A storm in a D cup.

One of the features of scientific life is that non-scientist friends, and friends-of-friends, often ask about the soundness of the latest health scare, or latest cure-all, to have hit the newspapers or bookstores. In almost all cases, the only honest instant response is "I don't know, it's not my field; sorry.". Occasionally, though, a question comes up that is intriguing enough, or surprising enough, to add "... but I will do my best to find out." I got one of those questions a few weeks ago, from someone who had heard a old interview, recorded in the early 2010s (see 'links'), with the medical anthropologists Sidney Ross Singer and Soma Grismaijer. It was about their 1995 book *Dressed to Kill*. The startling conclusion of this book was that most mammary cancer seems to be caused by the wearing of bras.

I had never heard the hypothesis before, and I could not immediately think of any reason that there could be a connection between bras and cancer, but lack of an ability to understand how cause and effect are linked is never a reason to reject an idea out of hand. The importance of keeping an open mind is illustrated well by the story of the mid nineteenth century Viennese doctor, Ignaz Semmelweis, and I tell this story as part of the 'scientific thinking' workshop I give to new graduate students who come here to study. Semmelweis was working in an obstetric clinic and his duties, like those of many other doctors, involved both care of the living and performing autopsies on the dead. The hospital had a huge problem with puerperal fever. Semmelweis noticed that, if he performed the then-unusual action of washing his hands between doing a post-mortem on a woman who had died of puerperal fever and examining a living woman, the living woman was much less likely to develop the fever than if he did not wash his hands. He concluded that something invisible, something that could cause the fever, could travel on unwashed hands from dead women to living ones. Bacteria and viruses had yet to be discovered, and Semmelweis was ridiculed, his ideas remaining mostly unadopted and countless people continuing to die in the practices of his colleagues. Only after bacteria were discovered, decades later, was there a mechanism to explain what Semmelweis had deduced many years before. Then the idea of hand-washing was taken seriously, and death rates plummeted. The main message of the story is that a lack of obvious mechanism is never a reason to reject a possible connection between two things. A second message may be that discoveries of connections where there are no obvious mechanisms may be the most important kinds of discovery to make, which is one reason the question about bra-wearing, bizarre as it seemed, intrigued me. I should say I have no axe to grind on this topic – I don't care whether

women wear bras or not and, for women I meet in ordinary social or professional situations, I am unlikely even to notice.

There are two main sources of data behind the argument in the book and interview (and I should say I am basing this account on the interview alone, having not read the book). One is based on the anthropologists' interviews with women about bra-wearing habits, which seemed to indicate that bra wearing for more than 12 hours per day was associated with greatly increased rates of cancer. The other is that recorded rates of mammary cancer in women in societies that do not wear bras are much lower (as low as they are in Western men) than they are in women in those in societies that wear bras; also, allegedly, when a bra-less society becomes Westernized and bra wearing begins, rates of cancer rise. Assuming these data are true, they demonstrate a correlation but of course this does not prove causality. It may be, for example, that the Western women who chose to wear bras most make this choice in response to an underlying feature that is also linked to tumour rates: total breast size would be a possible example. For the Westernizing societies, it may simply be that improved health surveillance and diagnosis arrives along with the Western clothing, and cancers that were present but not recorded before are now detected properly. For this reason, the authors were met with scepticism from the medical community, and the authors responded by proposing a possible mechanism (concerned with impeded lymphatic drainage). In the interview, they repeatedly said that their work was being impeded, because (they said in the interview) both fashion and medical industries make money by selling bras and treating the problem. Importantly, they said that no study had been performed to gainsay them and implied that this was because people had too much to lose if they found the hypothesis was right. This struck me as highly unlikely and quite at odds with the spirit of free enquiry I have always experienced. The book was published back in 1995 and the interview done in the early 2010s, so I realized that there was a chance that a proper study had been done since that interview. To provide an answer, I just had to find it.

