

Review

Dairy, chronic disease risk, and the comparator problem: What substitution analyses reveal

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Abstract: Epidemiological evidence links dairy consumption with neutral or modestly favorable chronic disease outcomes, shaping clinical practice guidelines worldwide. However, assessing dairy in isolation is inadequate for guiding practice, because the health implications of any food are significantly influenced by the foods it displaces. Substitution analyses directly address this gap: rather than questioning whether dairy is inherently harmful or beneficial, these studies investigate whether dairy is associated with better or worse outcomes relative to specific alternatives. This narrative review integrates evidence from prospective cohort studies, systematic reviews, and meta-analyses published between January 2000 and February 2026 that use food and nutrient substitution models to evaluate the comparative health impacts of dairy. The literature consistently indicates that dairy is associated with more favorable outcomes than red and processed meats with respect to cardiovascular disease (CVD) and all-cause mortality, and suggests that saturated fat from dairy poses a lower cardiovascular risk than saturated fat from meat. Conversely, dairy is surpassed by whole plant foods, including nuts, legumes, and whole grains, as well as fish, across outcomes such as CVD, type 2 diabetes, cancer, and all-cause mortality. Within the dairy category, fermented products such as yogurt and cheese demonstrate more favorable associations than non-fermented dairy. When dairy intake is reduced or eliminated, nutritional adequacy for key micronutrients, including calcium and iodine, can be maintained through targeted dietary strategies and supplementation. Health professionals and researchers are encouraged to adopt the comparative perspective offered by substitution analyses, recognizing that the health implications attributed to dairy are largely a function of what it replaces, or what replaces it, within the overall dietary pattern, rather than reflecting an inherent property of dairy in isolation.

Keywords: Dairy, Substitution analysis, Cardiovascular disease, Type 2 diabetes, Cancer, Mortality

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1. Introduction

The evidence base concerning dairy consumption and chronic disease presents mixed findings and remains subject to ongoing scientific debate: in a global analysis using the China Kadoorie Biobank and the UK Biobank, complemented by an updated meta-analysis, regular dairy consumption was associated with a higher risk of coronary heart disease among Chinese adults, whereas total dairy consumption was associated with a lower risk of cardiovascular disease among British adults [1]. Uncertainty persists regarding the essentiality of dairy for skeletal health and the extent to which its saturated fat content poses cardiovascular risks. Differences across dairy subtypes and between study populations further complicate the formulation of universal conclusions [1]. Divergent dietary guidelines illustrate this ambiguity: approximately 38% of clinical practice guidelines advocate the consumption of low-fat dairy, increasing to 60% among guidelines directed at cardiovascular diseases (CVD) [2].

Prospective cohort studies, systematic reviews, and meta-analyses generally indicate that dairy consumption is neutral or slightly beneficial for major chronic disease outcomes, including the risk of type 2 diabetes (T2D), obesity, hypertension, and CVD mortality [3–8]. However, these studies leave the critical question, “Compared to what?” unanswered. Assessing dairy in isolation is inadequate for informing dietary advice, because each food choice involves selecting among alternatives, and the health implications of that choice depend on what is displaced. Substitution analyses explicitly address this comparative issue by modeling the effect of replacing one specific food with another under isocaloric conditions [9]. This review integrates findings from substitution analyses and provides an overview of methodological considerations, key comparisons, and practical implications for dietary guidance.

The emergence of substitution analyses as a methodological priority reflects an evolution in nutritional epidemiology—from single-nutrient models to whole-food assessments to dietary pattern research—driven by the recognition that dietary choices are inherently comparative and that the health implications of any food depend fundamentally on the dietary context in which it is consumed. In the context of dairy, this issue is particularly important: the same food may appear protective when compared with red meat, and comparatively less favorable when compared with nuts or whole grains. This context-dependence has contributed to apparent contradictions in public communication of dairy research and highlights the importance of asking “Compared to what?”, a question with direct clinical implications [9].

2. Methods

This narrative review was conducted by searching PubMed for studies published in English between January 2000 and February 2026. The search incorporated combinations of terms, including “dairy”, “milk”, “cheese”, “yogurt”, “substitution”, “replacement”, “chronic disease”, “cardiovascular disease”, “mortality”, “type 2 diabetes”, and “cancer”. Inclusion criteria allowed studies reporting substitution or replacement analyses in human populations using prospective cohort designs, as well as systematic reviews or meta-analyses synthesizing such data. Exclusion criteria included studies using only cross-sectional designs, those reporting exclusively animal or *in vitro* data, or those lacking quantification or characterization of a substitution effect. When systematic reviews or meta-analyses were available, findings from individual cohorts that contributed to pooled estimates were reported through those pooled sources, in accordance with conventional methodology for narrative reviews. Additionally, reference lists of all included studies were screened to identify supplementary relevant sources not identified through the primary database search. Studies were prioritized based on their explicit use of isocaloric substitution or replacement models, with systematic reviews and meta-analyses given precedence over individual cohort studies when pooled estimates were available. As this is a narrative review with no original data analysis, no statistical software was employed.

3. Methodological limitations and biases in dairy research

Several characteristics of research on dairy in isolation constrain the strength of its conclusions. A systematic review conducted by Chartres et al. assessed 40 cohort studies and 3 case-control studies on dairy consumption and CVD outcomes, finding that all studies carried a high risk of bias. Specifically, 33 studies were rated as “critical” risk according to the Risk of Bias in Non-Randomized Studies of Exposure tool. The principal source of bias was inadequate control for dietary confounders; numerous studies failed to adjust for fruit and vegetable intake, which is independently and inversely correlated with CVD risk [10].

Notably, the aforementioned systematic review found that industry-sponsored studies reported lower hazard ratios (HR) for CVD outcomes (HR: 0.78; 95% CI: 0.65–0.94; $n = 3$) than non-industry-sponsored studies (HR: 0.97; 95% CI: 0.93–1.02; $n = 18$). This difference was statistically significant (ratio of HRs: 0.80; 95% CI: 0.66–0.97; $p = 0.03$), indicating a systematic underestimation of risk among studies with industry funding compared to those with non-industry support. Furthermore, industry-funded studies were more likely to categorize total dairy as a single group (100% versus 83% in non-industry-sponsored studies), masking variation among subtypes.

