## Another update. Red meat doesn't kill you, but the spin is fascinating

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The latest news: eating red meat doesn't do any harm. But why isn't that said clearly? Alarmism makes better news, not only for journalists but for authors and university PR people too.

I've already written twice about red meat.

In May 2009 Diet and health. What can you believe: or does bacon kill you?based on the WCRF report (2007).

In March 2012 How big is the risk from eating red meat now? An update.

In the first of these I argued that the evidence produced by the World Cancer Research Fund (WCRF) for a causal relationship was very thin indeed. An update by WCRF in 2010 showed a slightly smaller risk, and weakened yet further the evidence for causality, though that wasn't reflected in their press announcement.

The 2012 update added observations from two very large cohort studies. The result was that the estimates of risk were less than half as big as in 2009. The relative risk of dying from colorectal cancer was 1.21 (95% Confidence interval 1.04-1.42) with 50 g of red *or* processed meat per day, whereas in the new study the relative risk for cancer was only 1.10 (1.06-1.14) for a larger 'dose', 85 g of red meat. Again this good news was ignored and dire warnings were issued.

This reduction in size of the effect as samples get bigger is exactly what's expected for spurious correlations, as described by loannidis and others. And it seems to have come true. The estimate of the harm done by red meat has vanished entirely in the latest study.

### The EPIC study

This is the European Prospective Investigation into Cancer and Nutrition, another prospective cohort study, so it isn't randomised [read the original paper]. And it was big, 448,568 people from ten different European countries. These people were followed for a median time of 12.7 years, and during follow-up 26,344 of them died.

The thing that was different about this paper was that red meat was found to pose no detectable risk, as judged by all-cause mortality. But this wasn't even mentioned in the headline conclusions.

**Conclusions**: The results of our analysis support a moderate positive association between processed meat consumption and mortality, in particular due to cardiovascular diseases, but also to cancer.

To find the result you have to dig into Table 3.

### Table 3 Association between consumption of red and processed meat, and poultry and all-cause mortality in EPIC.

	Observed	Calibrated
	HR <sup>a</sup> (95% CI)	HR <sup>a</sup> (95% CI)
Red meat (per 100 g)	1.02 (0.98 to 1.06)	1.02 (0.98 to 1.06)
Processed meat (per 50 g)	1.09 (1.06 to 1.12)	1.18 (1.11 to 1.25)
Poultry (per 50 g)	0.96 (0.92 to 0.99)	0.95 (0.87 to 1.04)

<sup>a</sup>stratified by age (one-year age groups), sex, study center, adjusted for education (five categories), body weight (continuous), body height (continuous), total energy intake (continuous), alcohol consumption (continuous), physical activity (four categories), smoking status (seven categories), smoking duration (six categories); CI, confidence interval; HR, hazard rate.

So, by both methods of calculation, the relative risk from eating red meat is negligible (except possibly in the top group, eating more than 160 g (7 oz) per day).

There is still an association between intake of processed meat and all-cause mortality, as in previous studies, though the association of processed meat with all-cause mortality, 1.09, or 1.18 depending on assumptions, is, if anything, smaller than was observed in the 2012 study, in which the relative risk was 1.20 (Table 2).

### Assumptions, confounders and corrections.

The lowest meat eaters had only 13% of current smokers, but for the biggest red meat eaters it was 40%, for males. The alcohol consumption was 8.2 g/day for the lowest meat eaters but 23.4 g/day for the highest-meat group (the correlations were a bit smaller for women and also for processed meat eaters).

These two observations necessitate huge corrections to remove the (much bigger) effects of smoking and drinking if we want find the association for meat-eating alone. The main method for doing the correction is to fit the Cox proportional hazards model. This model assumes that there are straight-line relationships between the logarithm of the risk and the amount of each of the risk factors, e.g smoking, drinking, meat-eating and other risk factors. It may also include interactions that are designed to detect whether, for example, the effect of smoking on risk is or isn't the same for people who drink different amounts.

Usually the straight-line assumption isn't tested, and the results will depend on which risk factors (and which interactions between them) are included in the calculations. Different assumptions will give different answers. It simply isn't known how accurate the corrections are when trying to eliminate the big effect of smoking in order to isolate the small effect of meat-eating. And that is before we get to other sorts of correction. For example, the relative risk from processed meat in Table 3, above, was 9% or 18% (1.09, or 1.18) depending on the outcome of a calculation that was intended to increase the accuracy of food intake records ("calibration").

The **Conclusions** of the new study don't even mention the new result with red meat. All they mention is the risk from processed meat.

In this population, reduction of processed meat consumption to less than 20 g/day would prevent more than 3% of all deaths. As processed meat consumption is a modifiable risk factor, health promotion activities should include specific advice on lowering processed meat consumption.

