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In Praise of Randomisation: The importance of causality in medicine and its subversion by philosophers of science

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I TAKE IT TO BE the job of scientists to try to distinguish between what is true from what is false by means of observation and experiment. That job has been made harder by some philosophers of science who appear to give academic respectability to relativist, and even postmodernist, postures. Luckily it has not been made very *much* harder, because these philosophers argue mainly with each other and practising scientists are hardly aware of their existence.

There is, I maintain, no real problem of any importance in the nature of evidence in most laboratory experiments. My real job is investigation of single ion channels. The results come in the form of distributions so they are perfectly suited to analysis by likelihood methods (Colquhoun *et al.*, 2003; Lape *et al.*, 2008). Of course there are problems in ambiguities about how likelihood is calculated, in indeterminacy of free parameters, in the distinguishability of reaction mechanisms and so on, but these are all quite well understood. Clinical studies are much harder, but when they are designed properly they too can give consistent and strong evidence for the efficacy of a treatment. The problems arise only when it is impossible to do properly designed experiments, or when commercial considerations prevent properly designed experiments being done even when they could be done.

I shall concentrate mainly on clinical studies, because they are where most of the problems arise.

The problems that I see in obtaining evidence to justify the correctness of a proposition fall into several categories. Some of these impediments to discovering the truth are nothing to do with profound principles, but merely reflections of human frailty. Here are some of them. I shall deal here with only the first and last.

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1 *Causality.* It isn't always possible to do a proper experiment. In large areas of medicine, the lack of clear evidence for causality is a major problem. Nowhere is that problem greater than in studies of the effect of diet on health. How what we eat affects our health is a question of enormous interest, yet it is a question that is almost impossible to answer.

2 *Commercial bias*. This has been documented widely (e.g. Lexchin and Light, 2006).

3 *Hubris and self-promotion*. The management culture that has engulfed universities has promoted dishonest self-promotion. Bibliometrists, with their futile attempts to sum up scientific achievement with a few numbers, have done as much harm to science as homeopaths and postmodernists

4 *Relativism and postmodernism*. I have left this category to the last, because, harmful though the effects of some philosophers of science may be, they have little influence.

Classification of diseases

In addition to these problems of principle, one suspects that a very major problem arises from the inadequate labels that are given to the conditions that are being tested. If you are testing a treatment for tuberculosis or malaria, the definition of the condition is pretty clear, but if you are trying to treat epilepsy or depression it is very far from clear. Even for conditions that are caused by single amino acid mutations in proteins of known function, it has turned out that there isn't just a single mutation that causes the disease, In conditions like slow channel congenital myasthenic syndrome (mutation in the nicotinic acetylcholine receptor), or hyperekplexia (mutation in the glycine receptor), there are almost as many single amino acid mutations as there are families with the condition. Each mutation causes a rather similar malfunction of the protein, and so a rather similar phenotype, but there is not just one hyperekplexia but dozens. The same, presumably, will turn out to be true of much more complex conditions like epilepsy and depression. This may be a big problem but it can't stop one trying and isn't a problem of principle so it won't be discussed further here.

I shall use the case of hormone replacement therapy to illustrate the importance of randomisation, and the case of processed meat and cancer to illustrate the problems that arise in the absence of randomised tests. Finally I shall discuss the opposition to randomisation that has come from some philosophers of science.

Causality and randomisation

It was clearly established in the 1930s, largely by R. A. Fisher, that random assignment of treatments to patients (or in his case, usually field plots) was the essential underlying condition for causal inference. He also established the idea of estimation by maximising likelihood and so provided a solution to the problem of inverse probability.

Randomisation is a rather beautiful idea. It allows one to remove, in a statistical sense, bias that might result from all the sources that you hadn't realised were there. If you are aware of a source of bias, then measure it. The danger arises from the things you don't know about, or can't measure (Senn, 2003, 2004). Although it guarantees freedom from bias only in a long run statistical sense, that is the best that can be done. Everything else is worse. The one essential bit of reading is Fisher's parable of the Lady Tasting Tea (Senn, 2003).

Everyone knows about the problem of causality in principle. *Post hoc ergo propter hoc*; confusion of sequence and consequence; confusion of correlation and cause. This is not a trivial problem. It is probably the main reason why ineffective treatments often appear to work. It is traded on by the vast and unscrupulous alternative medicine industry. It is, very probably, the reason why we are bombarded every day by conflicting advice on what to eat. This is a bad thing, for two reasons. First, we end up confused about what we should eat. But worse still, the conflicting nature of the advice gives science as a whole a bad reputation. Every time a white-coated scientist appears in the media to tell us that a glass of wine per day is good/bad for us (delete according to the phase of the moon) the general public just laugh.

