Dairy products and prevention of type 2 diabetes: implications for research and practice

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A growing body of scientific evidence has linked dairy intake to a reduced type 2 diabetes (T2D) risk. Using an evidence-based approach, we reviewed the most recent and strongest evidence on the relationship between dairy intake and the risk of T2D. Evidence indicates that dairy intake is significantly associated with a reduced T2D risk, and likely in a dose-response manner. The association between low-fat dairy and T2D risk reduction appears consistent. A beneficial impact is suggested for regular-fat dairy. The role of specific dairy products needs to be clarified. Potential underlying mechanisms include the role of dairy products in obesity and metabolic syndrome, as well as several dairy components, such as calcium, vitamin D, dairy fat, and specifically trans-palmitoleic acid. To conclude, there is strong, consistent, and accumulating evidence that dairy intake reduces the risk of T2D. More research is needed to better understand the role of regular-fat and specific dairy products. Well-designed randomized controlled trials and mechanistic studies are needed to support these findings. Efforts to translate this evidence into clinical practice and public health guidance are needed.

Keywords: dairy products, milk, dairy, diabetes, T2D, metabolic syndrome

INTRODUCTION

Diabetes is a global epidemic with major health, social, and economic implications. Over the last three decades, the prevalence of diabetes has more than doubled, and more than 371 million people worldwide now have diabetes (1). In 2012, diabetes was the cause of 4.8 million deaths and the estimated health care cost of diabetes was $471 billion worldwide (1).

Type 2 diabetes (T2D) accounts for at least 90% of all diabetes cases and its rates have been increasing at an alarming rate in every country (2). Lifestyle has been identified as playing a major role in the development and prevention of T2D. T2D usually develops during adulthood and is associated with obesity, physical inactivity, and unhealthy diets (2).

A growing body of scientific evidence has linked dairy products to a reduced risk of T2D. Potential underlying mechanisms remain to be fully elucidated but may include a beneficial role of dairy products in obesity and metabolic syndrome (MetS), two important risk factors for T2D, as well as a beneficial role of certain dairy components such as calcium, vitamin D, dairy fat, and specifically trans-palmitoleic acid.

Unfortunately, dairy products remain largely under-consumed by all age groups. An astonishing number of Americans (more than 80% men and 90% women) do not meet the minimum dairy requirements of the Dietary Guidelines for Americans (DGA) (3). A large proportion of Canadians also do not meet the minimum daily recommendations established by Health Canada, with an average intake for adults being 1.52 servings, which is well below the 2–4 recommended daily servings (4). Under-consumption of dairy products has also been reported in many other parts of the world (5–7).

Given the increasing amount of evidence on the beneficial role of dairy products in T2D risk reduction, ensuring optimal dairy intake may represent an additional key strategy against this epidemic. In this review, we aim to examine and synthesize the scientific evidence on the association between dairy products and T2D risk, and identify opportunities for future research. Using a comprehensive evidence-based approach, we reviewed the evidence on the relationship between dairy product intake and the risk of T2D. Online databases were searched until March 2013 for relevant peer-reviewed articles. Priority was given to the most recent and strongest available evidence, with a focus on meta-analyses, randomized controlled trials (RCTs), and prospective cohort studies.

Dairy and Type 2 Diabetes

Systematic Reviews and Meta-Analyses

Three meta-analyses of prospective cohort studies on dairy products and T2D were identified (Table 1). In a meta-analysis by Tong et al. the highest dairy consumption, compared to the lowest category, significantly reduced the risk of T2D by 14% (combined relative risk (RR) 0.86, 95% confidence interval (CI) 0.79–0.92) (8). A significant inverse association with T2D was also observed for low-fat dairy and yogurt. High-fat dairy and whole (regular-fat) milk were not found to be associated with T2D. A dose-response analysis showed a decrease of 6% in T2D risk per each additional daily serving of total dairy (RR 0.94, 95% CI 0.92–0.97). A dose-response
relationship between low-fat dairy consumption and T2D was also present, with a 10% risk reduction per additional serving (RR 0.90, 95% CI 0.85–0.95).

