
Letters to the Editor

Meta-analysis of effect of saturated fat intake on cardiovascular disease: overadjustment obscures true associations

Dear Sir:

The recent article by Siri-Tarino et al (1), which reported on a meta-analysis of prospective cohort studies evaluating the association of saturated fat with coronary heart disease (CHD), stroke, and cardiovascular disease (CVD) observed that “there is no significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD.” This finding has generated some interest in the media (2, 3). However, we believe that the interpretations of the results presented in this article are overstated and could be a result of flaws in the methodologic design of the study.

The meta-analysis involves data from 16 studies that evaluate the effect of saturated fat intake on CHD incidence or mortality and from 8 studies that evaluate the effect of saturated fat intake on stroke incidence or mortality. The results for CVD include any events for either CHD or stroke. The authors state that “wherever possible, risk estimates from the most fully adjusted models were used in the estimation of the pooled [relative risks].” It is well established that saturated fat intake is associated with increased concentration of serum cholesterol (4), and that serum cholesterol concentrations are associated with CHD and CVD (5). Therefore, serum cholesterol concentrations lie on the causal chain between saturated fat intake and CHD and CVD and to adjust for serum cholesterol concentrations in a meta-analysis will obscure the effect of saturated fat intake on these health outcomes. Yet 7 of the 16 studies included in the meta-analysis of CHD events, and 4 of the 8 studies included in the meta-analysis of stroke events, were adjusted for serum cholesterol concentrations. These studies accounted for nearly half of all CHD and CVD events included in the meta-analyses (*see Table 1*). Adjustment for serum cholesterol concentrations will inevitably bias the estimates of effect of saturated fat intake toward the null hypothesis. A meta-analysis of nonadjusted data would have produced different (and more informative) results.

Siri-Tarino et al (1) do not mention this as a potential limitation of their study, nor do they calculate estimates of the effect of saturated

fat intake on CHD and CVD using unadjusted data from the identified cohort studies. Without this further analysis, the conclusion that, “our meta-analysis showed that there is insufficient evidence from prospective epidemiologic studies to conclude that dietary saturated fat is associated with an increased risk of CHD, stroke, or CVD” is unsupported.

PS and MR are supported by the British Heart Foundation. The authors declared no conflicts of interest.

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TABLE 1

Studies included in the meta-analysis that adjusted for serum cholesterol concentrations¹

| Outcome | Studies adjusted for serum cholesterol concentrations | Total no. of studies | Individuals included from studies adjusted for serum cholesterol concentrations | Total no. of individuals | Events from studies adjusted for serum cholesterol concentrations | Total no. of events |
|---------------------|---|----------------------|---|--------------------------|---|---------------------|
| CHD | 7 | 16 | 59,428 | 214,182 | 3640 | 8644 |
| Stroke | 4 | 8 | 138,769 | 179,436 | 1101 | 2362 |
| CVD (CHD or stroke) | 10 | 21 | 188,430 | 347,747 | 4641 | 11,006 |

¹ CHD, coronary heart disease; CVD, cardiovascular disease.

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doi: 10.3945/ajcn.2010.29504.