Ben Goldacre has referred memorably to the newspapers' ongoing 'Sisyphean task of dividing all the inanimate objects in the world into the ones that either cause or cure cancer' (Goldacre, 2008). This has even given rise to a blog, 'The Daily Mail Oncological Ontology Project' <http://thedailymail oncologicalontologyproject.wordpress.com/>.

It wouldn't be so bad if the problem were restricted to the media. It is much more worrying that the problem of establishing causality often seems to be underestimated by the authors of papers themselves. It is a matter of speculation why this happens. Part of the reason is, no doubt, a genuine wish to discover something that will benefit mankind. But it is hard to avoid the thought that hubris and self-promotion may also play a role. Anything whatsoever that purports to relate diet to health is guaranteed to get uncritical newspaper headlines.

At the heart of the problem lies the great difficulty in doing randomised studies of the effect of diet and health. There can be no better illustration of the vital importance of randomisation than in this field. And, notwithstanding the generally uncritical reporting of stories about diet and health, one of the best accounts of the need for randomisation was written by a journalist, Gary Taubes, and it appeared in the *New York Times* (Taubes, 2007).

The case of hormone replacement therapy

In the 1990s hormone replacement therapy (HRT) was recommended not only to relieve the unpleasant symptoms of the menopause, but also because cohort studies suggested that HRT would reduce heart disease and osteoporosis in older women. For these reasons, by 2001, 15 million US women (perhaps 5 million older women) were taking HRT (Taubes, 2007). These recommendations were based largely on the Harvard Nurses' Study. This was a prospective cohort study in which 122,000 nurses were followed over time, starting in 1976 (these are the ones who responded out of the 170,000 requests sent out). In 1994, it was said (Manson, 1994) that nearly all of the more than thirty observational studies suggested a reduced risk of coronary heart disease (CHD) among women receiving oestrogen therapy. A meta-analysis gave an estimated 44% reduction of CHD. Although warnings were given about the lack of randomised studies, the results were nevertheless acted upon as though they were true. But they were wrong. When proper randomised studies were done, not only did it turn out that CHD was not reduced: it was actually increased.

The Women's Health Initiative Study (Rossouw *et al.*, 2002) was a randomised double blind trial on 16,608 postmenopausal women aged 50–79 years and its results contradicted the conclusions from all the earlier cohort studies HRT increased risks of heart disease, stroke, blood clots, breast cancer (though possibly helped with osteoporosis and perhaps colorectal cancer). After an average 5.2 years of follow-up, the trial was stopped because of the apparent increase in breast cancer in the HRT group. The relative risk (HRT relative to placebo) of CHD was 1.29 (95% confidence interval (1.02–1.63) (286 cases altogether) and for breast cancer 1.26 (1.00–1.59) (290 cases). Rather than there being a 44% reduction of risk, it seems that there was actually a 30% increase in risk. Notice that these are actually quite small risks, and on the margin of statistical significance. For the purposes of communicating the nature of the risk to an individual person it is usually better to specify the absolute risk rather than relative risk. The absolute number of CHD cases per

10,000 person-years is about twenty-nine on placebo and thirty-six on HRT, so the increased risk to any individual is quite small. Multiplied over the whole population though, the number is no longer small.

Several plausible reasons for these contradictory results are discussed by Taubes (2007): it seems that women who choose to take HRT are healthier than those who don't. In fact the story has been a bit more complicated since then: the effect of HRT depends on when it is started and how long it is taken (Vandenbroucke, 2009).

This is perhaps one of the most dramatic illustrations of the value of randomised controlled trials (RCTs). Reliance on observations of correlations suggested a 44% reduction in CHD, the randomised trial gave a 30% increase in CHD. Insistence on randomisation is not just pedantry. It is essential if you want to get the right answer.

Now back to the 'Sisyphean task of dividing all the inanimate objects in the world into the ones that either cause or cure cancer'.

The case of processed meat

In 2008, just about every newspaper carried a story with a headline like 'Why eating just one sausage a day raises your cancer risk by 20 per cent'. What was the basis for this statement? It was not made by a diet crank or supplement huckster but came from the World Cancer Research Fund report, *Food, nutrition, physical activity, and the prevention of cancer: a global perspective* (Marmot, 2007). This is a very weighty piece of work, chaired by Professor Sir Michael Marmot, famous for his pioneering work on the relationship between poverty and health. As one would expect of an eminent epidemiologist, it considers carefully the problem of causality: chapter 3 is devoted to it. Nonetheless, because most diet studies are not randomised, no amount of careful scrutiny can solve the problem. The recommendations of this study include the following.

