



Mini Review

Modelled Substitution of Meat with Dairy Products and Cardiometabolic Risk: A Mini-Review of Epidemiological and Mechanistic Evidence

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Abstract: Background: Epidemiological evidence consistently links higher consumption of red and processed meat with increased risk of type 2 diabetes (T2D) and adverse cardiometabolic outcomes, whereas dairy intake—particularly full-fat and fermented varieties—has shown neutral or protective associations. Understanding how substituting meat with dairy influences long-term metabolic and cardiovascular health can inform dietary recommendations and refine risk prediction models. Objective: This mini-review summarizes current epidemiological and mechanistic evidence on the modelled substitution of meat with dairy products in relation to T2D and broader cardiometabolic risk, with particular emphasis on findings from large-scale prospective studies. Evidence synthesis: Substitution analyses from multiple cohorts, including ATTICA, EPIC, and the Nurses' Health Studies, indicate that replacing one daily serving of red or total meat with dairy—especially fermented or full-fat forms—tends to reduce T2D risk by approximately 15–40% and may favorably influence lipid and blood pressure profiles. Proposed mechanisms include improved lipid and glucose metabolism, enhanced insulin sensitivity, modulation of the gut microbiota, and attenuation of systemic inflammation and oxidative stress, through dairy-derived bioactive compounds such as calcium, vitamin D, odd-chain fatty acids, and probiotics. Conclusions: Current evidence suggests that replacing meat with dairy products, particularly fermented and full-fat types, may modestly reduce long-term cardiometabolic risk, including T2D. This substitution framework highlights the importance of dietary quality and food-source replacement, offering a practical, evidence-based approach to metabolic and cardiovascular disease prevention.

Keywords: type 2 diabetes; cardiometabolic risk; red meat; fermented dairy; full-fat dairy; modelled substitution; Mediterranean diet

1. Background

Type 2 diabetes mellitus (T2D) and cardiometabolic diseases together represent a major global public health burden. According to the 11th edition of the International Diabetes Federation (IDF) Diabetes Atlas, approximately 589 million adults (11.1% of the global adult population) were living with diabetes in 2024, a prevalence projected to rise to 853 million by 2050. Notably, over 43% of cases remain undiagnosed, reflecting substantial gaps in prevention and early detection. The increasing incidence of T2D and cardiometabolic disorders, including among younger and middle-aged adults, underscores the urgent need to identify modifiable lifestyle determinants, among which diet plays a central role [1].



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Current nutritional recommendations from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) emphasize limiting red and processed meat consumption due to consistent associations with insulin resistance, low-grade inflammation, dyslipidemia, and increased cardiovascular risk [2,3]. Epidemiological studies and meta-analyses consistently demonstrate that high intake of red and processed meat is associated with increased risk of T2D and cardiometabolic disease across diverse populations [4–6]. Proposed biological mechanisms include increased oxidative stress and endothelial dysfunction related to heme iron, accumulation of advanced glycation end-products, and gut microbiota-derived metabolites such as trimethylamine-N-oxide, all of which may contribute to impaired glucose metabolism and chronic inflammation.

In contrast, the relationship between dairy intake and cardiometabolic outcomes appears more nuanced and potentially protective depending on dairy type and processing characteristics. Dairy products provide high-quality protein, calcium, magnesium, and bioactive lipids, while fermented varieties such as yogurt and kefir additionally deliver probiotics and bioactive peptides that may improve insulin sensitivity, endothelial function, and inflammatory profiles [7,8]. Recent systematic reviews suggest that dairy consumption is generally neutral to modestly beneficial for cardiometabolic health, with higher intake associated with approximately 17% lower all-cause mortality, 22% lower risk of major cardiovascular events, and around 34% lower stroke risk [9]. Yogurt consumption, in particular, has been linked with lower T2D incidence, with reported risk reductions ranging from 14% to 27% depending on intake level and product type [9]. Complementary umbrella reviews indicate modest inverse associations between total dairy or yogurt intake and cardiovascular outcomes as well as hypertension risk, although findings vary according to geographic context, dietary patterns, and food processing practices [10–13].