In six of 43 studies (14%), unfavorable results were juxtaposed with favorable conclusions, including three of 14 studies with industry affiliations (21%) and three of 29 without industry ties (10%), resulting in a risk ratio for discordance of 2.07 (95% CI: 0.48–8.99). However, this finding did not show a statistically significant association with food industry ties [10].

Lifestyle confounding presents an additional threat to validity. In certain populations, high intake of high-fat dairy and butter clusters with unfavorable behavioral patterns, including preferences for sweets and tobacco use [11]. Failure to adjust for these correlated behaviors can result in spurious associations and an overestimation of dairy-related risk [11]. In other populations where milk consumption is associated with health-conscious behaviors, the direction of confounding reverses, and neglecting to adjust for favorable habits may lead to underestimation of risk [12]. Methodological heterogeneity in the categorization of dairy fat content is also a concern [6]. Measurement error magnifies these concerns: food frequency questionnaires routinely capture less than half of the true inter-individual variability in whole milk intake [13], and publication bias has been observed in meta-analyses of milk consumption and all-cause mortality or stroke, indicating that risks linked to milk consumption may be systematically undervalued [12]. Taken together, these limitations support adopting a more rigorous comparative framework through substitution analysis.

It is equally important to recognize that studies reporting favorable outcomes for plant-based dietary patterns are not immune to comparable methodological challenges. Confounding bias can operate in both directions. In populations where plant-based eating clusters with health-conscious behaviors such as regular physical activity, non-smoking, and higher socioeconomic status, favorable associations may be at least partly attributable to these correlated factors rather than to diet alone [14]. Conversely, as noted above, unaccounted confounding variables may inflate apparent risks in populations where dairy consumption is associated with unfavorable lifestyle patterns. In Western cohorts, socioeconomic status and educational attainment are strongly correlated with healthful plant-based dietary patterns, introducing deep, residual lifestyle confounding that even comprehensively adjusted observational models struggle to isolate completely [15–18]. These considerations apply across all observational dietary research and should be borne in mind when interpreting substitution analyses as well as non-substitution studies.

4. The substitution analysis framework: contextualizing the health implications of dairy

Substitution models are predicated on the principle that,

because total energy intake within individuals tends to remain relatively stable over time, a sustained increase in the consumption of one food item is generally accompanied by a decrease in others [9]. Ibsen et al. delineate two primary types of models: nonspecified substitution models, which compare a food to an unspecified array of alternatives determined by background dietary patterns; and specified substitution models, which compare two particular foods directly [9]. Because nonspecified models do not specify which foods are displaced, their outcomes are heavily influenced by the composition of the background diet and can be difficult to interpret across populations. Consequently, specified models are preferred for generating actionable dietary guidance, as they provide explicit comparisons and identify optimal dietary substitutions rather than merely characterizing a food relative to an indeterminate mix of alternatives [9]. This distinction is particularly important in dairy research: findings may appear favorable when the implicit comparator is a nutrient-poor food such as red or processed meat. However, outcomes may seem less advantageous when the comparator is a whole plant food or fish [19–20]. Figure 1 illustrates this concept by positioning selected foods along a continuum of relative all-cause mortality risk, with dairy serving as the reference point; all depicted foods are derived from specified substitution analyses in which the comparator is explicitly defined.

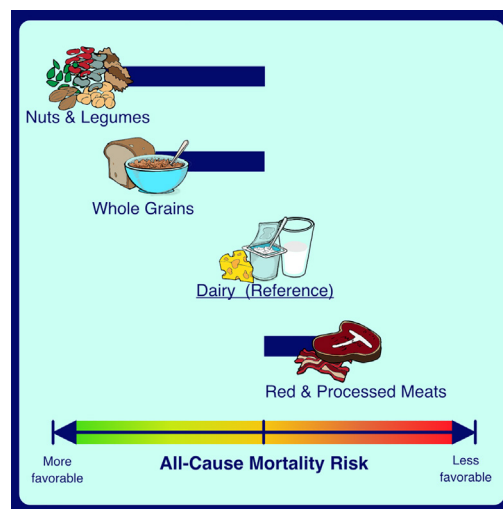


Figure 1. Whole-food substitutions and all-cause mortality: Relative favorability of food groups

Note. Positions on the continuum were derived from isocaloric per-serving substitution hazard ratios reported by Ding et al. across three prospective US cohorts ($n = 217,755$; follow-up up to 32 years) [19]. Each hazard ratio reflects the association with all-cause mortality when one daily serving of dairy is replaced with the indicated food, or vice versa, under isocaloric conditions. Raw hazard ratios were normalized to a 0–100 scale using the formula: $\text{Score} = (\text{HR}_{\text{worst}} - \text{HR}_{\text{food}}) / (\text{HR}_{\text{worst}} - \text{HR}_{\text{best}}) \times 100$, where HR_{best} and HR_{worst} represent the lowest and highest hazard ratios within this food set, respectively. The resulting scale reflects relative favorability

within this specific substitution model only and does not permit cross-outcome comparisons. Dairy serves as the reference category (HR = 1.00).

5. Strengths and limitations of substitution analyses

Substitution analyses offer a more clinically actionable comparative framework than analyses of absolute food intake because they explicitly model dietary trade-offs rather than treating foods in isolation [9]. However, several important limitations should be considered when interpreting the findings reviewed here. First, even specified substitution models cannot fully disentangle the effect of replacing one food from correlated changes elsewhere in the diet or lifestyle. Residual confounding remains a concern in all observational designs. Second, these models assume a hypothetical isocaloric exchange, which may not reflect how dietary behavior changes in practice. In real-world settings, reducing one food may result in non-isocaloric and non-specific dietary shifts that do not mirror the model's assumptions. Third, dietary assessment through food frequency questionnaires introduces measurement error that may attenuate substitution effect estimates and may differ in its error structure between the two foods being compared, potentially biasing results in unpredictable directions. Fourth, the assumption that total energy intake remains constant across the substitution is a modeling constraint, not an empirically verified observation, and its validity may vary across populations and dietary contexts. A further consideration is between-study heterogeneity: meta-analyses in this area report substantial variability in effect estimates across included studies, with I^2 values occasionally exceeding 90% for specific substitution comparisons and prediction intervals that frequently cross the null, indicating that the true effect in a future study could be negligible or reversed [20]. These limitations do not undermine the value of substitution analyses, which remain the most direct observational tool available for addressing comparative dietary questions, but they warrant epistemic caution when translating findings into clinical guidance [9].