The first port of call of any medical scientist hungry for high-quality information is PubMed, the free-to-anyone, open-access service that literally millions of articles in the medical literature (see 'links'). A quick search revealed that, since the interview, someone had indeed taken the question of a link between bra wearing and mammary cancer seriously. A paper by Lu Chen and colleagues (see 'links') appeared in the journal *Cancer Epidemiolology, Biomarkers and Prevention*, in 2014. It is the only paper I found that addresses the question head-on.

The structure of the Chen paper illustrates nicely the problems of performing research on human beings. If we were exploring a question of whether something caused cancer in a short-lived experimental animal, the conventional design would be to split young animals into two groups, give one group the suspected carcinogen, 'blind-code' the animals when being examined, so that people monitoring them did no know to which group they belonged, record any cancers and then, at the end, compare the frequencies in the two groups. There are obvious problems in following this plan with humans. Obviously nobody can arbitrarily divide girls into two groups and insist that one group wears bras from puberty and the other does not. And, even if this were ethically and practically possible, which it is not, beginning the experiment now might mean a sixty year wait for results. So the best that Lu and colleagues could do was to look at a cohort of local women (local to Seattle, in this case), and look backwards at their medical histories and at the choices these women made about bra wearing, to see if there was any correlation between bras and mammary tumours.

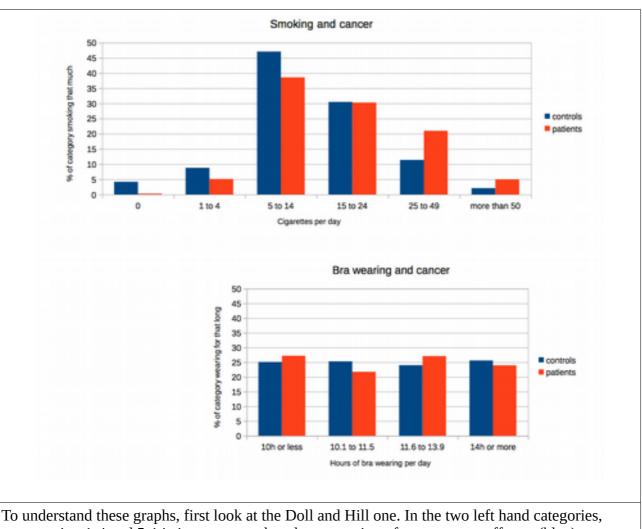
Clearly, there is a weakness in this type of study. In a culture in which the wearing of bras is almost ubiquitous, girls and women who chose not to wear one, or to wear one for only very limited periods of the day, may have been in some way atypical. They may, for example, have smaller breasts, though this may not matter much to cancer risk – there only is a very limited correlation between breast size and risk, and even this tiny association is apparently relevant only for women who are very lean when young (see the 'Egan' paper in the 'links' section). More significantly, people who chose not to follow mainstream fashion in one thing, especially something that is as politically sensitive as a garment whose existence may be taken to imply that the natural female figure is in some way unacceptable, may well refuse to follow other fashions too. They may, for example, eat and drink differently, live in different environments, compared to most of their peers; they might also pay more attention to checking their own bodies. There is therefore a risk of finding a difference in breast cancer rates that is really about something other than clothing.

More significantly, the Chen study had to make another huge compromise (I am not writing this as a criticism – I applaud Chen and colleagues for doing the study at all, and all study designs that involve humans also involve compromise). Although it is the most common internal cancer in women, mammary cancer is still not all that common: in the USA just over one in a thousand women is diagnosed with the disease each year. Looking at differences in cancer rates in a large population of initially-healthy women, some of whom wear bras and some of whom do not, would require a very large study, especially because almost every woman in Seattle does wear a bra. The

kind of money and time needed would simply not be made available for what most cancer specialists assume would be a wild goose chase anyway. So Chen and colleagues chose an alternative study design. They started with a cohort of just over a thousand women who had already been diagnosed with mammary cancers, and a 'control' group of women with no history of breast cancer. The groups were of a similar age profile. All of these women were asked about their lifetime bra-wearing habits, and also other aspects of their medical history. Only one participant reported having never worn a bra: she was excluded from the analysis, presumably because there was nobody with whom to compare her. So the study was left with a comparison of lifetime brawearing habits in women who had become breast cancer patients and those who had not. Observant readers will realize that this was not the original question: is the new form of the question valid?