In their meta-analysis of four prospective cohort studies on diabetes, Elwood et al. demonstrated that milk or dairy consumption was protective against T2D (RR 0.92, 95% CI 0.86–0.97). Each additional daily serving was significantly associated with a reduction in diabetes incidence by 4–9% (9). In another meta-analysis with mostly similar cohort studies, the highest vs. lowest dairy intake (3–5 vs. 1.5 servings per day) was associated with a lower risk of incident T2D (odds ratio (OR) 0.86, 95% CI 0.79–0.93) (10). Furthermore, in the 2010 DGA, the Dietary Guidelines Advisory Committee (DGAC) concluded that moderate evidence indicates that dairy products are associated with a reduced risk of T2D after their systematic review of literature (11).

### PROSPECTIVE COHORT STUDIES

Several prospective cohort studies, published thereafter, have also been conducted to evaluate the potential role of dairy products in T2D prevention (Table 1).

The Australian Diabetes Obesity and Lifestyle Study (AusDiab), a population-based, prospective survey with follow-up of 5 years, consisting of 5,582 adults demonstrated a significant inverse association between the highest tertile of dairy intake and risk of diabetes in men, after adjustment for age, sex, energy intake, and various other clinical characteristics (adjusted OR 0.86, 95% CI 0.79–0.93) (10). Furthermore, in the 2010 DGA, the Dietary Guidelines Advisory Committee (DGAC) concluded that moderate evidence indicates that dairy products are associated with a reduced risk of T2D after their systematic review of literature (11).
Conversely, in another Australian prospective cohort study, the Blue Mountains Eye Study (BMES), after adjustment for covariates including energy intake, fiber from vegetables, dietary glycemic load, and calcium, total dairy consumption was not found to be associated with T2D (adjusted OR 1.50, 95% CI 0.47–4.77) (13). No association was also observed for reduced/low-fat dairy (adjusted OR 1.09, 95% CI 0.57–2.09), or regular-fat dairy (adjusted OR 0.87, 95% CI 0.48–1.57), and T2D risk. However, compared with subjects in the lowest intake quartile of regular-fat dairy products, those in the highest quartile had a 59% lower risk of MetS (multivariate adjusted OR 0.41, 95% CI 0.23–0.71).

A prospective analysis of the Inter99 Study, a Danish population-based lifestyle intervention, assessed the association between specific types of dairy products and T2D incidence. Glucose regulation, an important underlying mechanism in the development of T2D, was also investigated (14). No significant association was found between total dairy intake and T2D incidence (OR 0.95, 95% CI 0.86–1.06). There was also no association between specific dairy products and T2D, but cheese and fermented dairy appeared to have a beneficial effect on glucose regulation indices. A linear inverse association was demonstrated between cheese and 2 h plasma glucose (β = −0.048, 95% CI −0.095 to −0.001). Fermented dairy products (cheese, yogurt, and buttermilk) were also inversely associated with fasting plasma glucose and hemoglobin A1c.

The Whitehall II prospective cohort study was a London-based study of the working staff of Civil Service departments (15). Ten-year follow-up of 4,186 participants indicated that total dairy consumption was not significantly associated with T2D [hazard ratio (HR) 1.30, 95% CI 0.95–1.77]. Neither high-fat dairy, low-fat dairy, total milk, yogurt, cheese nor fermented products were associated with T2D risk. However, fermented dairy products were significantly associated with an inverse risk of overall mortality.

The Data from the Epidemiological Study on Insulin Resistance Syndrome (DESIR) study was a prospective cohort study of French adults, followed for 9 years (16). Adjustment was made for potential confounders including fat intake, and analysis of 3,435 participants demonstrated that total consumption of dairy products, excluding cheese, was inversely associated with incident impaired fasting glycemia and T2D (adjusted OR 0.85, 95% CI 0.76–0.94). Cheese consumption was not associated with T2D (adjusted OR 0.93, 95% CI 0.82–1.06), but an inverse relationship was found between cheese and incident MetS (adjusted OR 0.82, 95% CI 0.71–0.95).

