Letters to the Editor

Saturated fat and heart disease

Dear Sir:

In a meta-analysis of observational studies, Siri-Tarino et al (1) concluded that there was no association of intake of saturated fat with risk of cardiovascular disease. There are several weaknesses in their report, which question the validity of their conclusions.

First, the notion that there exists such a thing as ''the effect of saturated fat'' is flawed. A lower intake of saturated fat implies an increased intake of some other source of calories to maintain caloric balance. Different substitutions for saturated fat have different effects on risk of coronary heart disease (CHD) and need to be discussed separately.

Replacement of saturated fat by polyunsaturated fat lowers both plasma concentrations of LDL cholesterol and the LDL/HDL-cholesterol ratio (2). Moreover, replacement of saturated fat by polyunsaturated fat is also associated with a lower risk of CHD in prospective cohort studies (3) and with lower risk of CHD in randomized trials (4). Thus, the benefit of replacing saturated by polyunsaturated fat is proven beyond reasonable doubt. However, Siri-Tarino et al failed to find this effect in their meta-analysis, just as they failed to find a significant association of saturated fat with CHD in general. The null results of their meta-analysis may reflect a lack of statistical power or an overreliance on mathematical models. To estimate the effect of replacing saturated by polyunsaturated fat, Siri-Tarino et al selected 5 studies that reported relative risks adjusted for intake of carbohydrate, protein, and fats but not of polyunsaturated fat. They then combined these 5 numbers and presented the outcome as the effect of replacing saturated by polyunsaturated fat. It requires a leap of faith to assume that the outcome of such a calculation truly represents what happens when saturated fat is replaced by polyunsaturated fat.

A major weakness of the meta-analysis is the imprecision of dietary assessment methods used in the underlying studies. About half of the studies used 1-d dietary assessments or some other unvalidated method. Food intake varies from day to day, and there is a substantial literature showing that a single 24-h recall provides a poor estimation of the usual dietary intake of an individual (5). Such methods cannot reliably rank individuals by their long-term intake, especially within populations with a uniformly high saturated fat intake. Such imprecision in the assessment of disease determinants systematically reduces the strength of association of determinants with the disease. This is referred to as *attenuation* (6) or *regression dilution bias* (7). Observational studies that used such dietary assessment methods failed to show an association between diet and serum cholesterol concentrations (6). This shows the shortcomings of such dietary methods, because the effect of diet on serum cholesterol concentrations has been well established in randomized controlled trials (2, 8). Thus, the lack of a significant association between saturated fat intake and CHD may well reflect the consequences of regression dilution bias.

Intakes of saturated fat, and to a lesser extent *trans* fats, are important determinants of LDL cholesterol, which is a causal risk factor for CHD. Intake of saturated fat in the United States and Europe has fallen markedly since the first recommendations on dietary fat quality were issued 50 y ago. The resulting fall in LDL cholesterol led to a distinct decrease in CHD (9), especially in the early period before the arrival of statins in the 1990s. CHD and stroke still account for most deaths in the United States and Europe and increasingly also in other parts of the world. We believe that the conclusions of Siri-Tarino et al are invalid and are likely to mislead the general population.

Our final comment concerns conflicts of interest. Involvement with industry does not discredit scientists, but it does need to be disclosed. Siri-Tarino et al reported the various grants that funded their research but otherwise stated ''No conflicts of interest.'' However, the website of the senior author (RMK) mentions advisory activities for the dairy industry (10). We wonder whether these should have been disclosed under the American Society for Nutrition Journals' Conflict of Interest Guidelines for Authors.

Neither MBK nor his family had any financial or other interest in the subject-matter of this letter which may be considered as constituting a real, potential, or apparent conflict of interest. Except for travel and hotel costs for scientific meetings of Nestlé Research in 2006 and 2007, MBK has not accepted in the past 5 y and will not accept in the foreseeable future money or favors from companies involved with foods, beverages, or drugs. MBK possesses no stock or other equity in such companies. IAB had no personal conflict of interest with the food or pharmaceutical industry. She does not receive honoraria or other payments from industry, except for the reimbursement of costs to participate in scientific meetings. RC's affiliation, the Clinical Trial Service Unit, has a policy of all staff not accepting honoraria or other payments from industry, except for the reimbursement of costs to participate in scientific meetings. RC had no personal or family conflict of interests with the food industry or with the pharmaceutical industry. JMG received unrestricted research grants from Unilever (for the Alpha Omega Trial; www.alphaomegatrial.com), from the Dutch Dairy Association (for a meta-analysis on dairy intake and cardiovascular diseases), and from Alpro Foundation (for an epidemiologic analysis on α-linolenic acid intake and cardiovascular diseases). RPM received unrestricted research grants from the Dutch Dairy Association, Raisio Nutrition Ltd, Malaysian Palm Oil Board, and Sime Darby Research Sdn Bhd for studies on dietary effects on risk markers related to the metabolic syndrome. RPM had no personal or family conflict of interests with any industry.

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