Growing emphasis in nutritional epidemiology has shifted from nutrient-based analyses toward food-based substitution models, which better reflect real-world dietary behavior by evaluating what foods replace others under isocaloric conditions. Evidence from systematic reviews and meta-analyses indicates that replacing dairy products with red or processed meat is associated with approximately 11–20% higher risks of mortality and cardiometabolic disease, and up to 41% higher risk of T2D when processed meat is considered [12]. Conversely, substituting red or processed meat with dairy products—particularly fermented or full-fat varieties—may be associated with lower cardiometabolic risk, supporting the concept that dietary quality and replacement patterns may be more informative than single-food restriction alone.

Despite accumulating evidence, important gaps remain. Much of the available literature has focused on replacing meat with plant-based foods, while comparatively fewer studies have examined meat–dairy substitutions. Furthermore, data from Mediterranean populations are limited, and only a small number of studies have applied isocaloric substitution models capable of isolating food-specific effects independent of total energy intake. Although Mediterranean centers within large European cohorts such as EPIC have explored associations between meat and dairy intake and cardiometabolic outcomes, few investigations have specifically modeled the substitution of meat with dairy products [14].

Findings from the 20-year ATTICA prospective cohort (2002–2022) help address this gap, representing one of the few long-term studies from a Mediterranean population to evaluate the cardiometabolic implications of replacing meat with dairy products within a culturally relevant dietary context [15]. Beyond their immediate epidemiologic relevance, such findings support a broader paradigm shift toward food-based substitution frameworks emphasizing dietary balance and realistic dietary replacement strategies rather than categorical elimination approaches.

Against this background, the aim of the present mini-review is to synthesize current epidemiological and mechanistic evidence on the modeled substitution of meat with dairy products in relation to T2D and broader cardiometabolic outcomes. According to the PICOS framework, the review focuses on: Population—adult populations included in observational and clinical studies; Intervention/Exposure—substitution of total, red, or processed meat with dairy products (including full-fat and fermented varieties); Comparison—continued meat consumption or alternative dietary patterns; Outcomes—T2D incidence and cardiometabolic outcomes such as hypertension, dyslipidemia, and glycemic markers; and Study design—prospective cohort studies, clinical investigations, and systematic reviews/meta-analyses.

2. Methods

2.1. Search Procedures

A targeted literature search was conducted in PubMed/MEDLINE, Scopus, and Web of Science for articles published up to [October, 2025]. Search terms combined concepts related to meat intake (e.g., “red meat”, “processed meat”), dairy (e.g., “dairy”, “full-fat”, “fermented”, “yogurt”, “kefir”), and substitution modeling (e.g., “food substitution”, “isocaloric substitution”, “replacement”), together with outcomes of interest (“type 2 diabetes”,

“cardiometabolic”, “hypertension”, “dyslipidemia”). We included studies in adults reporting associations of meat–dairy substitutions (or closely related comparative analyses) with T2D and/or cardiometabolic outcomes, including prospective cohorts, clinical/intervention studies, and systematic reviews/meta-analyses. Animal-only studies, pediatric populations, and reports without relevant outcomes were excluded. Reference lists of eligible articles and recent reviews were additionally screened to identify further relevant publications.

2.2. Evidence Synthesis

The final evidence base included prospective cohort studies, systematic reviews/meta-analyses, and mechanistic investigations examining the substitution of meat with dairy products and related cardiometabolic outcomes. Major prospective cohorts included large population-based studies from North America and Europe, such as the Nurses’ Health Study, Health Professionals Follow-Up Study, EPIC-InterAct, and the Danish Diet, Cancer and Health Study, as well as Mediterranean data from the ATTICA cohort. These studies primarily investigated associations between meat and dairy consumption patterns, or modeled isocaloric substitutions, in relation to T2D incidence, cardiovascular outcomes, blood pressure, lipid profiles, and markers of glycemic control. Included studies varied in design and sample size but consistently focused on adult populations and long-term cardiometabolic outcomes. Recent systematic reviews and meta-analyses were additionally considered to contextualize observational findings and explore mechanistic pathways related to insulin sensitivity, inflammation, lipid metabolism, and gut microbiome modulation.