1 Don't get overweight.

2 Be moderately physically active, equivalent to brisk walking for at least thirty minutes every day

3 Consume energy-dense foods sparingly. Avoid sugary drinks. Consume 'fast foods' sparingly, if at all.

4 Eat at least five portions/servings (at least 400 g or 14 oz) of a variety of non-starchy vegetables and of fruits every day. Eat relatively unprocessed cereals (grains) and/or pulses (legumes) with every meal. Limit refined starchy foods.

5 People who eat red meat to consume less than 500 g (18 oz) a week, very little if any to be processed.

6 If alcoholic drinks are consumed, limit consumption to no more than two drinks a day for men and one drink a day for women.

7 Avoid salt-preserved, salted, or salty foods; preserve foods without using salt. Limit consumption of processed foods with added salt to ensure an intake of less than 6 g (2.4 g sodium) a day.

8 Dietary supplements are not recommended for cancer prevention.

These all sound pretty sensible but they are very prescriptive. And of course the recommendations make sense only insofar as the various dietary factors *cause* cancer. If the association is not causal, changing your diet won't help. In section 3.4 the report says

> … causal relationships between food and nutrition, and physical activity can be confidently inferred when epidemiological evidence, and experimental and other biological findings, are consistent, unbiased, strong, graded, coherent, repeated, and plausible.

The case of processed meat is dealt with in chapter 4.3 (p. 148) of the report.

> Sausages, frankfurters, and 'hot dogs', to which nitrates/nitrites or other preservatives are added, are also processed meats. Minced meats sometimes, but not always, fall inside this definition if they are preserved chemically. The same point applies to 'hamburgers'.

The evidence for harmfulness of processed meat was described as 'convincing', the highest level of confidence in the report, though this conclusion has been challenged (Truswell, 2009).

Meat is only harmful if the association is causal. How well does the evidence obey the criteria for the relationship being causal? Twelve prospective cohort studies showed increased risk for the highest intake group when compared to the lowest (Fig. 12.1), which was statistically significant in three. One study reported non-significant decreased risk and one study reported that there was no effect on risk.

> Meta-analysis was possible on five studies, giving a summary effect estimate of 1.21 (95% CI 1.04–1.42) per 50 g/day with low heterogeneity (Figs. 12.2 and 12.3).

This is presumably where the headline value of a 20% increase in risk came from.

Support came from a meta-analysis of fourteen cohort studies, which reported a relative risk for processed meat of 1.09 (95% CI 1.05–1.13) per 30 g/day (Larsson and Wolk, 2006). Since then another study has come up with

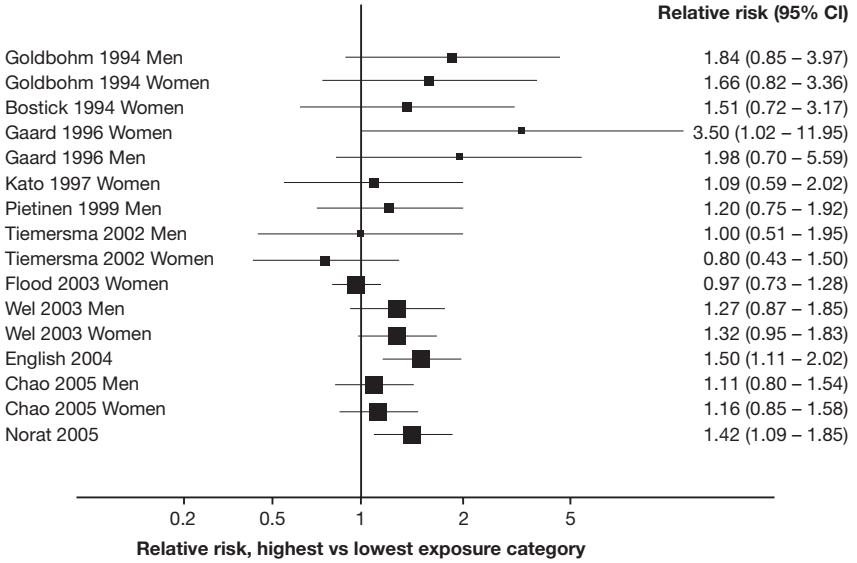

Figure 12.1. Processed meat and colorectal cancer: cohort studies (fig. 4.3.5 in Marmot, 2007).