Data from 37,038 women from the Nurses’ Health Study II, followed for 7 years, was used to evaluate whether dairy consumption during adolescence was associated with the development of T2D in adulthood (17). After adjustment for risk factors present in adolescence, those in the highest quintile of dairy consumption during adolescence (two servings per day) had a reduced risk of T2D by 38%. Adjusting for risk factors present in adulthood also showed a significant inverse association between adolescent dairy intake and T2D (RR 0.73, 95% CI 0.54–0.97). A 43% reduction in risk of T2D was observed for women with consistently high-dairy intakes (from adolescence to adulthood), highlighting the importance of persistence in dairy consumption. A 25% risk reduction was also observed for the highest dairy consumption (two servings per 1,000 kcal), and a 26 and 28% risk reduction with low- and high-fat dairy, respectively.

In a nested case-cohort analysis within eight countries of the European Prospective Investigation into Cancer and Nutrition (EPIC) Study, consisting of a subcohort of 16,835 participants, total dairy consumption was not associated with T2D (HR 1.01, 95% CI 0.83–1.34) (18). Both the consumption of cheese and fermented dairy products (cheese, yogurt, and thick fermented milk) were inversely associated with T2D (HR 0.88, 95% CI 0.76–1.02 and HR 0.88, 95% CI 0.78–0.99, respectively).

**RANDOMIZED CONTROLLED TRIALS**

To our knowledge, no RCTs to date have specifically assessed the association between dairy products and the risk of incident T2D. However, in a randomized crossover trial of 12 months, the consumption of low-fat dairy (four servings per day) was associated with improved insulin resistance, without adversely affecting body weight and lipid status (19).

**REGULAR/HIGH-FAT DAIRY**

While the evidence appears to be relatively consistent with respect to a beneficial role of low-fat dairy products in the prevention of T2D, the role of regular/high-fat dairy, as well as dairy fat itself, is less clear. In a recent systematic review of observational studies (20), the majority of studies suggested that high-fat dairy products were inversely associated with T2D, either significantly or non-significantly.

In a prospective cohort analysis of the Cardiovascular Health Study (CHS), *trans*-palmitoleic acid, a naturally occurring *trans* fatty acid found in dairy and ruminant fat, was shown to significantly and considerably reduce the risk of incident T2D, with a risk reduction of 62% (21). Dairy fat content appeared to be directly related to *trans*-palmitoleic acid levels, and whole-fat but not low-fat dairy, was also inversely associated with the risk of T2D. In another subsequent prospective cohort study, the Multi-Ethnic Study of Atherosclerosis (MESA), *trans*-palmitoleic acid was associated with a 48% lower risk of incident T2D (22). A pooled meta-analysis of these two independent cohorts indicated a 29% lower incidence of diabetes for each 0.05% point of higher *trans*-palmitoleic acid concentrations (22).

**SPECIFIC TYPES OF DAIRY PRODUCTS**

The evidence regarding the role of specific types of dairy products such as milk, yogurt, and cheese is limited. Milk has generally been assessed as part of total dairy consumption, and limited evidence exists on milk specifically. It appears that milk consumption may be associated with a reduced risk of T2D, with no association for regular-fat or whole milk and T2D (8, 9, 15). Limited evidence suggests that yogurt is inversely associated with T2D (8, 12, 14). Cheese consumption may be associated with a reduced risk of T2D, but this needs to be confirmed as some findings are not statistically significant (14–16, 18). Finally, a protective role of fermented dairy products as a whole (including yogurt, cheese, buttermilk, and fermented milk), is suggested against T2D (14, 18).
Vitamin D also has an indirect effect via the regulation of extracellular calcium for normal calcium flux through cell membranes and adequate Ca\(^{2+}\) pool (37). Vitamin D may enhance insulin receptor expression and insulin responsiveness for glucose transport (38). Moreover, vitamin D directly activates peroxisome proliferator activator receptor-\(\delta\), a transcription factor involved in fatty acid metabolism (39, 40).

T2D has also been shown to be associated with systemic inflammation (41, 42). Insulin sensitivity and \(\beta\)-cell survival may be improved through the direct effect of vitamin D on the generation of cytokines (10). Vitamin D also down-regulates genes encoding pro-inflammatory cytokines involved in insulin resistance (43). The anti-inflammatory mechanism may also be modulated by the regulation of Ca\(^{2+}\) levels (10).

