently.

Studies in the United States on larger cohorts depicted varied results for different demographics, even after

adjusting for confounders. In a mixed sample, with large whites, the analysis on regular consumption of dairy had no significant impact on T2D, but the change in, the then, incumbent patterns altered the results. The research followed 65,929 women from the Nurses' Health Study (NHS; 1984–2012), 89,565 women from the NHS II (1991–2013), and 41,808 men from the Health Professionals Follow-Up Study (1986–2012).^[16,17] In all three cohorts, there was a positive correlation between the consumption of dairy fat and white ethnicity, current tobacco use, TFA consumption, and total calorie intake. Furthermore, in all three cohorts, the consumption of dairy fat was negatively correlated with the use of postmenopausal hormones in women, as well as with baseline levels of hypertension and hypercholesterolemia, AHEI score, glycemic load, and intakes of alcohol, whole-grain carbohydrates, fruits, vegetables, animal and vegetable fat. When compared to energy from carbs, the consumption of dairy fat did not significantly increase the risk of type 2 diabetes in the study of three cohorts. However, there was a significant correlation found between the risk of T2D and substituting animal fat from other sources or refined grain carbohydrates for the same number of calories from dairy fat. Conversely, substituting whole grain carbohydrates for dairy fat resulted in a significantly lower risk of T2D - 7% lower risk (HR: 0.93; 95% CI: 0.88, 0.98).

A following study, which evaluated the change in dairy patterns for incidence impact concluded that when compared to maintaining steady intakes, increasing yogurt consumption by >0.5 serving/d was linked with an 11% (95% CI: 4%, 18%) lower risk of T2D, while increasing cheese consumption by >0.5 serving/d was associated with a 9% (95% CI: 2%, 16%) greater risk. An 11-year follow-up study on American Indians reported consumption of dairy products was modest (0.03 serving/1000 kcal for low-fat dairy products and 0.11 serving/1000 kcal for full-fat dairy products). After adjusting for demographic and diet variables, participants who reported the highest full-fat food intake had a lower risk of developing diabetes [HR (95% CI): 0.79 (0.59, 1.06); P-trend = 0.03]. Consuming dairy products low in fat did not correlate with diabetes. In conclusion, American Indians who took part in the study indicated consuming few dairy products. Individuals who consumed more full-fat dairy products were less likely to develop diabetes than those who consumed less.^[18]

Within Asia, Japan and China depicted varied outcomes, the population in Japan showed a higher incidence of T2D with consumption of high fat milk [RR: 1.02 (0.85, 1.24)], whereas in China the relation was inverse [Table 1] [RR: 0.74 (0.67, 0.82)].^[19-21]

Discussion

The global prevalence of diabetes is a significant public health concern, with millions of individuals affected,

and an even larger population at risk of developing the condition.^[22] This review aimed to comprehensively examine the relationship between dairy product consumption and the risk of T2D, considering various forms of dairy products and diverse geographic populations. The findings from the reviewed studies indicate a complex and multifaceted relationship between dairy consumption and T2D risk. Notably, the impact of specific dairy products on prediabetes and diabetes varies across different regions and populations. The inconsistencies in results may be attributed to the diversity in dietary habits, lifestyle factors, genetic predispositions, and other confounding variables.^[23]

While it is hypothesized that dairy products protect against type 2 diabetes, based on the review one key observation is the divergent effects of dairy products on T2D risk. While some studies, like the Hoorn trials, suggest a decreased incidence of prediabetes associated with high-fat fermented dairy, other investigations, such as those in the Netherlands and the United States, present indifferent or even contrasting results [Figure 2].^[24] These variations highlight the importance of considering regional dietary patterns and lifestyle factors in understanding the impact of dairy consumption on metabolic health.^[25,26]

Furthermore, the positive association between high milkfat and a decreased risk of prediabetes is intriguing. Plausible mechanisms, such as improved insulin sensitivity and reduced fat-cell lipid accumulation, have been suggested by researchers. However, it is essential to recognize that these potential benefits may not universally apply, particularly for individuals with co-morbidities like obesity, cardiovascular diseases, or hypertension. The inclusion of diverse populations in this review, ranging from Australia to the United States, allowed for a comprehensive analysis of the global scenario. Interestingly, the study in Iran aligns with global trends, emphasizing the inverse association between increased intake of low-fat dairy and reduced T2D risk. This consistency across different regions supports the notion that certain aspects of dairy consumption,