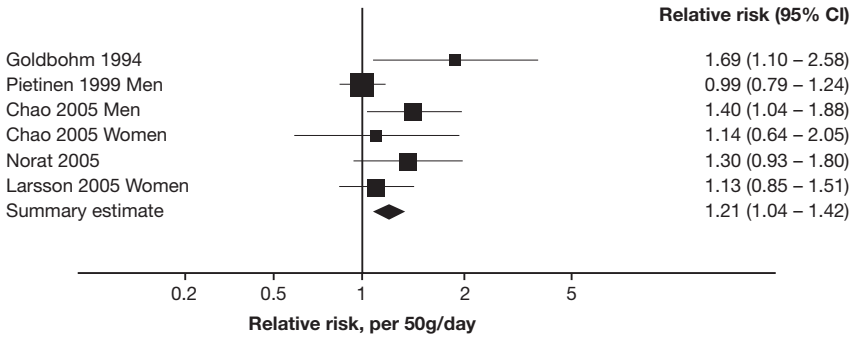

Figure 12.2. Processed meat and colorectal cancer: cohort studies (fig. 4.3.6 in Marmot, 2007).

similar numbers (Sinha *et al.*, 2009). This consistency cannot be taken as evidence for causality. Observational studies on HRT were just as consistent, but they were wrong.

The accompanying editorial (Popkin, 2009) points out that there are rather more important reasons to limit meat consumption, like the environmental footprint of most meat production, water supply, deforestation and so on.

So there is certainly some tendency for the relative risk to be just above 1. But being observational data there can be no guarantee that they are unbiased. The size of the effects is quite small. It is smaller than the reported beneficial effect of HRT in observational studies and that effect too was quite consistent, but it was plain wrong.

The other criteria for causality are 'graded, coherent, repeated, and plausible'. Graded means that there is a relationship between intake (dose) and response. The report says

> A dose–response relationship was also apparent from cohort studies that measured in times/day (Fig. 12.4).

It is at this point my credulity gets a bit strained. Any pharmacologist looking at the six dose–response curves in Figures 12.3 and 12.4 would say that the technical description would be 'bloody horizontal'. They are certainly the least convincing dose–response relationships I have ever seen. Nevertheless a meta-analysis came up with a slope for response curve that just reached the 5% level of statistical significance.

The conclusion of the report for processed meat and colorectal cancer was as follows.

> There is a substantial amount of evidence, with a dose–response relationship apparent from cohort studies. There is strong evidence for plausible mechanisms operating in humans. Processed meat is a convincing cause of colorectal cancer.

But the dose–response curves (Figs. 12.3 and 12.4) look appalling, and it is reasonable to ask whether public policy should be based on a 1 in 20 chance of being quite wrong (1 in 20 *at best*—see Senn, 2008). I certainly wouldn't want to risk my reputation on odds like that, never mind use it as a basis for public policy. So we are left with plausibility as the remaining bit of evidence for causality.

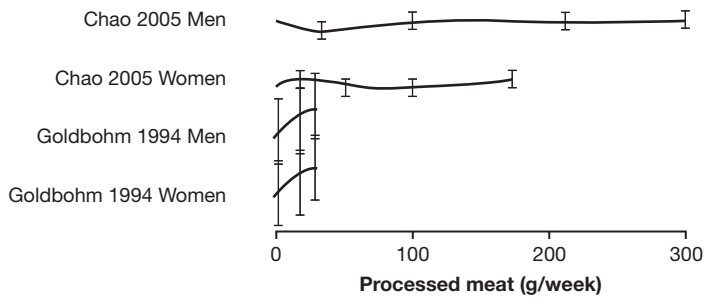

Figure 12.3. Processed meat and colorectal cancer: dose response (fig. 4.3.7 in Marmot, 2007).

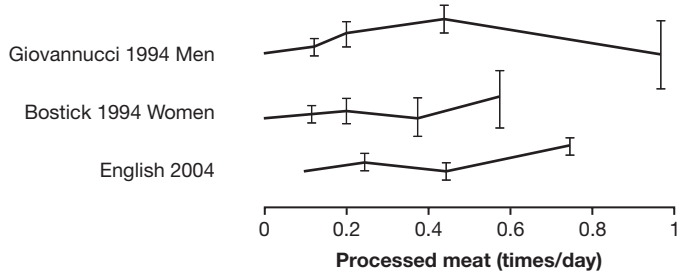

Figure 12.4. Processed meat and colorectal cancer: cohort studies (fig. 4.3.8 in Marmot, 2007).