### DAIRY FAT AND TRANS-PALMITOLEIC ACID

The trans isomer of palmitoleic acid (trans-16:1n-7) is a natural source of palmitoleic acid, mainly obtained via the diet from dairy or ruminant fat. Trans-palmitoleic acid may have similar actions to that of endogenous cis-palmitoleic acid (22, 26). Up-regulation of adipose-derived cis-palmitoleic acid improves hepatic and peripheral insulin resistance, diminishes metabolic dysregulation, and suppresses hepatic de novo lipogenesis (20, 22, 44). Higher trans-palmitoleic acids levels are also associated with lower triglycerides, fasting insulin, blood pressure, and C-reactive protein (21, 22).

Other dairy-derived fatty acids have also been associated with lower T2D risk but findings are less consistent (22). A recent meta-analysis of cohort studies has indicated that dietary saturated fat is not associated with risk of T2D (45).

### LIMITATIONS

Our review of the most recent studies on dairy products and risk of T2D has some limitations. Most of the studies included in this review consisted of prospective cohort studies. The potential for bias in such observational studies is present in that individuals who have a regular consumption of dairy products may also engage in other healthful diet and exercise behavior. In most studies, adjustments were made for potential confounders, yet, the possibility of residual confounding cannot be completely eliminated.

### CONCLUSION

There is a strong and relatively consistent body of accumulating evidence indicating that dairy products may significantly reduce the risk of T2D and likely in a dose-response manner. The protective effect of low-fat dairy products against T2D appears consistent in the literature. Evidence on regular-fat dairy products suggests no association with T2D or a beneficial impact. The role of specific dairy products such as cheese and yogurt appears beneficial.

### IMPLICATIONS FOR FUTURE RESEARCH

More research is needed to better understand the role of regular-fat and specific types of dairy products on incidence of T2D and indices of glycemic regulation. Large RCTs are needed to confirm findings on the role of dairy in the management of cardiometabolic risk factors, particularly in at risk population, such as those with prediabetes.

Randomized controlled trials are also warranted to increase our understanding of the role of individual dairy nutrients per se.
Moreover, mechanistic studies are essential to understand the underlying mechanisms regarding dairy products and specific dairy components in preventing T2D.

**IMPLICATIONS FOR PRACTICE**

Given the evidence regarding dairy products in T2D prevention, translation into practice, and clinical and public health guidance is warranted. The value of having an adequate intake of dairy products is to be reinforced especially during weight loss and among those with prediabetes and MetS.

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**Table 2 | Potential mechanisms of dairy products in preventing type 2 diabetes.**

| Component       | Mechanism                                                                                      |
|-----------------|-----------------------------------------------------------------------------------------------|
| Obesity and weight | Favorable effect of dairy products during weight loss through fat mass reduction and preservation/augmentation of lean mass. Reduction of lipogenesis and increase in lipolysis by high calcium intake. Prevention of fat absorption via the formation of calcium insoluble soaps. Increased fat oxidation by calcium. Role of whey protein in muscle sparing and lipid metabolism. |
| Metabolic syndrome | Reduced risk of MetS via improvement of several cardiometabolic risk factors (e.g., blood lipids, blood pressure, abdominal fat). |

**DAIRY COMPONENTS**

- **Calcium**
  - Regulation of insulin-mediated intracellular processes in insulin-responsive tissues.
  - Secretory function of pancreatic ß-cells.
  - Phosphorylation of insulin receptors.
  - Down-regulation of regulator genes encoding pro-inflammatory cytokines involved in insulin resistance.
  - Indirect effect via the regulation of extracellular calcium.
  - Reduction of lipogenesis and increase in lipolysis by high calcium intake.
  - Down-regulation of regulator genes encoding pro-inflammatory cytokines involved in insulin resistance.

- **Vitamin D**
  - Direct effect on insulin secretion by binding to vitamin D receptors in pancreatic ß-cells.
  - Indirect effect via the regulation of extracellular calcium.
  - Protection against systemic inflammation by counteracting cytokine generation.

- **Trans-palmitoleic acid**
  - Improvement of hepatic and peripheral insulin resistance, metabolic regulation, and suppression of hepatic de novo lipogenesis.
  - Lower levels of triglycerides, fasting insulin, blood pressure, and C-reactive protein.

- **Meta-analysis**
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