3. Modelled Substitution of Meat with Dairy Products

Evidence from prospective cohorts and recent systematic reviews suggests that replacing red or processed meat with dairy products may be associated with favorable cardiometabolic outcomes. Large North American cohorts, including the Nurses’ Health Study and Health Professionals Follow-Up Study, reported lower risk of incident T2D when meat was replaced by dairy products, while European studies such as EPIC-InterAct and the Danish Diet, Cancer and Health Study highlighted potential benefits of fermented dairy intake for metabolic and cardiovascular outcomes [14,16,17]. Similarly, population-based studies from Scandinavian countries suggested that fermented dairy products were inversely associated with cardiometabolic risk, whereas non-fermented dairy showed neutral or inconsistent associations [17,18]. Within the Mediterranean context, findings from the ATTICA cohort indicated directionally consistent but borderline inverse associations between isocaloric substitution of total or red/processed meat with full-fat or fermented dairy and long-term incidence of T2D and composite cardiometabolic outcomes [15].

Despite overall consistency in directionality, several methodological limitations should be acknowledged. Most evidence derives from observational cohort studies, which preclude causal inference and remain vulnerable to residual confounding and measurement error related to self-reported dietary intake [9,12,14]. Definitions of dairy categories vary substantially across studies, particularly regarding fat content and fermentation status, complicating direct comparisons [12,18]. In addition, substitution models represent statistical estimates under isocaloric assumptions and may not fully capture real-world dietary behaviors or cultural dietary patterns [14,17]. Finally, evidence from Mediterranean populations remains relatively limited compared with Northern European and North American cohorts, highlighting the need for further longitudinal studies integrating repeated dietary measurements and objective biomarkers [14,15].

4. Mechanisms beyond Substitution of Meat with Dairy Products in Relation to Cardiovascular Health

Several biological mechanisms may explain the cardiometabolic associations observed when meat is replaced with dairy products, extending beyond the statistical framework of dietary substitution models. High intake of red and processed meat has been linked to increased cardiometabolic risk through multiple pathways, including oxidative stress mediated by heme iron, accumulation of advanced glycation end-products (AGEs), and elevations in branched-chain amino acids (BCAAs) and carnitine that may impair insulin signaling and glucose homeostasis. In addition, gut microbial metabolism of carnitine and choline produces trimethylamine-N-oxide (TMAO), a metabolite associated with inflammation, endothelial dysfunction, and atherosclerotic processes [4,6,14,19].

Conversely, dairy products—particularly full-fat and fermented varieties—contain complex nutrient matrices that may confer metabolic and vascular benefits. Dairy-derived odd-chain saturated fatty acids (C15:0 and C17:0), calcium, vitamin D, and bioactive peptides have been associated with improved insulin sensitivity and lipid metabolism. Fermented dairy products provide probiotics and fermentation-related compounds that may beneficially modulate gut microbiota composition, strengthen intestinal barrier integrity, and reduce low-grade inflammation [12,17,18]. Additional components such as the milk fat globule membrane (MFGM), vitamin K₂,

and fermentation-derived peptides have been proposed to enhance endothelial function and nitric oxide bioavailability, thereby contributing to vascular protection [6,11,20].

Collectively, these mechanisms support the biological plausibility of epidemiologic findings suggesting that replacing meat with selected dairy products may contribute to improved cardiometabolic profiles. Importantly, these pathways likely act synergistically through modulation of inflammation, lipid metabolism, endothelial function, and glucose regulation, emphasizing that food matrix interactions may be more relevant than isolated nutrient effects.

5. Discussion

The ATTICA study contributes novel evidence to the growing literature on the cardiometabolic impact of food substitutions, particularly the exchange of meat with dairy products. Over two decades of follow-up, isocaloric replacement of total or red/processed meat with full-fat or fermented dairy was associated with a borderline inverse association with T2D incidence, while similar trends were observed for composite cardiometabolic outcomes including hypertension and dyslipidemia [15]. Although these results did not reach conventional statistical significance, the direction and magnitude of the associations align with findings from other large-scale cohorts and systematic reviews published in 2023–2025 [9,11,12,21].