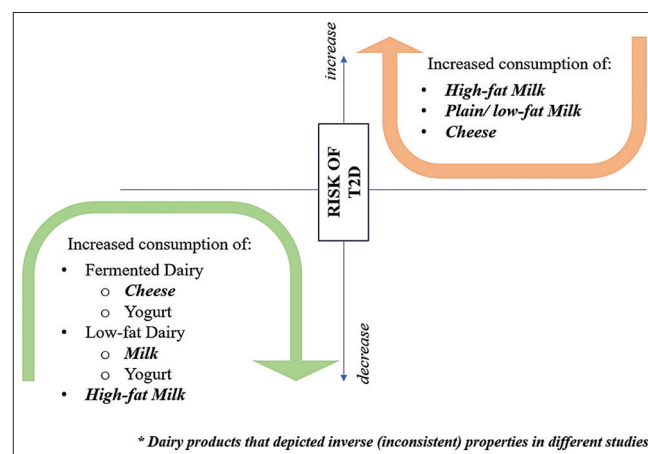


Figure 2: Impact of certain dairy products on T2D risk

Table 1: Overview of studies across geographies on impact of dairy consumption on T2D with related confounding factors

Region	Sample	F.Y	Dairy items included	Biomarker	Confounding factors	Confounder models	Impact
Australia	4,891	12	High-fat dairy, milk, cheese, yogurt, ice cream	Fasting plasma glucose (FPG); 2-h glucose levels (2hPG)	Education, smoking, physical activity, family history, cardiovascular disease, BMI, blood pressure	Model 1 adjusted for age, sex, and energy intake. Model 2 additionally adjusted educational level, alcohol, smoking, physical activity, and family history of type 2 diabetes. Model 3 additionally adjusted for food group including fruits, vegetables, grains, legumes, nuts, meat, and juice	High-fat dairy, milk and cheese associated with lower risk of T2D - (RR servings/d: 0.92; 95% CI: 0.85, 1.00); (RR: 0.89; 95% CI: 0.80, 0.99) and (RR: 0.74; 95% CI: 0.56, 0.96), respectively
Netherlands	74,132	12	Total dairy, fermented dairy, milk, yogurt, cheese, cream, ice cream	FPG, A1C	Metabolic risk factors, lifestyle behaviors, food intake, education, physical activity and BMI	Model 1 adjusted for age, sex, energy intake, and follow-up duration. Model 2 additionally adjusted education, smoking behavior, alcohol use, physical activity level, and family history of diabetes. Model 3 additionally adjusted for food groups associated with type 2 diabetes	No strong significant relation. A slightly higher risk of prediabetes was linked to plain and low-fat milk in the top quartiles vis-a-vis the lowest (RR: 1.17; 95% CI: 1.05, 1.30; <i>P</i> 0.04 and RR: 1.18; 95% CI: 1.06, 1.31; <i>P</i> : 0.01)
Iran	639	9	Milk, yogurt, cheese, and ice cream	FPG, 2-h plasma glucose (2-hPG)	Smoking status, food intake fruit, legumes, etc., and body weight	Model 1 was adjusted for age, sex, physical activity, change in body mass index, family history of diabetes, and total energy intake. Model 2 was further adjusted for dietary factors, including wholegrain intake and energy	Increasing low-fat dairy, milk and yogurt consumption led to reduced risk of T2D - (OR=0.56; 95% CI: 0.35 to 0.90), (OR=0.59; 95% CI: 0.37 to 0.92) and (OR=0.55; 95% CI: 0.33 to 0.93), respectively, when compare with stable consumption
USA	197,289	16	High-fat dairy, milk, cheese, yogurt, icecream	FPG, A1C	BMI, smoking, physical activity, medication use, history of chronic diseases, menopausal status, and diet	3 cohorts based on gender, with models adjusted for confounders.	When compared to calories from carbs, dairy fat did not appear to be related to a higher risk of type 2 diabetes (HR top and bottom quintiles: 0.98; 95% CI: 0.95, 1.02).
USA	192,347	4	Total dairy, fermented dairy, milk, yogurt, cheese, cream, ice cream	FPG, A1C	Age, race, BMI, smoking, physical activity, and family history	3 cohorts based on gender, with models adjusted for confounders.	Decreasing total dairy by >1.0 serving/d was associated with an 11% (95% CI: 3%, 19%) higher risk of T2D Increasing yogurt consumption by >0.5 serving/d was associated with an 11% (95% CI: 4%, 18%) lower T2D risk.
USA	277	11	Milk, yogurt, cheese, and ice cream	FPG, A1C	Education, smoking, BMI, physical activity	Model 1 adjusted for age, sex, study, and energy. Model 2 additionally adjusted smoking, dairy	Full fat dairy intake led to lower risk [HR (95% CI): 0.79 (0.59, 1.06); <i>P</i> - trend=0.03