6. Dairy compares favorably when replacing red and processed meat

The most consistent finding from substitution analyses is that dairy compares favorably to red and processed meats across mortality and cardiometabolic outcomes [19–21]. Ding et al. examined three cohort studies totaling 217,755 participants over 32 years and reported that substituting one daily dairy serving with red or processed meat was associated with a 5% higher mortality risk (HR: 1.05; 95% CI: 1.01, 1.09) [19]. A systematic review by Kiesswetter et

al., which included 15 studies, reported that replacing 200 g/day of low-fat dairy with red meat was associated with higher all-cause mortality (summary relative risk [SRR]: 1.11; 95% CI: 1.06, 1.16), higher coronary artery disease (CAD) risk (SRR: 1.13; 95% CI: 1.08, 1.18), and higher type 2 diabetes risk (SRR: 1.20; 95% CI: 1.16, 1.25), each at moderate certainty of evidence. The CAD estimate pooled three cohorts, and the corresponding estimate for whole-fat dairy replaced with red meat was similar (SRR: 1.12; 95% CI: 1.07, 1.17); in both analyses the prediction interval crossed the null, indicating that the association in a future study could be attenuated or reversed [20]. Similarly, a prospective cohort study of 409,885 men and women in Europe determined that replacing 100 kcal/day of red and processed meat with an isocaloric serving of yogurt or cheese was associated with a 16% and 15% lower risk of CHD, respectively (HR: 0.84; 95% CI: 0.76, 0.92 and HR: 0.85; 95% CI: 0.79, 0.92) [22].

These benefits may be attributable to several adverse properties of red and processed meats. Heme iron, which is abundant in red meat, has been associated with a higher risk of cardiovascular disease and type 2 diabetes in dose-response meta-analyses of prospective cohort studies [23–24]; more broadly, higher red meat consumption has been associated with increased cardiovascular disease and T2D risk in meta-analyses of prospective cohort studies [25]. These associations have been hypothesized to involve oxidative stress, systemic inflammation, and impaired insulin signaling, supported in part by biomarker analyses linking heme iron intake to unfavorable profiles of insulinemia, lipids, and inflammation [26], although such mechanisms have not been firmly established as causal in humans. Nitrate and nitrite additives characteristic of processed meats have additionally been proposed as contributing factors, although the evidence is outcome-specific: in the Danish Diet, Cancer and Health cohort, nitrate from additive-permitted meat sources was associated with higher all-cause mortality (highest compared with lowest quintile, HR: 1.19; 95% CI: 1.14, 1.25), whereas plant-sourced nitrate was inversely associated (HR: 0.83; 95% CI: 0.80, 0.87); the same analysis found no association between additive-permitted meat-sourced nitrate and cardiovascular mortality (HR: 1.07; 95% CI: 0.96, 1.19) [27]. Heterogeneity exists across studies in this area, attributable in part to differences in dairy product classifications, background dietary patterns, and the amount of dairy consumed across populations, with northern European cohorts showing the highest intake and Asian cohorts the lowest, factors that Ding et al. identified as among the most important reasons for inconsistent findings [19]. Key findings from comparisons of dairy with red and processed meat are summarized in Table 1.

Table 1. Dairy vs. red and processed meat and within-dairy comparisons

Food substitution (Isocaloric)		Key source (s)	Outcome	Effect estimate	95% CI
Dairy vs. Red and processed meat	Low-fat dairy (200 g/d) → Red meat (142 g/d)	[20]	All-cause mortality	SRR 1.11	1.06, 1.16
	Dairy (1 serving/d) → Red/processed meat	[19]	All-cause mortality	HR 1.05	1.01, 1.09
	Low-fat dairy (200 g/d) → Red meat (125-142 g/d)	[20]	CAD	SRR 1.13	1.08, 1.18
	Total meat SFA → Dairy SFA (isoenergetic)	[21]	CVD	HR 0.91	0.86, 0.96
Within-dairy comparisons	Cheese (20 g/d) → Whole-fat milk (200 g/d)	[28]	All-cause mortality	HR 1.06–1.12 (sex-specific)	Men: 1.03, 1.10; Women: 1.07, 1.18
	Cheese (20 g/d) → Low-fat yogurt (200 g/d)	[28]	All-cause mortality	HR 1.11 (both sexes)	Men: 1.02, 1.20; Women: 1.03, 1.20

Note. CAD: coronary artery disease; CVD: cardiovascular disease; SFA: saturated fatty acids; SRR: summary relative risk; HR: hazard ratio. Effect estimates represent the association with the food in the second column, replacing the food in the first column under isocaloric conditions. Single-study findings not pooled

7. Dairy saturated fat versus meat saturated fat and CVD risk

Substitution analyses clarify the differing cardiovascular implications of saturated fat from dairy versus meat. Substitution estimates for saturated fat from meat versus dairy are presented in Table 1. In the European Prospective Investigation into Cancer and Nutrition Netherlands cohort of 35,767 participants followed for 15 years, Vissers et al. found that replacing 1% of energy from dairy-derived saturated fatty acids (SFA) with meat-derived SFA was associated with a 6% higher CHD risk (HR: 1.06; 95% CI: 1.02, 1.10) [29]. Similarly, in EPIC-Norfolk ($n = 22,050$) and EPIC-Denmark ($n = 53,375$), the association between SFA intake and myocardial infarction risk differed by carbon-chain length: in the Danish cohort, intakes of lauric acid (C12: 0) and myristic acid (C14: 0), which are relatively enriched in dairy fat, were inversely associated with myocardial infarction risk (HR for the highest versus lowest quintile: 0.80; 95% CI: 0.66, 0.96 for both), although no equivalent associations were observed in EPIC-Norfolk [30]. These outcomes may reflect the distinct fatty acid composition of dairy fat compared with meat fat. Dairy fat contains a greater proportion of short- and medium-chain SFA, as well as the longer-chain lauric acid (C12: 0) and myristic acid (C14: 0), whereas palmitic acid (C16: 0) predominates in both dairy and red meat fat [31–32]. The LDL-cholesterol response to dietary saturated fat also varies by carbon-chain length: in a meta-analysis of randomized trials, medium-chain triglyceride oil, composed almost exclusively of C6: 0–C10: 0 fatty acids, did not alter LDL cholesterol overall (0.02 mmol/L; 95% CI: -0.13, 0.17), although the effect differed by comparator (p for interaction = 0.008): LDL cholesterol rose when medium-chain