Anyone who had done much experimental work knows that it is possible to dream up a plausible explanation of any result whatsoever. Most are wrong and so plausibility is a pretty weak argument. Scientists should take heed if the journalist, H. L. Mencken, who said, in 1917,

> there is always a well-known solution to every human problem—neat, plausible, and wrong.

Much play is made on the fact that cured meats contain nitrates and nitrites, but there is no real evidence that the amount they contain is harmful.

The main source of nitrates in the diet is not from meat but from vegetables (especially green leafy vegetables like lettuce and spinach) which contribute 70–90% of total intake. The maximum legal content in processed meat is 10–25 mg/100g, but lettuce contains around 100–400 mg/100g with a legal limit of 200–400 mg/100g. Dietary nitrate intake was not associated with risk for colorectal cancer in two cohort studies (Food Standards Agency, 2004; International Agency for Research on Cancer, 2006).

To add further to the confusion, another cohort study on over 60,000 people compared vegetarians and meat-eaters. Mortality from circulatory diseases and mortality from all causes was not detectably different between vegetarians and meat eaters (Key *et al.*, 2009*b*). Still more confusingly, although the incidence of all cancers combined was lower among vegetarians than among meat eaters, the exception was colorectal cancer which had a *higher* incidence in vegetarians than in meat eaters (Key *et al.*, 2009*a*).

Mente *et al.* (2009) compared cohort studies and RCTs for effects of diet on risk of coronary heart disease. 'Strong evidence' for protective effects was found for intake of vegetables, nuts, and 'Mediterranean diet' and harmful effects of intake of trans-fatty acids and foods with a high glycaemic index. There was also slightly less strong evidence for effects of mono-unsaturated fatty acids and for intake of fish, marine ω-3 fatty acids, folate, whole grains,

dietary vitamins E and C, beta carotene, alcohol, fruit, and fibre. But RCTs showed evidence only for 'Mediterranean diet', and none of the others.

As a final nail in the coffin of case–control studies, consider pizza. According to La and Bosetti (2006) data from a series of case–control studies in northern Italy lead to

> An inverse association was found between regular pizza consumption (at least one portion of pizza per week) and the risk of cancers of the digestive tract, with RRs of 0.66 for oral and pharyngeal cancers, 0.41 for oesophageal, 0.82 for laryngeal, 0.74 for colon and 0.93 for rectal cancers.

What is one meant to make of this? Pizza should be prescribable on the National Health Service to produce a 60% reduction in oesophageal cancer? As the authors say 'pizza may simply represent a general and aspecific indicator of a favourable Mediterranean diet'. On the basis of this sort of study, the finding is uninterpretable.

Is the observed association even real?

The most noticeable thing about the effects of red meat and processed meat is not only that they are small but also that they only just reach the 5 per cent level of statistical significance. It has been explained clearly why, in these circumstances real associations are likely to be exaggerated in size (Ioannidis, 2008*b*; Ioannidis, 2008*a*; Senn, 2008) and why many, even most, claimed effects are not real anyway (Ioannidis, 2005). The inflation of the strength of associations is expected to be bigger in small studies, so it is noteworthy that the large meta-analysis by Larsson and Wolk (2006) comments 'In the present meta-analysis, the magnitude of the relationship of processed meat consumption with colorectal cancer risk was weaker than in the earlier meta-analyses.'

This is all consistent with the well known tendency of randomised clinical trials to show initially a good effect of treatment but subsequent trials tend to show smaller effects. The reasons, and the cures, for this worrying problem are discussed by Chalmers (Chalmers, 2006;Chalmers and Matthews, 2006; Garattini and Chalmers, 2009).

What about randomised studies?

The only form of reliable evidence for causality comes from randomised controlled trials. The difficulties in allocating people to diets over long periods of time are obvious and that is no doubt why there are far fewer RCTs than there are observational studies. But when they have been done the results often con-

tradict those from cohort studies. The RCTs of hormone replacement therapy mentioned above contradicted the cohort studies and reversed the advice given to women about HRT.

Three more illustrations of how plausible suggestions about diet can be refuted by RCTs concern nutritional supplements and weight-loss diets.

Many RCTs have shown that various forms of nutritional supplement do no good and may even do harm (see Cochrane reviews <http://tinyurl.com/dd89j7>). At least we now know that anti-oxidants *per se* do you no good. The idea that anti-oxidants might be good for you was never more than a plausible hypothesis, and like so many plausible hypotheses it has turned out to be a myth. The word anti-oxidant is now no more than a marketing term, though it remains very profitable for unscrupulous salesmen.