Contd...

Table 1: Contd...

Region	Sample	F.Y	Dairy items included	Biomarker	Confounding factors	Confounder models	Impact
EU - 8 countries	16835	11	Milk, yogurt, curd, ice cream, cheese, milk beverages	Self-reported FPG	Education, smoking, physical activity, BMI, other nutrients, supplements intake	intake, and physical activity Model 3 adjusted for BMI and alternate nutrient intake Model 1 adjusted for age and sex. Model 2 additional adjusted BMI, education, smoking, alcohol, energy and food intake	No statistically significant association. Intake of fermented dairy reduced the risk of diabetes to some extent
China	64191	6.9	Powdered and fresh milk	FPG, A1C	Age, energy, BMI, income, occupation, education	4 models adjusted for confounders	With a daily serving of 25g/d milk the RR of T2D reduced: 0.46 (0.32, 0.64) for daily consumers 0.74 (0.67, 0.82)
Japan	59796	5	Milk, yogurt, cheese	2-h plasma glucose (2-hPG)	Age, BMI, family history, smoking, alcohol intake, hypertension, exercise	6 models adjusted for confounders and different product consumption	With difference in top and bottom quintiles of dairy products esp. milk has an impact on increased risk of T2D RR: 1.18 (0.90, 1.56) for men and RR 1.12 (0.80, 1.57) for women

particularly low-fat options, may offer protective effects against T2D.

The common similarities in the studies were the use of a similar instrument – the food frequency questionnaire (FFQ), and similar confounding factors including age, gender, smoking, education, and other food items consumption. The models used for sensitivity analysis had similar adjustments, so a critical review to validate the instruments and factors might be necessary.

The biomarker data through FPG, HbA1C, and 2hPG may also need another review, because as per studies heptadecanoic acid (17:0), pentadecanoic acid (15:0), and trans palmitoleic acid (trans-16:1n-7) are related to incidence diabetes, which are not directly inferred from the measure used in our studies.^[27]

Nevertheless, the observed variations in outcomes across studies underscore the need for standardized methodologies and unified criteria when investigating the relationship between dairy consumption and T2D risk. The diverse study designs, participant characteristics, and measurement methods for dairy intake may contribute to the disparities in reported results.

Conclusion

In conclusion, this review synthesizes evidence from diverse populations and geographical regions to explore the intricate relationship between dairy product consumption and the risk of type 2 diabetes. The findings suggest that the impact of dairy on metabolic health is complex

and context-dependent. High-fat dairy, particularly fermented products, may exhibit protective effects in some populations, while low-fat dairy consumption is consistently associated with a reduced risk of T2D across various regions.

The conflicting results across studies emphasize the need for further research and a nuanced understanding of the interactions between dairy products and metabolic health.^[28,29] The critical review of parameters included in the studies – confounders, instruments, biomarkers, and models is necessary to draw more rational conclusions. Future investigations should strive for standardized methodologies, considering diverse populations, and accounting for confounding factors. Additionally, personalized dietary recommendations based on individual health conditions and risk factors may be crucial for optimizing the preventive and therapeutic potential of dairy consumption in the context of type 2 diabetes.

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Conflicts of interest

There are no conflicts of interest.

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