triglyceride oil displaced predominantly unsaturated fatty acids, with weak evidence of a reduction when it displaced longer-chain SFA [33]. Although LDL cholesterol is causally implicated in atherosclerotic CVD, as established by Mendelian randomization studies and lipid-lowering trials [34–35], these differences among individual fatty acids do not by themselves account for the more favorable cardiovascular profile of dairy fat relative to meat fat, since dairy fat is also comparatively rich in the longer-chain lauric and myristic acids; this difference is instead more plausibly attributable to the dairy food matrix [36]. Dairy also contains beneficial non-fat components, including calcium, magnesium, and phosphate [29, 36]. These intrinsic qualities of the dairy food matrix, including its mineral content and fermentation byproducts, may further help explain the observed cardiovascular differences [36].

This pattern was extended by Vogtschmidt et al. in the UK Biobank study involving 120,496 participants monitored over a median period of 10.5 years [21]. The study modeled isoenergetic substitutions of SFA derived from specific meat sources with dairy SFA. Replacing total meat SFA with total dairy SFA was associated with a 9% lower CVD risk (HR: 0.91; 95% CI: 0.86, 0.96). Substituting SFA from processed red meat with yogurt SFA was associated with a 20% decrease in CVD risk (HR: 0.80; 95% CI: 0.68, 0.94). Furthermore, replacing processed poultry SFA with dairy products was associated with substantial risk reductions (HR range: 0.58–0.67), although these estimates derive from a low mean and narrow range of poultry SFA intake in this cohort and should be interpreted with caution [21]. This food-source specificity is complemented by randomized evidence that reducing saturated fat intake lowers cardiovascular risk: in a Cochrane review of long-term trials, reducing dietary saturated fat reduced combined cardiovascular events

by 17% (RR: 0.83; 95% CI: 0.70, 0.98; 12 trials, 53,758 participants; moderate-certainty evidence), and meta-regression indicated that greater reductions in saturated fat, reflected in greater reductions in serum cholesterol, produced greater reductions in risk. Subgroup analyses in that review could not distinguish replacement with polyunsaturated fat from replacement with carbohydrate, underscoring that the comparator remains central to interpretation [37]. Collectively, these data support the substitution of fat from dairy for fat from red and processed meats as a strategy for reducing cardiovascular risk, although the dairy-specific estimates derive from a limited number of cohorts and their magnitude varies.

8. Within-dairy comparisons for CVD and mortality risk

Considerable variability also exists across dairy subtypes with respect to CVD and mortality risk. Fermented dairy products, such as cheese and yogurt, appear superior to non-fermented dairy. In two large Swedish cohorts comprising 61,433 women and 45,339 men, Michaëlsson et al. found that each additional daily glass of non-fermented milk was associated with higher all-cause mortality (HR: 1.15; 95% CI: 1.13, 1.17 in women; HR: 1.03; 95% CI: 1.01, 1.04 in men), whereas high intakes of fermented milk products and cheese were associated with lower mortality [38]. In the Danish Diet, Cancer and Health cohort, comprising 55,775 participants followed for a median of 19 years, Laursen et al. found that substituting fermented cheese with whole-fat milk was associated with a 6–12% increase in all-cause mortality (HR range: 1.06–1.12 across sexes; see Table 1). Furthermore, replacing fermented cheese with low-fat yogurt was associated with an 11% increase in mortality in both sexes (HR: 1.11 in both sexes; see Table 1) [28]. This is notable because it contradicts the common assumption that yogurt is healthier than cheese based on its saturated fat content. The authors suggested that the relative advantage of cheese may, in part, be ascribed to its fermentation-derived vitamin K2 [28], although evidence regarding dietary vitamin K2 benefits remains inconclusive, and the observed association could potentially be influenced by residual confounding from other dietary components [39] or the unique effects of the cheese matrix on blood lipid metabolism [40]. Consistent with these within-dairy observations, an umbrella review of prospective studies found that cheese consumption was associated with modestly lower risks of all-cause mortality, cardiovascular mortality, and incident cardiovascular disease [41]. Substitution analyses comparing low-fat and high-fat dairy are limited, and a systematic review and meta-analysis of prospective studies found that substituting these products for one another yielded largely null associations across health outcomes [20].

However, evidence from the ATTICA cohort, involving 1,988 Greek adults monitored over 20 years, found that,

among fermented products, replacing low-fat yogurt with whole-fat yogurt was associated with an increased risk of CVD (HR: 1.35; 95% CI: 1.02, 1.58), whereas replacing cheese with low-fat yogurt was associated with risk reductions for both feta cheese (HR: 0.75; 95% CI: 0.59, 0.91) and hard cheese (HR: 0.73; 95% CI: 0.45, 0.95) [42]. These data suggest that both fermentation and the fat content of dairy products may influence health outcomes. It should be noted that within-dairy substitution comparisons are derived predominantly from Northern European and US cohorts, and findings may not generalize to populations in which dairy varieties, fermentation practices, and baseline dietary patterns differ substantially.