5.1. Potential Mechanisms Linking Meat Consumption to Cardiometabolic, and Type 2 Diabetes Risk

A substantial body of evidence supports the adverse metabolic and cardiovascular implications of red and processed meat consumption. Several interrelated biological mechanisms have been proposed to explain these associations. Excessive intake of heme iron promotes oxidative stress, β -cell dysfunction, and impaired insulin secretion, while the accumulation of advanced glycation end-products (AGEs) disrupts insulin signaling and induces endothelial damage. Elevated levels of branched-chain amino acids (BCAAs) and carnitine, abundant in meat, have been linked to impaired glucose homeostasis and insulin resistance. Moreover, gut microbial metabolism of carnitine and choline produces trimethylamine-N-oxide (TMAO), a pro-inflammatory metabolite implicated in atherosclerosis, endothelial dysfunction, and overall cardiometabolic dysregulation. Collectively, these mechanisms delineate a biologically plausible pathway through which high intake of red and processed meat contributes to both insulin resistance and the broader spectrum of cardiometabolic risk, encompassing T2D, dyslipidemia, and cardiovascular disease [4,6,14,19].

5.2. Mechanistic Rationale for the Protective Effects of Dairy Products

In contrast to meat, full-fat and fermented dairy products exhibit complex nutrient matrices that may confer both metabolic and vascular benefits. These foods provide a rich source of odd-chain saturated fatty acids (C15:0 and C17:0), calcium, vitamin D, and probiotics—nutrients and bioactive components known to enhance insulin sensitivity, reduce oxidative stress, and improve lipid metabolism [12,17]. Full-fat dairy intake has been inversely associated with fasting glucose, Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), and triglyceride levels in metabolomic studies, suggesting a potential role in maintaining metabolic homeostasis.

Fermented dairy products, such as yogurt and kefir, contribute additional bioactive peptides and short-chain fatty acids that beneficially modulate gut microbiota composition, strengthen intestinal barrier integrity, and attenuate low-grade inflammation—mechanistic pathways closely linked to improved insulin sensitivity. Clinical evidence supports this concept: probiotic-enriched fermented milk has been shown to lower fasting glucose, glycated hemoglobin (HbA1c), and C-reactive protein concentrations among individuals with T2D [12,22].

Moreover, constituents unique to dairy, including the milk fat globule membrane (MFGM), vitamin K₂, and fermentation-derived peptides, appear to exert vasculoprotective actions by enhancing insulin signaling, promoting lipid oxidation, and reducing systemic inflammation [20,22,23]. Taormina et al. further demonstrated that MFGM and fermentation peptides improve nitric oxide bioavailability and endothelial function, contributing to vascular resilience [11].

Collectively, these mechanistic insights provide biological plausibility for the epidemiological observations that dairy consumption—particularly of full-fat and fermented varieties—may lower cardiometabolic risk when it replaces meat in the diet.

5.3. Epidemiologic Consistency with Prior Cohorts and Reviews

The findings from the ATTICA cohort align closely with international evidence examining the substitution of meat with dairy products in relation to T2D and cardiometabolic outcomes. Data from the Nurses' Health Study

and the Health Professionals Follow-Up Study demonstrated that replacing meat with dairy was associated with a 22% lower risk of T2D after multivariable adjustment [5]. Similarly, large European cohorts such as EPIC-InterAct and the Danish Diet, Cancer, and Health Study reported inverse associations between fermented dairy intake and both T2D and cardiovascular disease (CVD) outcomes, reinforcing the consistency of these findings across diverse populations [12,14,24,25].

Population-based research from Sweden further supported these results, showing that fermented milk, cream, and butter were inversely associated with incident T2D, whereas non-fermented milk and processed cheese were positively associated [18]. Collectively, these studies indicate that the metabolic and cardiometabolic effects of dairy are not homogeneous but depend substantially on product type, fat composition, and degree of fermentation.

Recent systematic reviews strengthen this evidence base. Kiesswetter et al. and Givens et al. confirmed that the beneficial associations of dairy extend beyond glycemic regulation to improvements in blood pressure, lipid metabolism, and overall cardiometabolic health, underscoring the systemic relevance of food substitution strategies in chronic disease prevention [9,12].

Within the ATTICA cohort, the modeled substitution of total meat with full-fat or fermented dairy yielded directionally consistent associations with these prior findings, while substitutions involving white meat or low-fat dairy were not significant. Adjustment for adiposity did not materially alter the estimates, suggesting that body mass index was unlikely to mediate the observed associations. However, further adjustment for inflammatory and lipid markers—specifically C-reactive protein and total cholesterol—modestly attenuated the associations, implicating inflammatory and lipid-metabolic pathways as potential mediators linking dietary substitution patterns with reduced cardiometabolic risk [15].