The randomised Women's Health Initiative Dietary Modification Trial (Prentice *et al.*, 2007; Prentice, 2007) showed minimal effects of dietary fat and cancer, though the conclusion has been challenged on the basis of the possible inaccuracy of reported diet (Yngve *et al.*, 2006).

Contrary to much dogma about weight loss, Sacks *et al.* (2009) found no differences in weight loss over two years between four very different diets. They assigned randomly 811 overweight adults to one of four diets. The percentages of energy derived from fat, protein, and carbohydrates in the four diets were 20, 15, and 65%; 20, 25, and 55%; 40, 15, and 45%; and 40, 25, and 35%. No difference could be detected between the different diets: all that mattered for weight loss was the total number of calories.

The impression one gets from RCTs is that the details of diet are not as important as has been inferred from non-randomised observational studies.

So does processed meat give you cancer?

After all this, we can return to the original question. Do sausages or bacon give you colorectal cancer? The answer, sadly, is that nobody really knows. I do know that, on the basis of the evidence, it seems to me to be an exaggeration to assert that 'The evidence is convincing that processed meat is a *cause* of bowel cancer.'

In the UK there were around five cases of colorectal cancer per 10,000 population in 2005 <http://info.cancerresearchuk.org/cancerstats/types/bowel/incidence/>, so a 20% increase, even if it were real, and genuinely causative, would result in six rather than five cases per 10,000 people, annually. That makes the risk sound trivial for any individual. On the other hand there were 36,766 cases of colorectal cancer in the UK in 2005. A 20% increase would

mean, if the association were causal, about 7,000 extra cases as a result of eating processed meat, but no extra cases if the association were *not* causal.

For the purposes of those making public health policy about diet, the question of causality is crucial. One has sympathy for the difficult decisions that they have to make, because they are forced to decide on the basis of inadequate evidence.

The decision about whether to eat bacon and sausages has to be a personal one. It depends on your attitude to the precautionary principle. My own inclination would be to ignore any relative risk based on observational data if it were less than about two. The National Cancer Institute (Nelson, 2002) advises that relative risks less than 2 should be 'viewed with caution', though they do not say what 'viewing with caution' means in real life. Hardly any of the relative risks reported in the WCRF report (Marmot, 2007) reach a relative risk of 2. Almost all are less than 1.3 (or greater than 0.7 for alleged protective effects). Perhaps it is best to stop worrying and get on with your life. At some point it becomes counterproductive to try to micromanage `people's diet on the basis of dubious data. There is a price to pay for being too precautionary. It runs the risk of making people ignore information that *has* got a sound basis. It runs the risk of excessive medicalisation of everyday life. And it brings science itself into disrepute when people laugh at the contradictory findings of observational epidemiology.

If it were not already obvious, the examples discussed above make it very clear that the only sound guide to causality is a properly randomised trial. The only exceptions to that are when effects are really big. The relative risk of lung cancer for a heavy cigarette smoker is twenty times that of a non-smoker and there is a very clear relationship between dose (cigarettes per day) and response (lung cancer incidence), as shown in Figure 12.5 (Doll and Peto, 1978). That is a 2000% increase in risk, very different from the 20% found for processed meat (and many other dietary effects). Nobody could doubt seriously the causality in that case.

The question of how diet and other 'lifestyle interventions' affect health is fascinating to everyone. There is compelling reason to think that it matters. For example one study demonstrated that breast cancer incidence increased almost threefold in first-generation Japanese women who migrated to Hawaii, and up to fivefold in the second generation (Kolonel, 1980). Since then enormous effort has been put into finding out why. The first great success was cigarette smoking but that is almost the *only* major success. Very few similar magic bullets have come to light after decades of searching (asbestos and mesothelioma, or UV radiation and skin cancer, count as successes). The WCRF report (Marmot, 2007) has over 4,000 references and we still don't know.

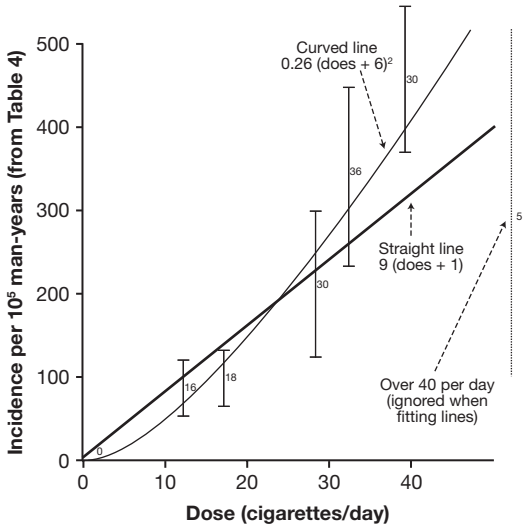

Figure 12.5. Dose–response relationship standardised for age. The numbers of onsets in each group is given, and 90% confidence intervals are plotted (Doll & Peto 1978).