Several important controversies within dairy research remain unresolved and merit explicit acknowledgment. With respect to fat content, substitution analyses comparing low-fat and high-fat dairy products have generally yielded null associations across health outcomes [20], suggesting that fat content alone may not be the primary determinant of dairy's health effects. However, evidence from cohort data suggests that, among fermented products specifically, fat content may modulate risk [42]. This is consistent with systematic-review evidence indicating that the cardiovascular associations of dairy depend more on the type of dairy food than on its fat content [43]. The dairy matrix hypothesis proposes that the complex food environment of dairy, encompassing mineral content, fermentation byproducts, milk fat globule membranes, and bioactive peptides, may explain why dairy saturated fat behaves differently from meat saturated fat, but the precise constituents and mechanisms responsible remain incompletely characterized [36]. Similarly, while fermented dairy products consistently demonstrate more favorable associations than non-fermented dairy, the proposed biological mechanisms, including vitamin K2 produced during fermentation, short-chain fatty acids, and probiotic effects, are biologically plausible but have not been definitively established as causal pathways in humans [39–40]. Readers are encouraged to consider these open questions when interpreting the findings discussed throughout this review.

9. Dairy compares less favorably when replacing plant foods and fish

Although dairy exhibits benefits relative to red and processed meats, substitution analyses indicate the opposite trend when whole plant foods are used as the comparator [19–20, 44–45]. Whole plant foods—particularly whole grains, nuts, and legumes, including soy—are associated with more beneficial outcomes than dairy across mortality, CVD, T2D, and cancer [19–20, 44–46]. Replacing dairy with fish is associated with reduced CHD risk [20, 47], as detailed in the subsequent section on mortality, CVD, and life expectancy. Tables 1–4 provide a summary of key substitution findings across outcome domains.

Table 2. Dairy vs. plant foods: Mortality, CVD, and cancer

	Food substitution (Isocaloric)	Key source (s)	Outcome	Effect estimate	95% CI
Dairy vs. plant foods: mortality, CVD, and cancer	Dairy (1 serving/d) → Nuts/legumes	[19]	All-cause mortality	HR 0.86	0.78, 0.95
	Dairy (1 serving/d) → Whole grains	[19]	All-cause mortality	HR 0.89	0.84, 0.93
	Dairy (1 serving/d) → Nuts	[46]	All-cause mortality	HR 0.88	0.80, 0.97
	Dairy fat (5% energy) → Plant-derived oils	[48]	CVD	HR 0.90	0.87, 0.93
	Dairy fat (5% energy) → Whole grain carbohydrates	[48]	CVD	HR 0.72	0.69, 0.75
	Dairy fat (0.3% energy) → Omega-3 PUFA	[48]	CVD	HR 0.89	0.84, 0.94
	Butter (10 g/d) → Plant-derived oils	[49]	All-cause mortality	HR 0.83	0.79, 0.86
	Butter (10 g/d) → Plant-derived oils	[49]	Cancer mortality	HR 0.83	0.76, 0.90
	Cheese (30 g) → Avocado	[20]	CAD	RR 0.81	0.72, 0.90
	Yogurt (200 g/d) → Whole grains	[20]	All-cause mortality	RR 0.91	0.85, 0.97
	Yogurt (200 g/d) → Nuts (23 g/d)	[20]	All-cause mortality	SRR 0.82	0.72, 0.94
	Dairy milk → Soy milk (median intake)	[50]	Breast cancer	HR 0.68	0.55, 0.85
	Dairy (1 serving/d) → Whole grains	[46]	Cancer-specific mortality	HR 0.91	0.87, 0.95

Note. CAD: coronary artery disease; CVD: cardiovascular disease; PUFA: polyunsaturated fatty acids; RR: relative risk; HR: hazard ratio. Effect estimates represent the association with the food in the second column, replacing the food in the first column under isocaloric conditions. Single-study findings not pooled

Table 3. Dairy vs. alternatives: T2D (and dairy vs. fish)

	Food substitution (Isocaloric)	Key source (s)	Outcome	Effect estimate	95% CI
Dairy vs. alternatives: T2D (and dairy vs. fish)					
Dairy vs. fish (CHD)	Whole-fat dairy (1 serving/d) → Fish	[47]	CAD	RR 0.83	0.69, 0.99
	Whole-fat dairy (200 g/d) → Fish (pooled)	[20]	CAD	SRR 0.93	0.73, 1.18
Dairy vs. alternatives (T2D)	Dairy fat (5% energy) → Whole grain carbs	[51]	T2D	HR 0.93	0.88, 0.98
	Dairy fat (0.3% energy) → Alpha-linolenic acid	[51]	T2D	HR 0.95	0.90, 0.995
	Dairy protein (1% energy) → Plant protein-rich foods	[52]	T2D	HR 0.79	0.65, 0.97
	Dairy (200 g/d) → Peanuts/peanut butter (28 g/d)	[20]	T2D	SRR 0.98	0.93, 1.03
	Dairy (200 g/d) → Whole grains (30 g/d)	[20]	T2D	SRR 0.97	0.95, 1.00

Note. CAD: coronary artery disease; T2D: type 2 diabetes; RR: relative risk; SRR: summary relative risk; HR: hazard ratio. Effect estimates represent the association with the food in the second column, replacing the food in the first column under isocaloric conditions. Single-study findings not pooled

Table 4. Dairy protein vs. plant protein-rich foods: Mortality and CVD

	Food substitution (Isocaloric)	Key source (s)	Outcome	Effect estimate	95% CI
Dairy protein vs. plant Protein-rich foods: Mortality and CVD	Dairy (contributing 3% of energy as protein) → Plant protein-rich foods	[45]	All-cause mortality	HR 0.92	0.87, 0.96
	Dairy (contributing 3% of energy as protein) → Plant protein-rich foods (men)	[53]	CVD mortality	HR 0.89	0.84, 0.94
	Dairy (contributing 3% of energy as protein) → Plant protein-rich foods (women)	[53]	CVD mortality	HR 0.88	0.82, 0.95
	Dairy (2 oz-equivalents/d) → Nuts	[54]	CVD mortality	HR 0.81	0.67, 0.97

Note. CVD: cardiovascular disease; HR: hazard ratio. Effect estimates represent the association with the food in the second column, replacing the food in the first column under isocaloric conditions. Single-study findings not pooled