5.4. Contribution to Substitution Modeling Literature and Clinical Implications

The present findings expand upon existing evidence by employing an isocaloric substitution framework to assess the hypothetical exchange of one protein source for another under conditions of constant total energy intake. This analytical approach reflects realistic dietary modifications and mitigates confounding by total caloric intake—an inherent limitation in many traditional dietary analyses. Prior prospective studies, including the EPIC-InterAct consortium and pooled analyses from U.S. cohorts, have demonstrated that replacing red or processed meat with dairy, particularly fermented or higher-fat types, is associated with a reduced risk of T2D diabetes [14,26]. A recent meta-analysis further concluded that replacing dairy with red meat increases T2D incidence, whereas the inverse substitution—replacing meat with dairy—may be protective [16].

In this context, the ATTICA findings, though modest in magnitude, reinforce the conceptual and clinical value of dietary substitution frameworks. Rather than focusing solely on nutrient restriction or total intake, substitution modeling emphasizes the quality and direction of dietary change—what foods replace one another—and thereby provides a more nuanced and actionable basis for dietary guidance. Such models align with modern public health nutrition paradigms, which advocate for balanced, flexible, and culturally adaptable dietary strategies over restrictive or exclusionary approaches.

From a clinical standpoint, these findings support a shift toward food-based, quality-oriented dietary advice. Replacing portions of red or processed meat with fermented or full-fat dairy—within an isocaloric, nutrient-balanced framework—may yield small but clinically meaningful improvements in glycemic control, blood pressure regulation, and lipid metabolism. These benefits align with cardiometabolic prevention strategies that prioritize dietary quality, matrix interactions, and substitution patterns rather than categorical elimination of food groups.

Implementing this substitution-focused guidance in clinical and community settings could enhance dietary adherence and improve long-term metabolic outcomes, especially when integrated into Mediterranean-style or balanced omnivorous dietary patterns. Ultimately, these results highlight the importance of pragmatic dietary recommendations that optimize food quality and substitution rather than relying solely on reductionist metrics of single-nutrient limitation.

A summary of the key studies discussed, including their design and main findings, is provided in Supplementary Materials Table S1 to facilitate comparison across the available evidence.

6. Conclusive Remarks and Future Directions

The evidence summarized in this mini-review suggests that replacing total or red/processed meat with selected dairy products, particularly fermented and full-fat varieties, may be associated with modest improvements in T2D diabetes risk and broader cardiometabolic outcomes. Findings from prospective cohorts, including data from Mediterranean populations such as the ATTICA study, indicate consistent directionality toward benefit, although associations are generally modest and not uniformly statistically significant.

From a clinical and public health perspective, these findings support the growing emphasis on food-based dietary substitution approaches rather than isolated nutrient restriction. Substitution models provide a pragmatic framework for dietary guidance, emphasizing improvements in food quality and realistic dietary modifications that may enhance long-term adherence and cardiometabolic resilience.

Future research should focus on longitudinal studies incorporating repeated dietary assessments, objective biomarkers, and advanced analytical approaches such as metabolomics, microbiome profiling, and causal inference modeling to better clarify underlying biological mechanisms. In addition, further investigation in Mediterranean and other culturally diverse populations is warranted to enhance generalizability and refine food-based prevention strategies.

Overall, a substitution-focused dietary framework that prioritizes balanced food replacement rather than categorical elimination may represent a promising strategy for the prevention of type 2 diabetes and cardiovascular disease.

Supplementary Materials

The additional data and information can be downloaded at: <https://media.sciltp.com/articles/others/2603161024213163/JCMDE-25100138-SM.pdf>. Table S1: Summary of epidemiological and mechanistic evidence supporting meat-to-dairy substitution and cardiometabolic outcomes.

Author Contributions

I.K.: conceptualization, methodology, software; I.K.: data curation, writing—original draft preparation; D.V.: visualization, investigation; I.K.: supervision; O.T.: software, validation; I.K.: writing—reviewing and editing. All authors have read and agreed to the published version of the manuscript.

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No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

AI-assisted tools were used only for language improvement. The authors reviewed and edited the content and take full responsibility for the final manuscript.

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