The history of cancer epidemiology constantly hits the same practical problems that were faced by Chen. Transforming the question of "If some people do X and some do not, do the group who did X suffer more cancer?" into the question "Did a group of people with cancer do X more than people without it?" has often been a powerful way of identifying dangerous habits. Richard Doll and Bradford Hill's famous 1950 study on smoking faced very similar problems, including the issue that almost all men smoked then (as almost all women wear bras now). Doll and Hill used essentially the same experimental structure later used by Chen, and showed a strong association between smoking and lung cancer. So yes, the transformation of the question can be a worthwhile step especially if it allows a study to be made that would otherwise be impractical.

Back to the bras: the results of the statistical analysis showed no evidence that the women who had been diagnosed with breast cancer had, over their lives, worn a bra any more (hours per day, or started younger) than those who had no evidence of cancer. The point can be appreciated visually as well as in formal statistical tests: I have plotted the data below, together with the smoking data from Doll and Hill:



Waiting for the cells to grow: a laboratory blog at http://golgi.ana.ed.ac.uk/Davieslab/wftctg.html

To understand these graphs, first look at the Doll and Hill one. In the two left hand categories, representing 1-4 and 5-14 cigarettes per day, the proportion of non-cancer-sufferers (blue) was higher than lung cancer patients (red) but, in the right-hand categories that represent heavy smoking, the patients outnumbered the controls. This was an important observation in public health. Now look at the bra graph. Here there is essentially no pattern to suggest that wearing a bra for long periods is associated with cancer.

So, does this mean that bra-wearing is safe? Alas, as with all studies of this type, the best that can be hoped for is not a conclusion that something is 'safe', but rather that the risk of something must be less than some amount that is the minimum risk that the study could have detected. In the interview, the book's authors claimed that the wearing of a bra increased cancer risk tenfold, which is a dramatic claim: could the study have detected this? The answer depends on the relationship between 'dose' of bra wearing and its effect. For most cancer-causing substances, for example tobacco smoking, there is a clear relationship between the dose of the substance and risk of cancer. Small exposures generate moderate risk, medium exposures generate larger risk and large exposures generate very serious risk. You can see that in the Doll and Hill graph above. For anything that behaves like that, studying any part of the dose-response curve ought to indicate a problem. But if

the response curve flattens off in any range of doses, the relationship would be hard to detect. As a glance at the figure will show, the Chen study on bra wearing lumped bra-wearing habits of any time less than ten hours a day together, making it impossible to explore any relationship at really low 'doses'. The same applies to the high 'dose' end. If the dose-response was anything like linear across its whole range (double the dose, double the risk), then Chen's study would certainly have found an effect as large as the interview claims. But, if the response is increased by even tiny amounts of bra wearing and then hits a plateau, then it might not. This is not, therefore, an absolute proof of safety.

So what did I tell my friend? That I found only one good study. It proved that if you wear a bra at all, it makes no difference whether you wear it for your working day or your whole waking day. It found no evidence that bra wearing is a cancer risk, but the study design was not capable of proving, beyond all doubt, that there is no risk. And that the same answer applies to practically everything else that someone, somewhere, has thought might cause cancer (but not to smoking – that is definitely and indisputably dangerous).

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Links

Pubmed search: https://www.ncbi.nlm.nih.gov/pubmed

Lu Chen's paper: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4184992/

The Egan paper about breast size and cancer risk: <u>https://www.ncbi.nlm.nih.gov/pubmed/10231159</u> Richard Doll's paper on smoking: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2038856/</u>

The interview that provoked the question:

<u>http://feeds.bareoaks.ca/~r/NaturistLivingShow/~5/GpdEF0l6OzI/Health.mp3</u> (the interview is embedded in an audio podcast from a naturist community, with a general topic of clothing and health – the relevant interview starts 15 minutes into the podcast. Listeners will realize at once that the interview is not in the tradition of critical examination.)