9.1 Mortality, CVD, and life expectancy

Substituting whole plant foods for dairy products is consistently associated with lower mortality rates and reduced CVD risk across large, diverse cohort studies. A systematic review by Fernández-Fígares Jiménez and Storz [46] found that replacing one daily serving of dairy with nuts and legumes was associated with a 14% lower all-cause mortality risk; replacing dairy with whole grains with an 11% lower risk; and replacing dairy with nuts with a 12% lower risk [19, 46]. At the food level, replacing cheese (30 g) with avocado was associated with a 19% lower CAD risk [20]. Similarly, in the Atherosclerosis Risk in Communities cohort, Haring et al. found that replacing high-fat dairy with nuts (HR: 0.90; 95% CI: 0.78, 1.03) showed a directional but non-significant risk reduction in fully adjusted models [55]. Collectively, these findings suggest that substituting dairy with whole plant foods is consistently associated with lower mortality and cardiovascular risk.

Similar patterns are evident at the level of dietary fat. Chen et al. found that replacing 5% of energy from dairy fat with plant-derived oils, polyunsaturated fatty acids (PUFA), or whole grain carbohydrates was associated with 10%, 24%, and 28% lower CVD risk, respectively [48] (Table 2). Replacing dairy fat with marine omega-3 PUFA (0.3% of energy) was associated with an 11% reduction in CVD risk and a 13% reduction in CHD risk, plausibly mediated by substituting longer-chain dairy SFA with omega-3 PUFA, which improves lipid profiles [56]. Substituting butter specifically with plant-derived oils conferred meaningful additional benefit: Zhang et al. analyzed pooled data from 221,054 participants and found that replacing 10 g/day of butter with plant-derived oils was associated with 17% lower total mortality and 17% lower cancer mortality, with olive, canola, and soybean oils each independently associated with lower risk [49]. Similarly, Kiesswetter et al. found that substituting 5 g/day of butter with olive oil was associated with a 6% lower risk of all-cause mortality (SRR: 0.94; 95% CI: 0.92, 0.97)

[20]. Taken together, these results indicate that exchanging dairy fat for plant-derived or marine fat sources lowers both cardiovascular and overall mortality risk.

Substitution analyses comparing dairy with fish and poultry show directionally favorable but imprecise associations for CHD risk [20, 47, 55]. Substituting one daily serving of whole-fat dairy with fish was associated with a 17% lower relative risk (RR) of CAD in the Nurses' Health Study (RR: 0.83; 95% CI: 0.69, 0.99) [47], although the summary relative risk for replacing whole-fat dairy with fish was not statistically significant in a systematic review (SRR: 0.93; 95% CI: 0.73, 1.18) [20]. Bernstein et al. further observed that substituting fish with high-fat dairy was associated with increased CHD risk (RR: 1.24; 95% CI: 1.01, 1.53), whereas substituting dairy with poultry showed a non-significant reduction [47] (Table 3). Haring et al. also found that replacing high-fat dairy with fish (HR: 0.94; 95% CI: 0.75, 1.19) showed a directional but non-significant risk reduction in fully adjusted models, consistent with the broader pattern of variability across cohorts [55]. Overall, the evidence suggests a potential reduction in CHD risk when dairy is replaced with fish or poultry, although the lack of consistent statistical significance underscores the need for further research to clarify these relationships. Substitution estimates for dairy compared with plant foods across mortality and CVD outcomes are summarized in Table 2.

9.2 Protein source and mortality

Before reviewing specific findings on protein source and mortality, an important interpretive caveat must be acknowledged. The substitution analyses discussed in this section compare dairy products with plant protein-containing foods; they do not isolate the effect of protein as a macronutrient. These models reflect substitutions between complex food matrices that differ across multiple nutritional dimensions: plant protein sources are typically embedded in foods rich in dietary fiber, unsaturated fatty acids, and phytochemicals, whereas dairy represents a

distinct food matrix characterized by calcium, SFA, lactose, and bioactive peptides. Although some of these variables are commonly adjusted for in substitution analyses, many remain unaccounted for, such as phytochemical content and bioactive peptides. Accordingly, the associations reported in this section are more accurately interpreted as reflecting the substitution of dairy-containing foods with plant protein-rich foods, rather than the effect of protein source per se. This distinction should be considered when translating these findings into clinical or policy guidance [9].

Multiple substitution analyses have examined the association between replacing dairy with plant protein-rich foods (from sources that include whole grains, nuts, and legumes) and mortality risk [45, 52–54, 57]. In a prospective cohort study of 131,342 participants followed for up to 32 years, Song et al. found that replacing dairy (contributing 3% of energy as protein) with plant protein-rich foods was associated with an 8% reduction in all-cause mortality (HR: 0.92; 95% CI: 0.87, 0.96) [45]. Huang et al. observed consistent results in a larger cohort of 416,104 participants from the National Institutes of Health-American Association of Retired Persons Diet and Health Study, where substituting dairy products with plant protein-rich foods was also associated with an 8% reduction in all-cause mortality (HR: 0.92; 95% CI 0.89, 0.95) as well as lower CVD mortality in both women (HR: 0.88; 95% CI: 0.82, 0.95) and men (HR: 0.89; 95% CI: 0.84, 0.94) [53].

Additional evidence supports these life-expectancy benefits. A systematic review of seven cohorts and 13 randomized controlled trials by Lamberg-Allardt et al. identified an 11–12% reduction in CVD mortality associated with substituting dairy products with plant protein-rich foods [52]. In the Women's Health Initiative, Sun et al. followed 102,521 postmenopausal women over more than 1.8 million person-years and found that substituting 2 oz-equivalents/day of dairy products with nuts was associated with a 19% lower risk of CVD mortality (HR: 0.81; 95% CI: 0.67, 0.97) and a 30% lower risk of dementia mortality (HR: 0.70; 95% CI: 0.51, 0.96) [54]. Zheng et al. also conducted a systematic review encompassing more than 1.4 million participants, concluding that substituting plant protein for animal protein is associated with lower all-cause and cardiovascular mortality [57]. In one of the included cohort studies, Ortolá et al. found that substituting 1% of energy from dairy protein with plant protein was associated with less deficit accumulation over 8.2 years ($\beta = -0.51$; 95% CI: -0.91, -0.12), a validated measure of biological aging [58]. Collectively, this evidence suggests that substituting plant protein-rich foods for dairy products is consistently associated with improved longevity outcomes, particularly for cardiovascular mortality.

