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The Interphone study

Mobile madness

The threat to human health from mobile phones, if any, is much disputed. A shame, then, that a massive multinational study on the question has ended in chaos

LONG-TERM mobile-phone use increases risk of benign tumours!" "Clean bill of health for the mobile!" "Mobile phone-cancer link not proven!" Those who have followed the saga of whether or not mobile phones are damaging people's brains are used to contradictory headlines. A decade of coverage has left readers and viewers more confused than enlightened, with news reports alternating between alarming claims and soothing reassurances. Yet even by the standards of modern news, it is unusual to see such contradictory headlines about the same piece of research. Which is why a study, called Interphone, provides a cautionary tale.

Interphone began in 2000, ended in 2006, cost \$30m and involved around 50 scientists working in 13 countries on 14,000 people. It has, however, still to come to a settled conclusion- A draft of its supposed findings was circulated in June, and Elisabeth Cardis of the Centre for Research in Environmental Epidemiology in Barcelona, who led it, thought until recently that a final paper would be submitted this month. Now, though, it looks as if that will not even happen this year.

The contradictory headlines are the result of national research teams releasing single-country reports, despite the fact that

these inevitably involve smaller samples. The results from nine of the 13 single-country studies have been made available in this way, and the consequence is a farrago of misinformation. Many of the national reports suggest, for example, that ever having been a regular mobile-phone user offers statistically significant protection against some brain tumours. This finding is so counter-intuitive that it has led most of the people involved to acknowledge serious flaws in the study's design.

Please press "recall"

One problem was what statisticians call selection bias. Interphone began by gathering a group of people who had had the cancers of interest (glioma, meningioma, acoustic neurinoma and parotid gland tumour) and questioning them about their past use of mobile phones. The researchers then approached a number of healthy people in order to compare them with the cancer patients, and find out if there was a systematic difference in mobile-phone use between the two groups. Some of those approached agreed, and some declined. Of those who agreed to take part, 59% were regular mobile-phone users as defined by the study's protocol. Later on, those who had declined were recontacted and asked

about their mobile use. Among this group, only 34% were regular users. That meant those in the control group were more likely than average to be regular users, and therefore were not representative of the population at large.

Moreover, the definition of "regular mobile-phone use" was itself questionable. Anyone who had used a phone just once a week for at least six months qualified. That is a pretty low rate of usage. If phones really do cause cancer, but only at high exposure, employing such a generous definition of regular use means that the effect might be diluted into undetectability.

Another potentially serious flaw is that participants asked in 2001-02 about their mobile use a decade earlier will have been using analogue, not digital, handsets. That would lead to a different pattern of exposure and therefore of potential risk.

How the shift from analogue to digital phones might have changed things is anybody's guess. But both the selection bias and regular-phone-use definition might be expected to mask any adverse effect of phones. The most serious flaw in the study, however, is generally reckoned to be recall bias, which would tend to work in the opposite direction, by suggesting problems with phones that do not, in fact, exist.

Recall bias happened because the study was retrospective rather than prospective. In other words it looked at what people had done in the past rather than following their behaviour into the future. In practice, that meant asking them about past behaviour, and relying on the accuracy of their memories.

Even a healthy person would probably have difficulty recalling exactly how often

he used his mobile phone a decade ago, and which ear he routinely held it to. Someone subsequently diagnosed with a brain tumour might easily be biased, consciously or unconsciously, to exaggerate the former and misstate the latter. And that would be enough to account for the fact that several of the single-country studies found that ten years' mobile use was associated with an increased risk of brain tumours on the side of the head that people said was exposed to their handsets. It would also more significantly account for the studies' weird suggestion that the same amount of use stops tumours developing on the other side of the head.

The scientists involved in Interphone are, it must be said, well aware of these biases, and efforts to work out their effects and adjust for them were always part of the plan. In May Dr Cardis and her colleagues published a validation study in the

Journal of Exposure Science and Environmental Epidemiology. This compared the recollections of about 500 Interphone subjects with their actual mobile use according to the records of the network operators. The researchers found a high level of recall errors. Participants underestimated the number of calls they had made by an average of about 20%, and overestimated call duration by 40%. Ominously for the statisticians, the recall errors of those with tumours increased with time.

