See corresponding articles on pages 1192, 1201 and 1220.

Dairy foods, dairy fat, diabetes, and death: what can be learned from 3 large new investigations?

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Dairy products are a major component of most diets, contributing ~10% of calories in the United States (1). Surprisingly, for such a major share of the food supply, their health effects remain remarkably uncertain, insufficiently studied, and controversial. Dietary guidelines on dairy remain largely based on theoretical considerations about isolated nutrients (e.g., theorized benefits of calcium or vitamin D; theorized harms of total fat or saturated fat) or short-term dietary pattern studies of surrogate markers (2), rather than on the mounting evidence on how milk, cheese, yogurt, butter, and other dairy foods relate to major clinical endpoints. Such evidence on health outcomes is crucial, because dairy products appear to be a heterogeneous class with complex effects dependent upon the interplay of diverse nutrients and processing characteristics (e.g., probiotics, fermentation, milk fat globule membrane, and more) (3).

In this issue of the Journal, 3 new publications report on dairy consumption and risk of type 2 diabetes or mortality (4–6). Ardisson Korat et al. (4) evaluated estimated dairy *fat* consumption and onset of diabetes in 3 cohorts of US health professionals. After adjustment for other risk factors, higher dairy fat intake, in comparison with carbohydrate, was associated with lower diabetes risk in 1 cohort of middle-aged women, and was not significantly associated with diabetes in the other 2 cohorts or among all 3 cohorts combined. In subgroup analyses, dairy fat intake was associated with lower risk of diabetes at younger ages (<65 y) and in women, the 2 subgroups among whom 70–80% of diabetes cases occurred—although these interactions by age and sex did not achieve statistical significance. When dairy fat was statistically compared with carbohydrate from whole grains, the latter was associated with lower risk of diabetes (per 5% energy, 7% lower risk), whereas, compared with other animal fats (largely from red meat and poultry) or with carbohydrate from refined grains, dairy fat consumption was associated with lower risk of diabetes (per 5% energy, 4–17% lower risk). Dairy fat consumption was not associated with incident diabetes when compared with vegetable fat, polyunsaturated fat (total, ω-6, or ω-3), or monounsaturated fat from plant sources. Because dairy fat in these cohorts was associated with several unhealthy lifestyle factors, including higher BMI, more current smoking, less physical activity, fewer fruits and vegetables, and a less healthy overall dietary pattern, this suggests that residual confounding, if present—the major limitation of observational cohorts such as this one—would tend to cause bias toward dairy fat appearing more harmful (less beneficial) than it actually may be.

These findings add to a growing body of literature which call into question the soundness of conventional dietary recommendations to avoid dairy fat (7). As noted by Ardisson Korat et al. (4), dairy fat contains a complex mix of different SFAs, other unsaturated and conjugated fatty acids, and other constituents, each with varying biological effects (3). Physiologic effects of dairy fat further vary according to content of milk fat globule membrane, which alters cholesterol absorption (8) and perhaps skeletal muscle responses to exercise (9). Also, cheese, the major source of dairy fat in most diets, is a fermented food and a rich source of menoquinones which may improve insulin secretion and sensitivity through osteocalcin-related pathways (3). In a recent pooling project of de novo individual-level analyses from 16 prospective cohort studies across 4 continents (including 2 of the 3 US cohorts evaluated by Ardisson Korat et al.), objective blood biomarkers of odd-chain saturated fats and *trans*-palmitoleic acid, each found in dairy fats, were associated with significantly lower risk of diabetes (10). Together with these prior findings, the new results by Ardisson Korat et al. provide little support for metabolic harms of dairy fat, and indeed suggest potential benefits among younger adults, among women, and as a replacement for other animal fats or refined carbohydrates.

A second report in this issue of the Journal assessed how *changes* in dairy foods, assessed using serial questionnaires, related to incident diabetes in the same 3 US cohorts of health professionals (5). After multivariable adjustment, participants who decreased their total dairy intake by >1 serving/d over a 4-y period experienced 11% higher incidence of diabetes, compared with stable intake. Among dairy subtypes, changes in low-fat

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milk, whole milk, and cream were not significantly associated with diabetes, whereas decreases in ice cream, increases in some types of cheese, and decreases in yogurt were each associated with higher risk. Several factors complicate the interpretation of this analysis. Foremost, none of these findings were symmetrical for increases compared with decreases in intake: i.e., when decreased consumption of total dairy or a dairy subtype was linked to diabetes risk, increased consumption was not linked in the opposing direction, and vice versa. This counters expected biology and the important Bradford Hill criterion of dose-response, which for example has been evidenced in these cohorts for dietary changes and long-term weight gain (11). In addition, results for each of the dairy subtypes appeared generally inconsistent across the 3 cohorts, with little uniformity (I^2 values were not reported). Some of the findings counter expected causal biology − e.g., that decreasing ice cream increases diabetes − raising concern for reverse causation. The dietary instrument was also variably reliable for assessing different dairy foods: for example, as compared with multiple dietary records, the FFQ reliably measured consumption of yogurt ($r = 0.97$), but not hard cheese ($r = 0.38$). In light of the 26 prior cohort studies which have reported on dairy consumption and incident diabetes, in sum suggesting lower risk from total dairy and especially yogurt consumption (12), the internal inconsistencies of the present findings for *changes* in dairy foods raise more questions than they answer.

In the third publication in this issue, Pala et al. (6) investigated dairy consumption and death from cancer, cardiovascular disease, and all causes in a community-based Italian cohort. After adjustment for other risk factors, compared with no consumption, moderate milk intake (≤200 g or ∼6.5 ounces per day) was associated with ∼25% lower mortality, largely owing to ∼50% lower cardiovascular mortality, but consumption at higher levels was not associated with lower risk. Findings were similar for low-fat compared with whole-fat milk. Intakes of yogurt, cheese, and butter were not significantly associated with mortality. As the authors concluded, the lack of a linear dose-response for milk raises questions about the validity of the observed benefits, but none of the findings support the hypothesis that milk, yogurt, cheese, or butter consumption increases mortality.

The global pandemics of obesity and type 2 diabetes, together with high rates of cardiovascular disease and cancer, have stimulated a new popular frenzy around healthier eating. Although the resulting attention on diet-related health impacts, economic burdens, and corresponding policy solutions has been positive, the craze of competing popular diets and their proponents have simultaneously fueled confusion, controversy, and skepticism. For example, ignoring the preponderance of evidence, some popular books and social media headlines claim that dairy foods are toxic. At the same time, prevailing dietary guidelines exacerbate the confusion, remaining mired in outdated conceptual frameworks and hesitating to acknowledge new paradigms of complexity (7).

As is always true in science, these 3 new investigations cannot by themselves definitively eliminate confusion or answer all questions. Yet, these studies aimed to address crucial questions on dairy and health in large and well-designed prospective cohorts. Together, the findings provide little support that consumption of total dairy, dairy subtypes, or dairy fat is harmful, and they continue to build the case for possible benefits. As recently reviewed (3), the dizzyingly complex characteristics and molecular effects of different dairy foods belie any simplistic overall summary or synopsis. These 3 new studies highlight this complexity and the urgent need for additional long-term prospective studies, interventional trials, and mechanistic investigations of dairy foods and health.

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