The Danish Cohort Study: The Politics and Economics of Bias

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The latest update of the Danish cell phone-cancer study is being touted as the biggest and best ever. It shows "no link between mobile phone use and [brain] tumors," according to the press release.

Don't believe a word of it.

On October 20, the *British Medical Journal* released the third installment of the Danish Cancer Society's cohort study, which has been tracking some 400,000 mobile phones subscribers since the 1980s. The whole enterprise has been dogged by controversy and political suspicions since the first results were published ten years ago.

From the very beginning, the Danish project was criticized for eliminating more than 200,000 corporate subscribers, one third of the actual number of Danish cell phone users, the intended study population. The researchers had little choice: They did not know the names of the people using phones paid for by their employers and so had no way to match those on mobile phone subscriber lists with those on tumor registries. Everybody agrees that those who were dropped were the heaviest users. In the time period covered in the Danish project —from 1987 through 1995— cell phones were expensive and it's no stretch to assume that those who did not have to pay their own bills racked up the most talk time.

In an e-mail to *Microwave News,* IARC's Robert Baan, wrote that the exclusion of the corporate subscribers "seems remarkable." Baan coordinated last May's panel meeting that designated RF radiation from cell phones as a possible human carcinogen. He also pointed out that, as the authors of the Danish study have openly disclosed, all those corporate users ended up in the control group. In other words, these heaviest users were treated as if they did not use cell phones. In his report on the May IARC meeting,

Baan wrote that this “could have resulted in considerable misclassification in exposure assessment.” That’s just a smart way of saying that the study has a good measure of bias.

Bias can magnify or understate a risk. The bias that Baan is referring to will lower the observed tumor risks from cell phones. (Remember that the tumor risk is estimated by comparing the number of cell phone users who get tumors with the number of non-users who get tumors.) Here’s why: If cell phones do indeed lead to tumors, then obviously some people who use them will get one. And if those people are put in the control group instead of the user group, they will inflate the expected rate of tumors. The new normal will be higher than it should be. This bias explains why the IARC panel put much less weight on the Danish study than on the Interphone and Hardell efforts. The Interphone and Hardell studies used a case-control design; both point to a tumor risk. (The IARC panel reviewed the first Danish update, published in 2006, but not the latest one released two weeks ago.)

The Danish study has another, perhaps even more potentially fatal source of bias. The user population includes only those who had a cell phone in 1995 —that was about 20% of the population. The Danish Cancer Society treats everyone who took up cell phones after 1995 as if they had never used one. They too are in the control group. That’s hard to believe but true. Here’s a direct quote from the *BMJ* paper: “individuals with a subscription in 1996 or later were classified as non-users.”

The number of cell phone users in Denmark more than doubled between 1995 and 1997, to about 44% of the population. All those people who started using cell phones in 1996 and 1997 could have accumulated 10 or 11 years of cell phone use by the end of 2007, the cut off date for the *BMJ* paper analysis. All those post-1995 users are also in the controls together with the heavy corporate users. More bias on top of bias.

There are other sources of bias. For instance, there’s no way to know who used a cordless phone, which can deliver as much radiation exposure as a cell phone.

Despite all this, IARC, in a recent release, wrote that Danish cohort study “confirms the overall Interphone findings of no association, but with reduced potential for bias.” We’ve already addressed the bogus argument that Interphone showed no tumor risk —though we are still wondering who wrote those words. We find it hard to believe that it was Robert Baan; that leaves Joachim Schüz, IARC’s head of the section on environment and radiation, as the most likely to have been responsible. Schüz is also one of the principal authors of the Danish cohort study. (Is there some kind of internal RF dispute going on at IARC?)

No one doubts that Interphone had bias. That's what lowered all the risks and made the study appear to show that cell phones protect against brain tumors. Arguments about the role of various types of bias —primarily selection and recall bias— delayed the release of the Interphone paper for four years and finally forced Chris Wild, the director of IARC, to step in and force a compromise.

Is the bias in Interphone any worse than in the Danish study? We asked Lennart Hardell and Elisabeth Cardis, the leader of Interphone, whether they agreed with Schüz. They don't.

"It is very difficult to quantify and compare, but I would not say that there is less bias than in Interphone," Cardis replied. Hardell thinks the Danish cohort has more intrinsic bias than his and the Interphone studies. He sent us a list of all the various types of bias at work in the Danish study.

Michael Kundi of the Medical University of Vienna goes much further. The Danish study is "the most severely biased study among all studies published so far," he told us. Kundi explained that he had done calculations to correct the 2006 Danish paper for the "contamination" of having so many long-term users among the controls and had found a "highly significant increase of glioma [brain tumor] risk." He predicted that when he does similar corrections of the latest data, the risk "would be even more pronounced."

