

Mistaken Advice on Red Meat and Cancer

All scientific study is not created equal – there is sound science and junk science. Critical thinking should be applied every step of the way when reviewing evidence that informs policy. This article written by Dr. Guyatt of McMaster University, as published in the Financial Times November 24, 2015. Epidemiologist Dr. Dominique Alexander discusses the difference of Cause and Association: <https://vimeo.com/258311649>

The World Health Organization (WHO) announced recently that processed meats, such as salami and bacon, are on par with cigarettes as a "convincing" cause of cancer and that fresh red meat, like steak, is a "probable" cause. These statements overstate the evidence and mislead the public about their cancer risk from eating meat.

The determination of whether a substance causes cancer has traditionally relied upon three sources of evidence: animal models, data looking at possible mechanisms, and epidemiology. In the case of meat, the WHO committee determined that the evidence from animals was inadequate - simply put, feeding animals a diet rich in red meat does not give them cancer. The mechanistic evidence was strong-to-moderate, but these data alone cannot determine a mutagenic agent. Driving the WHO conclusion was the epidemiological data.

Epidemiology is a science that can establish associations (being in hospital is associated with death) but seldom cause and effect (being in hospital does not cause death). The great success story of epidemiological science was its ability to link smoking to cancer, with WHO designating tobacco as a "convincing" carcinogen in 1986. In that case, heavy smokers had a 9-to-25 times greater risk of contracting lung cancer than did non-smokers¹ a "relative risk" big enough to give researchers confidence that the association was a real. Ever since, however, standards for these risks in policy making have been dropping. This week's decisions on meat were based on relative risks of 1.17 to 1.18, a tiny fraction of those for smoking.

To keep things in perspective: for colon cancer, which was the focus of the WHO report, the absolute risk of contracting this cancer in one's lifetime is less than 4.5%. An increased relative risk of 1.17 raises the absolute risk to no more than 5.3%.

As two of the leaders in evidence based medicine, we were involved in the development an evidence ranking system, called "GRADE," adopted by over 90 groups world-wide, including the WHO. GRADE notes that unless relative risks are greater than 5, epidemiological studies typically provide only low-quality evidence. Although the smoking studies easily met that threshold, those used in the meat decision fell far below. Low-quality evidence means that the results are not trustworthy, and may well be proven wrong by future evidence. In such cases, the evidence is not convincing, and any recommendations would ordinarily be we would make a "weak", or "optional" recommendation, since the benefits do not clearly outweigh the potential harms.

The WHO has done the public a disservice in abandoning GRADE in its evaluation of the evidence, and greatly overstating confidence in a causal connection between red meat and cancer. Recent decades are littered with policies based on weak relative risks which, when properly tested in clinical trials, had to be reversed. For example, advice to take the antioxidant vitamins A and E was originally based on epidemiological data with modest reductions in relative risks of cancer in those who took the vitamins. The same was true with hormone replacement therapy and reduction in cardiovascular risk. Yet when randomized trials were conducted, they showed no benefit of antioxidant vitamins for cancer reduction, and no benefit—indeed, possible harm—of hormone replacement therapy on cardiovascular disease.

We see the same story with dietary guidelines: recommendations to restrict dietary cholesterol and limit fat to fight cancer were originally based principally on epidemiological data that clinical trials failed to confirm. Longstanding advice to restrict saturated fats has recently been challenged for the same reason. Now, it looks like we gained no benefit by eating egg white omelets, embarking on a low-fat diet, or quite possibly, giving up whole

milk for low-fat milk, let alone non-fat or skim.

The reason that weak associations are untrustworthy is that they could very well be due to bias associated with any number of factors in diet or lifestyle. With antioxidant vitamins, for instance, people who take vitamins do have lower rates of cancer, but it has nothing to do with the vitamins: factors related to genetics, lifestyle, and socioeconomic status are responsible. The same is true for eating meat. Vegetarians tend to be more alert to good health: they smoke less, exercise more, and have a higher socioeconomic status. By contrast, meat-eaters over the past 30-plus years are people who ignore their doctor's orders and are likely to be engaging in other insalubrious behaviors, all of which alone or in combination might explain the small relative risks associated with meat-eating.

Bias against red meat is another factor easily observable in the scientific literature and the popular press. Scientists try to adjust for these "confounding" variables, but measurements are incomplete and adjustments inadequate. Small relative risks are therefore just as likely to reflect bias as any true effect.

Randomized clinical trials provide far more trustworthy evidence regarding cause and effect. It is therefore perplexing that this week's WHO document does not even mention the relevant data: two large, multi-year RCTs, both funded by the National Institute of Health.

The first was Polyp Prevention Trial, which tested a high-fiber, high-fruit-and-vegetable, low-fat diet on more than 2,079 people for four years. In this multi-center trial, the intervention group significantly decreased red meat and processed meats, replacing them instead with chicken, yet researchers found no effect of this intervention, at the end of the trial or at the eight-year follow up, on the recurrence of colorectal cancer.

The second was the Women's Health Initiative, one of the largest randomized controlled trials ever conducted. The WHI tested a diet high in fruits and vegetables and low in fat, on nearly 49,000 women over 8 years. At year three, the only one for which the food data was published, the women on the low-fat diet reduced red meat by 20% compared to controls, a statistically significant amount, yet at the end of the trial, there was no effect on any of type of cancer, including colorectal cancer, ovarian cancer, endometrium cancer, or breast cancer.

It's possible that these trials didn't last long enough to see cancer develop, but they were both designed as cancer trials. They remain the most rigorous data to date, and neither support the hypothesis that red or processed meat causes cancer.

Sometimes we have little choice but to rely on epidemiological evidence. For instance, with potential toxins, such as inorganic arsenic, conducting clinical trials is unethical. On environmental issues, such as air pollution, such trials are impossible. However, for red and processed meat, the clinical trial evidence exists but has been unaccountably disregarded.

Ultimately, the WHO data might support a weak recommendation that the cautious among us might reduce our meat consumption, but certainly not a strong one of the sort we can legitimately make for smokers to reduce their cancer risk by quitting. And whereas smoking has no health benefit, meat is good source of nutrition, meaning that the trade-off for even the cautious among us might not be worth it. To say that red or processed meat is equivalent to smoking is profoundly misleading.

The consequences of the WHO decision may be vast. The government might decide to eliminate processed meat from federally funded programs and public institutions. Meat products may have to carry cancer warning labels. For scientists, the implications are that we cannot conduct clinical trials on any known carcinogen, and if we adopt the WHO conclusions, we will no longer be able to test the effects of processed meat on health. Such misguided conclusions create a dismal state of affairs for science and for public health policy. To prevent these

References:

¹ <http://monographs.iarc.fr/ENG/Monographs/vol1-42/mono38.pdf>, Table p. 215-216
<https://www.ft.com/content/42259e20-92b5-11e5-bd82-c1fb87bef7af>

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Written by Gordon Guyatt, Distinguished Professor, Department of Clinical Epidemiology & Biostatistics, Joint Member, Department of Medicine, McMaster University, Ontario; Benjamin Djulbegovic, Associate Dean, College of Internal Medicine; Professor, Department of Oncological Sciences; Distinguished Professor, Clinical and Translational Institute, Director, Evidence-based Medicine Research Group, University of South Florida.

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