The negative contribution of some philosophers of science

It seems surprising that the value of randomisation should still be disputed at this stage, and of course it is not disputed by anybody in the business. There is, though, a body of philosophers who do dispute it. And of course almost all practitioners of alternative medicine dispute it (because their treatments usually fail the tests). I had not come across the philosophers until I joined the London Evidence group, perhaps because I had long since decided that it was Fisher, rather than philosophers, who had the answers to my questions.

'Why there's no cause to randomize' is the rather surprising title of a report by Worrall (2004; see also Worral, 2010) from the London School of Economics. The conclusion of this paper is

> don't believe the bad press that 'observational studies' or 'historically controlled trials' get—so long as they are properly done (that is, serious thought has gone in to the possibility of alternative explanations of the outcome), then there is no reason to think of them as any less compelling than an RCT.

In my view this conclusion is quite wrong—it ignores the enormous difficulty of getting evidence for causality in real life, and it ignores the fact that historically controlled trials have very often given misleading results in the past,

as illustrated above. Worrall's fellow philosopher, Nancy Cartwright (2010), has made arguments similar to those of Worrall.

Many words are spent on defining causality but, at least in the clinical setting, the meaning is perfectly simple. If the association between eating bacon and colorectal cancer is causal then if you stop eating bacon you'll reduce the risk of cancer. If the relationship is not causal then if you stop eating bacon it won't help at all. No amount of 'serious thought' will substitute for the real evidence for causality that can come only from an RCT: Worrall seems to claim that sufficient brain power can fill in missing bits of information. It can't. I'm reminded inexorably of the definition of 'Clinical experience. Making the same mistakes with increasing confidence over an impressive number of years' in Michael O'Donnell's *A Sceptic's Medical Dictionary.*

At the other philosophical extreme, there are still a few remnants of postmodernist rhetoric to be found in obscure corners of the literature. Two extreme examples are the papers by Holmes *et al.* and by Christine Barry. Apart from the fact that they weren't spoofs, both of these papers bear a close resemblance to Alan Sokal's famous spoof paper, *Transgressing the boundaries: towards a transformative hermeneutics of quantum gravity* (Sokal, 1996). The acceptance of this spoof by a journal, *Social Text*, and the subsequent book, *Intellectual Impostures* (Sokal and Bricmont, 1998), exposed the astonishing intellectual fraud of postmodernism (for those for whom it was not already obvious). A couple of quotations will serve to give a taste of the amazing material that can appear in peer-reviewed journals. Barry (2006) wrote

> I wish to problematise the call from within biomedicine for more evidence of alternative medicine's effectiveness via the medium of the randomised clinical trial (RCT).
>
> Ethnographic research in alternative medicine is coming to be used politically as a challenge to the hegemony of a scientific biomedical construction of evidence.
>
> The science of biomedicine was perceived as old fashioned and rejected in favour of the quantum and chaos theories of modern physics.
>
> In this paper, I have deconstructed the powerful notion of evidence within biomedicine, …

The aim of this paper, in my view, is not to obtain some subtle insight into the process of inference but to try to give some credibility to snake-oil salesmen who peddle quack cures. The latter at least make their unjustified claims in plain English.

The similar paper by Holmes, Murray, Perron and Rail (Holmes *et al.*, 2006) is even more bizarre.

> **Objective** The philosophical work of Deleuze and Guattari proves to be useful in showing how health sciences are colonised (territorialised) by an all-encompassing scientific research paradigm 'that of post-positivism' but also and foremost in showing the process by which a dominant ideology comes to exclude alternative forms of knowledge, therefore acting as a fascist structure.

It uses the word fascism, or some derivative thereof, twenty-six times. And Holmes, Perron and Rail (Murray *et al.*, 2007) end a similar tirade with

> We shall continue to transgress the diktats of State Science.

It may be asked why it is even worth spending time on these remnants of the utterly discredited postmodernist movement. One reason is that rather less extreme examples of similar thinking still exist in some philosophical circles.

