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COMMENTARY

Will it be cheese, bologna, or peanut butter?

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Consumption of non-human milk and other dairy products has been at the center of debate about prevention of cardiovascular disease and dietary recommendations. In the seminal 7-Countries Study, the dairy-based cultures such as Finland and the Netherlands had the highest rates of coronary heart disease (CHD), whereas the areas with lower or no dairy consumption such as Crete and Japan had the lowest rates of CHD. Although many other variables likely contributed to differences in CHD rates, the high amounts of saturated fat in milk, combined with evidence that saturated fat raises serum cholesterol in controlled feeding studies, led to policies to de-emphasize dairy production in Finland and to recommendations that emphasize low-fat dairy foods.

Milk is a remarkably complex food that contains most essential nutrients, and its health effects may be modified by fermentation and other processing. Thus, its relation to cardiovascular disease (CVD) cannot be surmised simply by its content of saturated fat, and for this reason, long-term prospective studies of dairy foods are particularly important. Because the relation of dairy foods to risk of CVD has been examined in many studies, efforts to summarize this literature, such as the present paper by Guo et al. [1], are welcome. This is an advance beyond previous meta-analyses by this group and others because of the larger number of studies. Overall, no associations were found between total dairy and milk consumption and all-cause mortality, CHD or CVD, and dairy foods were described as largely “neutral”.

Like meta-analyses in general, this report has limitations that include potential publication bias and the challenges of summarizing data that are inevitably heterogeneous because of different populations, assessments of exposure and outcomes, analytic methods, and control of confounding. However, the study of diet is far more complicated than comparisons of pill verses placebo in randomized trials and also most other exposures evaluated in observational studies. Two related fundamental concepts in nutrition were not possible to address adequately in the Guo meta-analyses, largely because of limitations in the primary studies: the isocaloric principle and the importance of substitution. These concepts are critical in the design of a controlled experiment in animals or humans, and are similarly important in epidemiologic analyses.

The isocaloric principle is simply that total energy intake should be held constant; if not, the specific effect of the dietary factor being studied cannot be separated from the many important effects of unbalanced total energy intake. Also, over periods of months or a year, humans regulate energy consumption very closely, and increases or decreases in one source of energy are largely compensated by changes in other sources, either consciously or unconsciously [2]. Thus, with the exception of studies with weight change or body composition as the outcome, randomized experiments are almost always designed to be isocaloric. By analogy, epidemiologic studies of specific aspects of diet should almost always be adjusted for total energy intake; whether or not this is done can sometimes even affect directions of association [3]. This has now become fairly routine, and was done in some, but not all, of the studies summarized by Guo et al.

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More serious in the report by Guo et al. is the lack of results for specific substitutions for dairy foods; this was not possible because such analyses were rarely conducted in the primary studies. The issue of substitution is closely linked to the isocaloric principle: with energy held constant, if a specific source of energy is increased, the effect on health can depend importantly on the component of diet that is reduced. In designing a randomized dietary experiment, the choice of the control diet is just as important as defining the intervention diet; the results are likely to be strongly dependent on the comparison diet. The substitution issue has for some time been addressed in epidemiologic studies of macronutrients. For example, in examining different types of fat in relation to risk of coronary heart disease, the percent of energy from each type of fat was compared with the same percentage of energy from carbohydrate, and then each type of fat with each other [4]. This can be done easily in a model that includes total energy, each major type of fat (saturated, monounsaturated, polyunsaturated, and *trans* fats), protein, and alcohol. Carbohydrate, being left out, then serves as the reference source of energy [5].

Until recently, the substitution issue has been typically ignored in epidemiologic analyses examining specific foods or food groups. With total energy included in the model, by default, the food of interest is then compared with the mix of other foods in diets of the population being studied, in proportion to the calories contributed. This mix of other foods is not often particularly healthy: in our compilation of data from the U.S. National Health and Nutrition Survey (unpublished), about 40% of energy came from refined starch, sugar, and potatoes; other major contributors included red meat and partially hydrogenated oils (until recently). Thus, in the studies included in the Guo meta-analysis, dairy foods were compared with this mix of relatively unhealthy sources of energy. To conclude that dairy foods are "neutral" based on relative risks close to 1.0 could be misleading, as many would interpret this to mean that increasing consumption of dairy foods would have no effects on cardiovascular disease or mortality. Lost is that the health effects of increasing or decreasing consumption of dairy foods could depend importantly on the specific foods that are substituted for dairy foods. These potential substitutions are directly related to choices that individuals make every day, and to agricultural policies on a national and global level. For example, in making a sandwich for lunch the choices could include peanut butter, cheese, or bologna. Or, in making a salad options could include adding nuts, cheese, or bacon. On a national level, some countries have strong policy support for dairy and beef production but little for production of poultry, legumes, or nuts. To inform such decisions, epidemiologic analyses should directly compare intakes of these and other reasonable alternatives to dairy products, which can be readily done by comparing coefficients for these alternative foods when included in the same model [5]. Decisions will need to be made on a common scale for the different foods; this could be per unit of energy, protein, or servings/day. For example, Bernstein compared red meat, milk, and other major protein sources in relation to risk of coronary heart disease [6], and similar analyses have been conducted for risk of type 2 diabetes [7]. In another variant, different food groups were compared with respect to risk of CHD using percentage of total energy from protein as the common scale [8]. Also, compared to energy from dairy fat, intakes of similar energy intakes from vegetable fats and whole grains were associated with lower risk of cardiovascular disease [9].

Guo et al. acknowledge the lack of ability to examine specific alternative substitutions for dairy foods, which is a serious limitation. The optimal way to deal with this would be analyze and pool the primary data from the individual studies; substitution analyses of pooled data have been done for types of fat in relation in relation to risk of breast [10] and coronary heart disease [11], but thus far this does not seem to have been done for foods or food groups. This can also be done indirectly, and without formal statistical comparisons, by considering separate studies of individual foods, assuming that each has been compared with roughly the same mix of unhealthy foods. For example, consumption of nuts or plant protein has been inversely associated with risks of coronary heart disease [6, 8] and type 2 diabetes [7]; in contrast intake of red meat has been positively associated with these outcomes [6–8]. Thus, it is reasonable to assume that the lack of association with dairy foods reported by Guo et al. puts these foods somewhere in the middle of a spectrum of healthfulness, but not an optimal source of energy or protein. While awaiting additional direct analyses, and considering the vast literature on dietary fats and blood lipids, I'll pass on the cheese and butter and instead emphasize nuts, legumes, and olive oil in my diet. More broadly, the available evidence supports policies that limit dairy production and encourages production of healthier sources of protein and fats.

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