Well, you would save that number of lives if, and only if, the processed meat was the *cause* of death. Too many epidemiologists, the authors pay lip service to the problem of causality in the introduction, but then go on to assume it in the conclusions. In fact the problem of causality isn't even metnioned anywhere in either the 2012 study, or the new 2013 EPIC trial.



So is the risk of processed meat still real? Of course I can't answer that. All that can be said is that it's quite small, and as sample sizes get bigger, estimates of the risk are getting smaller. It wouldn't be surprising if the risk from processed meat were eventually found not to exist, just as has happened for red (unprocessed) meat

### The Japanese study

Last year there was another cohort study, with 51,683 Japanese. The results were even more (non-) dramatic [Nagao *et al*, 2012] than in the EPIC trial. This is how they summarise the results for the relative risks (with 95% confidence intervals).

"...for the highest versus lowest quintiles of meat consumption (77.6 versus 10.4 g/day) among men were 0.66 (0.45 - 0.97) for ischemic heart disease, 1.10 (0.84 - 1.43) for stroke and 1.00 (0.84 - 1.20) for total cardiovascular disease. The corresponding HRs (59.9 versus 7.5 g/day) among women were 1.22 (0.81 - 1.83), 0.91 (0.70 - 1.19) and 1.07 (0.90 - 1.28). The associations were similar when the consumptions of red meat, poultry, processed meat and liver were examined separately.

CONCLUSION: Moderate meat consumption, up to about 100 g/day, was not associated with increased mortality from ischemic heart disease, stroke or total cardiovascular disease among either gender."

In this study, the more meat (red or processed) you eat, the *lower* your risk of ischaemic heart disease (with the possible exception of overweight women). The risk of dying from any cardiovascular disease was unrelated to the amount of meat eaten (relative risk 1.0) whether processed meat or not.

Of course it's possible that things which risky for Japanese people differ from those that are risky for Europeans. It's also possible that even processed meat isn't bad for you.

### The carnitine study

The latest meat study to hit the headlines didn't actually look at the effects of meat at all, though you wouldn't guess that from the pictures of sausages in the headlines (not just in newspapers, but also in NHS Choices). The paper [reprint] was about carnitine, a substance that occurs particularly in beef, with lower amounts in pork and bacon, and in many other foods. The paper showed that bacteria in the gut can convert carnitine to a potentially toxic substance, trimethylamine oxide (TMAO). That harms blood vessels (at least in mice). But to show an effect in human subjects they were given an amount of carnitine equivalent to over 1 lb of steak, hardly normal, even in the USA.

The summary of the paper says it is an attempt to explain "the well-established link between high levels of red meat consumption and CVD [cardiovascular disease] risk". As we have just seen, it seems likely that this risk is far from being "well-established". There is little or no such risk to explain.

It would be useful to have a diagnostic marker for heart disease, but this paper doesn't show that carnitine or TMAO) is useful for that. It might also be noted that the authors have a maze of financial interests.

**Competing financial interests** Z.W. and B.S.L. are named as co-inventors on pending patents held by the Cleveland Clinic relating to cardiovascular diagnostics and have the right to receive royalty payments for inventions or discoveries related to cardiovascular diagnostics from Liposciences. W.H.W.T. received research grant support from Abbott Laboratories and served as a consultant for Medtronic and St. Jude Medical. S.L.H. and J.D.S. are named as co-inventors on pending and issued patents held by the Cleveland Clinic relating to cardiovascular diagnostics and therapeutics patents. S.L.H. has been paid as a consultant or speaker by the following companies: Cleveland Heart Lab., Esperion, Liposciences, Merck & Co. and Pfizer. He has received research funds from Abbott, Cleveland Heart Lab., Esperion and Liposciences and has the right to receive royalty payments for inventions or discoveries related to cardiovascular diagnostics from Abbott Laboratories, Cleveland Heart Lab., Frantz Biomarkers, Liposciences and Siemens.



The practical significance of this work was summed up the dietitian *par excellence*, Catherine Collins, on the BBC's Inside Health programme.

Listen to Catherine Collins on carnitine.

She points out that the paper didn't mean that we should change what we already think is a sensible diet.

At most, it suggests that it's not a good idea to eat 1 lb steaks very day.

And the paper does suggest that it's not sensible to take the carnitine supplements that are pushed by every gym. According to NIH

"twenty years of research finds no consistent evidence that carnitine supplements can improve exercise or physical performance in healthy subjects".

Carnitine supplements are a scam. And they could be dangerous.

### FOLLOW-UP

Another blog on this topic, one from Cancer Research UK also fails to discuss the problem of causality. Neither does it go into the nature (and fallibility) of the corrections for counfounders like smoking and alcohol,. Nevertheless that, and an earlier post on Food and cancer: why media reports are often misleading, are a good deal more realistic than most newspaper reports.

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