Re: Saturated Fat Intake and Lung Cancer Risk Among Nonsmoking Women in Missouri

Several (1–8), but not all (9–12), epidemiologic studies indicate that consumption of fat-rich diets increases risk of lung cancer. In 1993, we reported (13) a pronounced association between dietary fat and lung cancer risk. In a large, population-based, case–control study of nonsmoking Missouri women, risk of lung cancer increased across increasing levels of saturated fat intake. The odds ratio (OR) was more than sixfold greater for the highest quintile of consumption compared with the lowest quintile. We have since found that the ORs vary substantially according to the method of energy adjustment. In this correspondence, we report ORs based on two regression models other than the one used in the original analysis. The significantly elevated risk associated with saturated fat intake was not eliminated under these two models; however, the magnitude of most of the risk estimates and the consistency of a trend were clearly reduced using the alternative methods of energy adjustment (Table 1). For the reasons noted below, we believe our original estimates of risk were inflated and those resulting from the other methods are more valid.

The high correlation between saturated fat and total calories makes it difficult to assess the effect of saturated fat independent of its association with energy. In our original analysis (13), we entered both saturated fat and total calories as categorical variables in a standard multivariate model, since the nutrient residual method did not appear to offer any advantage. As others (14–16) have noted, the linear nutrient residual model is equivalent to the linear standard multivariate model. Furthermore, residuals do not convey an intuitive sense of nutrient intake, such as grams or calories of saturated fat consumed. At the time, we did not appreciate that the equivalence of the two methods ended when the nutrient intake data were categorized, a standard practice in epidemiologic studies.

As Brown et al. (17) and others (18) noted, when estimating the effect of increasing intake from dietary fat while keeping total energy intake constant (substitution effect), the standard multivariate model exaggerates the true variation in fat intake when data are modeled as quantile-categorical variables. Because the variability of the nutrient residuals provides a better estimate of the true variation in the nutrient of interest when total energy intake is fixed, the quantiles of the residual distribution provide a more valid description of the actual ORs to be expected when changing dietary composition. The multivariate nutrient density approach has the added advantage of being readily interpretable, representing the effect of changing the percentage of fat (or saturated fat) in the diet while keeping total energy intake constant.

Despite years of discussion about energy adjustment methods, we noted that only two observational studies of dietary fat and lung cancer (12,13) used any method of energy adjustment. In part, this circumstance reflects the fact that both the rationale and the appropriate method of energy adjustment remain controversial (19,20). In summary, computer simulations (17) and two analytic studies of dietary fat and cancer risk (13,21) now provide evidence that risk estimates and subsequent conclusions can be profoundly influenced by the method of energy adjustment.

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References


Table 1. Odds ratios (with 95% confidence intervals) of lung cancer among nonsmoking Missouri women according to quintiles of saturated fat intake: effect of energy adjustment method

<table>
<thead>
<tr>
<th>Energy adjustment method*</th>
<th>Quintile of saturated fat calories</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard multivariate†</td>
<td></td>
<td>1.0</td>
<td>1.6</td>
<td>1.8</td>
<td>2.9</td>
<td>6.2</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.9–2.9)</td>
<td>(0.9–3.4)</td>
<td>(1.3–6.0)</td>
<td>(2.6–14.6)</td>
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<td></td>
</tr>
<tr>
<td>Nutrient residual‡</td>
<td></td>
<td>1.0</td>
<td>1.4</td>
<td>1.7</td>
<td>1.9</td>
<td>1.6</td>
<td>&lt;.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.8–2.5)</td>
<td>(1.0–2.9)</td>
<td>(1.6–3.3)</td>
<td>(1.0–3.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariate nutrient density†</td>
<td></td>
<td>1.0</td>
<td>1.8</td>
<td>1.6</td>
<td>2.4</td>
<td>2.8</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.0–3.1)</td>
<td>(0.9–2.8)</td>
<td>(1.3–3.8)</td>
<td>(1.3–4.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*All three methods include as confounders age (continuous), smoking history (never smoked = 0; former smoker = 1), previous lung disease (no = 0; yes = 1), interview type (direct = 0; proxy = 1), and intakes of total calories, citrus fruits and juice, and beans and peas (quintiles).
†Independent variables include calories from saturated fat and total calories as categorical variables. Results originally reported in 1993 (13).
‡Reference category.
§Independent variables include residual calories as a categorical variable. Residual calories = observed saturated fat kcal − (estimated saturated fat kcal). In a linear model, estimated saturated fat kcal = α + β total kcal. The indicator variables are derived from the continuous residual values.
||Independent variables include proportion of total calories from saturated fat and total calories as categorical variables.


Notes

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Re: Correlating Nutrition to Recent Cancer Mortality Statistics

Wynder and Cohen (1) attribute the declining mortality from breast, prostate, and colon cancers (2) as well as from cardiovascular disease (3) to the reduction of total fat intake in the U.S. population in recent decades. The authors are fully aware of the differential effect of saturated, polysaturated, and monounsaturated fat on physiologic parameters and human disease risk—in fact, they have been major scientific contributors in this area. From the perspective of the U.S. population, it may make little difference to focus on total rather than saturated fat, although evidence incriminating saturated fat is strong for prostate cancer but weaker for cardiovascular disease and colorectal cancer and weaker still for breast cancer. The dominance, however, of the English language scientific and general press in the world scene has adversely affected the attitudes toward total fat intake in the Mediterranean countries in which most of the total fat is monounsaturated and is in the form of olive oil (4). There is strong evidence that consumption of olive oil may convey substantial protection against coronary heart disease (5), and several studies have indicated that it may also provide some protection against breast cancer (6) and possibly other forms of cancer (7) and even against osteoporosis (8). Mediterranean countries have lower rates of occurrence of these diseases and conditions in comparison to the United States, even though total fat intake has been as high or higher than that in the United States. The overall evidence points to a beneficial effect of olive oil on human health. Although the data may not be strong enough to dictate substitution of olive oil for other types of lipids in populations who do not traditionally consume it, they strongly suggest that the Mediterranean populations should not risk diverting from their olive oil-centered dietary habits.

Dietary guidelines have been widely perceived as indicating that total fat intake should be reduced. “Total fat,” however, is not a very useful term, because fats and oils are distinct categories in the broad group of lipids. It should be made clear that the evidence for the negative effects of dietary fat, such as it is, does not apply to monounsaturated triglycerides that dominate olive oil.

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References