Take, for example, the views expressed in papers such as Miles, Polychronis and Grey (Miles and Loughlin, 2006), Miles, Loughlin and Polychronis (Miles *et al.*, 2007) and Loughlin (2007). These papers form part of the authors' campaign against evidence-based medicine, which they seem to regard as some sort of ideological crusade, or government conspiracy. Bizarrely they seem to think that evidence-based medicine has something in common with the managerial culture that has been the bane not only of medicine but of almost every occupation (and which is noted particularly for its disregard for evidence). Although couched in the sort of pretentious language favoured by postmodernists, in fact it ends up defending the most simple-minded forms of quackery. Unlike Barry (2006), they don't mention alternative medicine explicitly, but the agenda is clear from their attacks on Ben Goldacre. For example, Miles, Loughlin and Polychronis (Miles *et al.*, 2007) say this.

> Loughlin identifies Goldacre [36] as a particularly luminous example of a commentator who is able not only to combine audacity with outrage, but who in a very real way succeeds in manufacturing a sense of having been personally offended by the article in question. Such moralistic posturing acts as a defence mechanism to protect cherished assumptions from rational scrutiny and indeed to enable adherents to appropriate the 'moral high ground', as well as the language of 'reason' and 'science' as the exclusive property of their own favoured approaches. Loughlin brings out the Orwellian nature of this manoeuvre and identifies a significant implication.

If Goldacre and others really are engaged in posturing then their primary offence, at least according to the Sartrean perspective adopted by Murray *et al.*, is not primarily intellectual, but rather it is moral. Far from there being a moral requirement to 'bend a knee' at the EBM altar, to do so is to 'violate one's primary duty as an autonomous being'.

This ferocious attack seems to have been triggered because Goldacre has explained in simple words what constitutes evidence and what doesn't. He has explained in a simple way how to do a proper randomised controlled trial of homeopathy. And he dismantled a fraudulent Qlink pendant, purported to shield you from electromagnetic radiation, which turned out to have no functional components (Goldacre, 2007). This is described as being 'Orwellian', a description that seems to me to be downright bizarre.

In fact, when faced with real-life examples of what happens when you ignore evidence, those who write theoretical papers that are critical about evidence-based medicine may behave perfectly sensibly. Although Andrew Miles edits a journal that has been critical of EBM for years, when faced with a course in alternative medicine run by people who can only be described as quacks, he rapidly shut down the course (see account by Colquhoun, 2010)

It is hard to decide whether the language used in these papers is Marxist or neoconservative libertarian. Whatever it is, it clearly isn't science. It may seem odd that postmodernists (who believe nothing) end up as allies of quacks (who'll believe anything). The relationship has been explained with customary clarity by Alan Sokal, in his essay 'Pseudoscience and Postmodernism: Antagonists or Fellow-Travelers?' (Sokal, 2006).

Conclusions

Of course RCTs are not the only way to get knowledge. Often they have not been done, and sometimes it is hard to imagine how they could be done (though not nearly as often as some people would like to say).

It is true that RCTs tell you only about an average effect in a large population. But the same is true of observational epidemiology. That limitation is nothing to do with randomisation, it is a result of the crude and inadequate way in which diseases are classified (as discussed above). It is also true that randomisation doesn't guarantee lack of bias in an individual case, but only in the long run. But it is the best that can be done. The fact remains that randomisation is the *only* way to be sure of causality, and making mistakes about causality can harm patients, as it did in the case of HRT.

Raymond Tallis (1999), in his review of Sokal and Bricmont, summed it up nicely

> Academics intending to continue as postmodern theorists in the interdisciplinary humanities after S & B should first read *Intellectual Impostures* and ask themselves whether adding to the quantity of confusion and untruth in the

> world is a good use of the gift of life or an ethical way to earn a living. After S & B, they may feel less comfortable with the glamorous life that can be forged in the wake of the founding charlatans of postmodern Theory. Alternatively, they might follow my friend Roger into estate agency—though they should check out in advance that they are up to the moral rigours of such a profession.

The conclusions that I have drawn were obvious to people in the business a quarter of a century ago. Doll and Peto (1980) said

> If we are to recognize those important yet moderate real advances in therapy which can save thousands of lives, then we need more large randomised trials than at present, not fewer. Until we have them treatment of future patients will continue to be determined by unreliable evidence.

The towering figures are R. A. Fisher and his followers who developed the ideas of randomisation and maximum likelihood estimation. In the medical area, Bradford Hill, Archie Cochrane and Iain Chalmers had the important ideas worked out a long time ago.

In contrast, philosophers seem to me to make almost no contribution to the accumulation of useful knowledge, and in some cases to hinder it. It is true that the harm they do is limited, but that is because they talk largely to each other. Very few working scientists are even aware of their existence. Perhaps that is just as well.

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