Saturated fatty acids and type 2 diabetes: more evidence to re-invent dietary guidelines

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Although saturated fatty acids (SFAs) are undoubtedly biologically active, several complexities preclude oversimplified predictions of their health effects. First, although attention has historically focused on blood LDL cholesterol, SFAs affect many other physiological pathways, including other blood lipids and lipoproteins and glucose—insulin responses. Second, different SFAs exist, with chain lengths ranging from 6 to 22 or more carbon atoms, and they have varying biological effects. Third, the relative effects of these SFAs also depend on the comparison nutrient, for example, other specific fatty acids, types of carbohydrate, or proteins. Fourth, dietary SFAs are obtained from remarkably diverse foods—red meat, poultry, processed meats, yoghurt, milk, cheese, butter, vegetable oils, and nuts, among others—that contain many other components that could modify their overall health effects. Finally, SFAs are derived not only from diet but also from endogenous synthesis (hepatic de-novo lipogenesis) in response to large, rapidly delivered doses of carbohydrate or total calories, which is especially important for even-chain SFAs (eg, 14:0 and 16:0).

In recent years, evidence for these complexities has revitalised scientific interest and investigation into the effects of SFAs on coronary heart disease and type 2 diabetes. In The Lancet Diabetes & Endocrinology, Nita Forouhi and colleagues present an important new study assessing plasma levels of SFAs and new-onset type 2 diabetes. This prospective investigation, nested within the EPIC study, included 12,403 cases of type 2 diabetes derived from 340,234 people across eight European countries. Plasma phospholipid SFAs were measured at baseline, providing an objective assessment of nine different circulating SFAs. After adjustment for other risk factors, odd-chain SFAs were associated with a lower incidence of type 2 diabetes (HR [95% CI] per 1 SD difference: pentadecanoic acid 0·79 [0·73—0·85] and heptadecanoic acid 0·67 [0·63—0·71]), as were very-long-chain SFAs (HRs ranged from 0·72 to 0·81, with 95% CIs of 0·61—0·92). Conversely, even-chain SFAs were associated with an increased incidence of type 2 diabetes (HR [95% CI] per 1 SD difference: myristic acid 1·15 [95% CI 1·09—1·22], palmitic acid 1·26 [1·15—1·37], and stearic acid 1·06 [1·00—1·13]). Results were consistent across the eight countries and in sensitivity analyses. When dietary correlates were assessed, odd-chain SFAs were associated most strongly with dairy products, as expected. Even-chain SFAs correlated more strongly with drivers of de-novo lipogenesis, including alcohol, soft drinks, and potatoes, than with direct dietary sources such as meat, butter, or cheese. Very-long-chain SFAs had weaker associations with diet than the other SFAs (although the strongest association was with nuts/seeds, which is one dietary source), which suggests that metabolic determinants could be especially important for plasma long-chain SFAs.
Several strengths of this research are evident, including its prospective subcohort design, its evaluation of several countries, the inclusion of a very large number of cases, the adjustment for many standardised covariates, and the assessment of dietary correlates. As the authors conclude, different SFAs were associated with type 2 diabetes in opposing directions, which provides clear evidence that SFAs are not a single homogeneous group.

What are the implications of this study? First, these results add to growing evidence that dairy fat might reduce insulin resistance and type 2 diabetes, benefits that might be greatest for cheese and yoghurt. Further research is needed to establish whether odd-chain SFAs have direct physiological benefits or are merely correlates of other beneficial compounds in dairy fat or other aspects of dairy fat-rich foods, such as probiotics or fermentation. Whatever the mechanism, these results add further challenges to prevailing dietary guidelines that recommend low-fat dairy products on the basis of the postulated bone benefits of calcium and theorised harms of total saturated fat content, rather than consideration of the complex nutrients and preparation methods of different dairy foods and the evidence for their direct health effects.

Second, the results confirm previous evidence that tissue concentrations of even-chain SFAs are linked to metabolic dysfunction—palmitic acid (16:0) seems to be especially harmful in animal and in-vitro models—and that, as reviewed elsewhere, these SFAs are mainly derived from endogenous hepatic synthesis, driven by consumption of starch, sugars, and alcohol. Thus, the present findings support adverse metabolic effects of refined carbohydrates and sugars and could also indicate, at least in part, reverse causation: underlying baseline metabolic dysfunction would increase de-novo lipogenesis, hepatic steatosis, circulating amounts of even-chain SFAs, and the future development of type 2 diabetes. Notably, the careful evaluation of dietary correlates was crucial to avoid prior erroneous interpretations from EPIC that circulating amounts of even-chain SFAs provide inference on effects of their direct dietary intakes. Additionally, the present findings draw attention to the need for investigation of the intriguing and remarkably understudied very-long-chain SFAs, the determinants (dietary and metabolic) and health effects of which remain largely unknown.

The consistent evidence for differing health effects of different SFAs, and their varying endogenous versus dietary determinants, remains under-recognised by many scientists, clinicians, media writers, and policy makers. Taken together with other advances in nutritional science, now is the time to redesign our process of setting dietary guidelines. We need to move away from unhelpful classifications and policies based on crude groupings of merely chemically related nutrients (eg, total saturated fat) and their predicted or postulated effects on risk—which, in addition to scientific dubiousness, create confusion for consumers and opportunities for manipulation by industry—and towards food-based guidelines that mainly consider prospective evidence for effects on clinical endpoints.

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References


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