Suitable (and legitimate) statistical massaging of all the data may be able to offset these biases in a way that could not so easily be done for the smaller data sets from individual countries. Nevertheless Dr Cardis admits the delays in releasing the report have been due to "the difficulty of interpreting the findings due to potential biases" and to the "conducting of additional analyses to try and disentangle the poten-

tial impacts of selection and recall errors on the risk estimates".

The Interphone researchers are split into three camps. One believes any increased incidence of tumours shown in the study is purely the result of the biases. Another thinks it really has found increased risks of certain tumours and wants to call for precautionary measures. A third group is just keeping quiet. One person who knows many of the scientists, but prefers not to be named, describes the relations between members of the three groups as "strained"-harsh language in the world of scientific research.

Regardless of what eventually gets published, some people have already decided the findings warrant action. Ronald Herberman, the director of the University of Pittsburgh Cancer Institute, made headlines in July with a memo to 3,000 members of his staff urging them to limit their use of mobile phones, to refrain from keeping their handsets near their bodies at night and to avoid using them when reception is weak as a phone will then boost the strength of its signal in order that the network can hear it. He based his warnings on "early unpublished data", and is believed to have been referring to Interphone.

Whatever the outcome, though, at least one lesson has been learnt. Follow-up studies now in the planning stage are expected to use prospective as well as retrospective data. In other words they will pick people at random and see what happens to them. That method takes longer to come to a conclusion-but it is more likely to be one you can trust. •

Electrosensitivity

Mind your phone

Sham radiation can cause real pain

WHETHER mobile phones can cause cancer remains moot (see previous story). But they are also accused by some of causing pain. A growing number of people around the world claim to be "electrosensitive", in other words physically responsive to the electromagnetic fields that surround phones and the other electronic devices that clutter the modern world. Indeed, at least one country, Sweden, has recognised such sensitivity as a disability, and will pay for the dwellings of sufferers to be screened from the world's electronic smog.

The problem is that, time and again, studies of those claiming to be electrosensitive show their ability to determine whether they are being exposed to a real electric field or a sham one is no better than chance. So, unless they are lying about their symptoms, the cause of those symptoms needs to be sought elsewhere.

Michael Landgrebe and Ulrich Frick, of the University of Regensburg, in Germany, think that the "elsewhere" in question is in the brain and, in a paper presented recently to the Royal Society in London, they describe an experiment which, they think, proves their point.

Dr Landgrebe and Dr Frick used a body scanner called a functional magnetic-resonance imager to see how people's brains react to two different kinds of stimulus. Thirty participants, half of whom described themselves as electrosensitive, were put in the imager and told that they would undergo a series of trials in which they would be exposed either to

an active mobile phone or to a heating device called a thermode, whose temperature would be varied between the trials. The thermode was real. The mobile phone, however, was a dummy.

The type of stimulus, be it the authentic heat source or the sham electromagnetic radiation, was announced before each exposure and the volunteers were asked to rate its unpleasantness on a five-point scale. In the case of heat, the two groups' descriptions of their experiences were comparable. So, too, was their brain activity. However, when it came to the sham-phone exposure, only the electrosensitives described any sensations—which ranged from pricking to pain. Moreover, they showed neural activity to match. Some of the same bits of their brains lit up as when they were exposed to high temperatures.

This suggests that electrosensitivity, rather than being a response to electromagnetic stimulus, is akin to well-known psychosomatic disorders such as some sorts of tinnitus and chronic pain. A psychosomatic disorder is one in which the symptoms are real, but are induced by cognitive functions such as attitudes, beliefs and expectations rather than by direct external stimuli.

The paradoxical upshot of Dr Landgrebe's and Dr Frick's experiment is that mobile phones do indeed inflict real suffering on some unfortunate individuals. It is just that the electromagnetic radiation they emit has nothing whatsoever to do with it.