Population-level modeling reinforces these findings while highlighting that the net benefit is driven primarily by what replaces dairy rather than by dairy reduction alone. Using representative Canadian data, Auclair et al. developed a model in which half of all dairy consumption

(reducing total intake from 230.8 g/day to 115.4 g/day) was substituted with equivalent weights of plant-based protein foods [59]. This substitution included a 1:1 replacement of fluid milk with a fortified soy beverage, resulting in a quadrupling of plant protein food intake to 153.2 g/day. The scenario was associated with an increase in life expectancy of up to 7.6 months (95% CI: 4.81, 9.89). Notably, a reduction in milk intake alone corresponded to a decrease of 0.18 months in life expectancy, whereas the introduction of plant protein foods resulted in an increase of 7.75 months, more than offsetting the adverse effect of reduced milk consumption [59]. Substitution estimates for dairy protein compared with plant protein-rich foods across mortality outcomes are presented in Table 4.

9.3 Type 2 diabetes

The comparative effects of dairy, or its components, and their alternatives on T2D risk have also been clarified through substitution analyses. Using data from three cohorts in the United States, Ardisson Korat et al. found that substituting 5% of energy derived from dairy fat with whole grain carbohydrates was associated with a 7% lower risk of T2D (HR: 0.93; 95% CI: 0.88, 0.98) [51], potentially due to the beneficial effects of whole grains on glucose tolerance and insulin sensitivity [60]. Additionally, replacing 0.3% of dairy fat energy with alpha-linolenic acid was associated with a 5% decrease in risk (HR: 0.95; 95% CI: 0.90, 0.995). Conversely, substituting 5% of energy from dairy fat with refined grains was associated with a modest, borderline statistically significant 4% higher risk of T2D (HR: 1.04; 95% CI: 1.00, 1.08) [51]. At the protein and dietary level, Lamberg-Allardt et al. documented a 21% reduction in T2D risk (HR: 0.79; 95% CI: 0.65, 0.97) when 1% of energy derived from dairy was exchanged for plant protein-rich foods [52]. At the whole-food level, Kiesswetter et al. reported no association with T2D incidence when 200 g/day of dairy was replaced with whole grains (30 g/day; SRR: 0.97; 95% CI: 0.95, 1.00) or with peanuts and peanut butter (28 g/day; SRR: 0.98; 95% CI: 0.93, 1.03), although both point estimates were directionally favorable [20]. This evidence further suggests that substituting dairy fat and protein with high-quality plant-based carbohydrates and plant protein sources is associated with reduced T2D risk. Key substitution estimates for dairy and T2D risk are summarized in Table 3.

9.4 Cancer

The impact of replacing dairy with plant-based alternatives on cancer risk and mortality has also been investigated. In a prospective cohort study involving 52,795 North American Seventh-day Adventist women, Fraser et al. determined that replacing median intakes of dairy milk with soy milk was associated with a 32% reduction in breast cancer risk (HR: 0.68; 95% CI: 0.55, 0.85),

potentially mediated by bovine sex hormones and insulin-like growth factor-1 present in dairy milk [50]. A systematic review conducted by Fernández-Fígares Jiménez and Storz [46], encompassing 17 cohort and case-cohort studies, extended this evidence: substituting one daily serving of dairy with whole grains was associated with a 9% lower risk of cancer-specific mortality (HR: 0.91; 95% CI: 0.87, 0.95). This evidence suggests a potential reduction in cancer mortality when dairy is replaced with plant-based foods in observational analyses, although findings are heterogeneous across cancer types; associations vary by organ site, and dairy itself has been associated with a lower risk of colorectal cancer in non-substitution analyses [61]. Further research is needed to clarify substitution-specific associations across different cancer types and subpopulations, identify relevant confounding factors, and determine whether these associations reflect causal relationships between dietary substitutions and cancer risk or mortality. Cancer-related substitution findings involving dairy and plant-based foods are also presented in Table 2.

10. Nutritional considerations when reducing dairy intake

Two nutrients, calcium and iodine, warrant attention when substantially reducing or eliminating dairy intake. Adequate calcium intake may be achieved without dairy through white beans, soybeans, calcium-set tofu, dark leafy greens (e.g., kale, collard greens), almonds, tahini, and fortified plant milks or juices [62]. One cup of fortified plant milk may supply approximately 25–35% of the WHO and FAO recommended nutrient intake and 35–50% of the United Kingdom's Daily Reference Value for adults [62]. However, the bioavailability of that calcium may depend on the fortification salt used, although the evidence is not uniform: in osteopenic postmenopausal women, fractional calcium absorption from a soy milk fortified with a proprietary calcium phosphate was comparable to that from cows' milk ($\alpha = 0.65$ compared with 0.66; $p > 0.05$) [63]. Human absorption studies indicate that soy milks fortified with calcium carbonate likewise provide calcium bioavailability equivalent to that of dairy milk [64], whereas tricalcium phosphate fortification has been associated with modestly lower fractional absorption [64] and, *in vitro*, with markedly lower calcium bioaccessibility than bovine milk (below 5% compared with approximately 30% for skimmed milk) [65]. Because human absorption data for non-soy matrices remain limited, and because the bioavailability of micronutrients added during fortification has not been established, absolute bioequivalences cannot yet be generalized to all plant-based beverages [65–66]. Supplementation is a viable option when nutritional targets cannot be met through diet alone [62]. Modelling research indicates that replacing cow's milk with non-calcium-fortified plant-based beverages leaves calcium intake below both the average requirement and the population

reference intake, whereas calcium-fortified beverages restore intake to at least the average requirement; vitamin D intake remained below the average requirement in every scenario modelled, including those retaining cow's milk [67]. Specifically, a model involving a 50% reduction in dairy intake was associated with a 14% increase in the prevalence of calcium inadequacy [59]. To the authors' knowledge, no substitution analyses have primarily assessed bone mineral density or fracture risk, and the comparative skeletal effects of dairy versus plant-based substitutes remain an area in need of further research.