As would be expected, the Danish paper has not been well received by those who have long pushed for caution and precautionary policies. Devra Davis, Denis Henshaw, Ron Herberman, Vini Khurana, Lloyd Morgan and Alasdair Philips have posted critical "rapid responses" on the *BMJ* Web site. Philips of U.K. Powerwatch was particularly outspoken about the new paper. "It's absolute rubbish," he said in an interview with *Microwave News.* "It's garbage in, garbage out."

Anders Ahlbom and Maria Feychting of the Karolinska Institute in Stockholm are more kindly disposed. In an editorial commissioned by *BMJ* and published with the Danish paper, they wrote that the results are "reassuring." They noted the potential for bias: "having a mobile phone subscription is not equivalent to using a mobile phone," they warned. They conceded that this would "dilute" a possible association, but they maintained it's a minor problem because the bias would have only "a small effect" for long-term users.

Somehow Ahlbom and Feychting don't address the fact that corporate subscribers and post-1995 users are in the controls. They are, of course, well aware of these sources of bias. Five years ago, they criticized the Danish study (the 2006 update) for these exact faults in a letter to the *Journal of the National Cancer Institute (JNCI).* Back then, they *did* express "concern" over the treatment of the corporate and post-1995 users. A "large proportion of the population started to use mobile phones after the cohort was defined and thus are included in the reference population," they wrote, admitting that the "same problem applies also to corporate users, who are not included as subscribers in the study." They warned: "All these circumstances would dilute any excess risk, were it to exist, and push the estimate toward the null." Elisabeth Cardis and U.K.'s Paul Elliott cosigned the letter to *JNCI.*

Ahlbom and Feychting also appear to have fogotten yet another source of bias which they had raised in *JNCI.* When the Danish team checked to see if members of the original 1987-1995 cohort

were still using a mobile phone in 2002, they found that only 61% of those questioned said that they still used a cell phone. This means that not only were the controls using cell phones but many of the so-called subscribers were not. This adds more bias to the already overflowing bucket of bias.

Is the COSMOS Study Another Source of Bias?

Why aren't those concerns as relevant today as they were five years ago? We were unable to ask Ahlbom and Feychting directly; they have both refused to be interviewed by *Microwave News* ever since we took them to task some years ago after they omitted an important paper showing tumor risks —one they both worked on!— in a report to the Swedish radiation protection authority.

Though Ahlbom and Feychting ignored the many biases of the Danish cohort study in their editorial, they didn't pass up the opportunity to highlight the recall and selection biases in the Interphone and Hardell case-control studies. In the process, they also take a swipe at the way Hardell did his case-control studies. What should be done next? Their answer: "Continued monitoring of health registers and prospective cohorts is warranted, but more case-control or other studies with built in selection and recall bias are not needed." This is, at least in part, another attack on Hardell: they are advising cutting off support for Hardell's work.

Ahlbom and Feychting neglect to mention that they are involved in the Swedish part of the only ongoing (or planned) prospective cohort study, the COSMOS project.

Officially launched last year —long after Ahlbom and Feychting wrote their critical letter to *JNCI* on the Danish cohort study— COSMOS is an international prospective cohort study. Because it will follow cell phone users in real time, it must continue for decades to allow for the long latency of brain tumor development. Denmark, Finland, the Netherlands, Sweden and the U.K. are participating. Germany planned to take part, but then dropped out over concerns about the project's feasibility. Schüz was a leader of the Danish component of the project before he moved to IARC. IARC now lists COSMOS as one of its current research projects.

COSMOS is attractive for the researchers and its sponsors alike. The major Swedish telecom companies —TeliaSonera, Telenor and Ericsson— are all helping pay for COSMOS. Because the project must continue to monitor the Swedish cohort for decades to come, COSMOS will keep Ahlbom and Feychting busy for the remainder of their careers at the Karolinska. The cell phone companies like it because COSMOS means business as usual —denial of tumor risks— for the foreseeable future as the results won't be published for many, many years. All the while, they can claim to be good corporate citizens for supporting health research. The governments like COSMOS too because they can continue to collect licensing fees worth billions without having to adopt precautionary policies that would incur the wrath of the companies that help them stay afloat.

The Karolinska group receives “practically all” the available funds for cell phone research in Sweden, according to Mona Nilsson, a freelance journalist and frequent critic of Ahlbom and Feychting. A lot of that money goes to the COSMOS project. For instance, Ahlbom recently received a SwKr3.2 million (~US$500,000) grant from Afa, an insurance company, to help pay for COSMOS. This is only one of many awards for COSMOS. Hardell attributes some of his troubles raising money to continue his epidemiological studies to Ahlbom’s major influence on who gets funding in Sweden. “We do not get any money,” he told us.

Here’s the question: Would the mobile phone companies continue to support COSMOS and the Karolinska group if Ahlbom and Feychting ever started ringing alarm bells over cell phones and cancer?

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