Consideration must also be given to iodine. The iodine content of dairy milk is primarily attributable to feed supplementation. Supplemental feeds contain approximately ten times more iodine than forage-based feeds, and iodine levels in milk are largely unaffected by environmental sources [68]. Most plant-based milk alternatives, however, are not fortified with iodine [69]. However, individuals reducing their dairy intake can meet their iodine requirements by using iodized salt or taking a daily supplement. Recommended iodine intakes are 150 micrograms for healthy adults, 90–130 micrograms for infants and children, 220 micrograms during pregnancy, and 290 micrograms during lactation [70]. Iodine requirements can also be met through occasional consumption of seaweed (e.g., dulse, nori), but it is important to note that the iodine content of seaweed is highly variable, and it is not recommended as a primary source of iodine [62].

Plant-based foods and products vary substantially in their nutritional composition. Certain highly processed plant-based alternatives, including some plant-based meats, beverages, and dairy substitutes, may differ considerably from whole plant foods in fiber content, sodium levels, and micronutrient profiles, and should not be assumed to provide equivalent health benefits. Consistent with this, a systematic review of novel plant-based foods found that their nutrient composition varies considerably across product types, brands, and primary ingredients, and that, on the limited health-outcome evidence available, shifts from animal-based foods to plant-based meats were associated with positive outcomes whereas findings for plant-based drinks were mixed and linked to micronutrient shortfalls [71]. Patients and clinicians should be encouraged to prioritize minimally processed plant foods when nutritional adequacy is the primary goal.

11. Implications for clinical practice

Dairy products should be considered within the broader context of overall dietary patterns, rather than evaluated in isolation. The literature on substitution analysis supports several actionable conclusions. First, replacing red and processed meats with dairy, particularly low-fat varieties and fermented products, is associated with lower risks

of mortality and cardiometabolic outcomes. Second, additional benefits may be achieved by substituting dairy with nuts, legumes, whole grains, or other plant-based protein sources, especially for CVD, T2D, cancer, and all-cause mortality. Third, when dairy consumption continues, fermented dairy products are preferable to non-fermented counterparts for mortality outcomes. Fourth, fish and plant-derived oils offer advantageous alternatives to dairy fat for reducing cardiovascular risk, particularly as replacements for butter. Healthcare professionals advising patients who reduce or eliminate dairy intake should recommend calcium-rich plant foods, fortified plant milks, or calcium supplements to meet nutritional requirements and should assess iodine status, especially in patients who also restrict iodized salt.

12. Strengths and limitations

This narrative review integrates a focused body of evidence from substitution analyses to address a clinically relevant, methodologically specific question. The substitution framework is a conceptual strength, as it provides comparative rather than absolute dietary assessments and more directly informs dietary guidance. However, several limitations should be acknowledged. As a narrative rather than systematic review, the study identification process was not designed to be exhaustive and carries a risk of selection bias. Studies were identified through a structured search but were not formally evaluated using a standardized risk-of-bias tool across all included publications. The evidence base is dominated by prospective cohort data from the United States and Northern Europe, limiting generalizability to populations with different dietary patterns, food compositions, and cardiometabolic risk profiles. All included substitution analyses are observational, and residual confounding cannot be excluded. Finally, this review focuses specifically on studies utilizing substitution or replacement models. Evidence from other study designs, including randomized controlled trials and studies reporting absolute dairy intake without a specified comparator, was not systematically incorporated, which constrains the scope of the conclusions drawn.

13. Conclusion

The health implications of dairy, as with any food, are inherently linked to the dietary context in which it is consumed. The existing literature on substitution analysis consistently indicates that dairy is associated with more favorable outcomes than red and processed meats regarding mortality and cardiometabolic outcomes. Additionally, dairy-derived SFA are associated with lower cardiovascular risk than those derived from meat. Conversely, replacing dairy with nuts, legumes, whole grains, and fish is

associated with lower risks of CVD, T2D, cancer, and all-cause mortality. Replacing dairy with plant protein-rich foods is associated with decreased all-cause and CVD mortality, reduced T2D risk, and a slowed biological aging. Within the dairy category, fermented products, particularly yogurt, are most strongly associated with favorable mortality outcomes. Substituting butter with plant-derived oils is associated with significantly lower total and cancer mortality, extending the relevance of substitution analyses to fats derived from dairy. Persistent methodological weaknesses in dairy research, including industry influence, lifestyle confounding, and the aggregation of heterogeneous products, necessitate caution when interpreting favorable associations from non-substitution studies. Ultimately, the most clinically informative question is not whether dairy is beneficial in isolation, but how it compares with specific alternatives within the context of an overall dietary pattern. Substitution analyses provide the most direct evidence available to address this question.

Future substitution research should prioritize several areas. First, well-designed randomized dietary intervention trials are needed to complement the observational substitution literature reviewed here and to clarify whether the associations observed between dairy substitutions and chronic disease outcomes are causal. Second, because the existing evidence base is drawn predominantly from North American and Northern European cohorts, substitution studies conducted in more diverse populations, including those in Asia, Africa, Latin America, and the Middle East, are needed to determine whether these findings generalize across differing dietary patterns, dairy subtypes, and genetic and cultural contexts. Addressing these gaps would strengthen the evidence base supporting comparative dietary guidance for dairy consumption worldwide.

Abbreviations

CAD: Coronary artery disease
CHD: Coronary heart disease
CI: Confidence interval
CVD: Cardiovascular disease
HR: Hazard ratio
PUFA: Polyunsaturated fatty acids
RR: Relative risk
SFA: Saturated fatty acids
SRR: Summary relative risk
T2D: Type 2 diabetes

Authors' contributions

Conceptualization, D.M.G.; investigation, D.M.G., C.W., and M.N.; writing—original draft preparation, D.M.G.; writing—review and editing, D.M.G., C.W., and M.N.; supervision, D.M.G. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

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Data availability statement

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

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