10 Years Later, Cell Phone Study Inconclusive

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MedPage Today Action Points

- Explain to interested patients that a large international study delivered inconclusive results on the link between cell phone use and brain cancer.

- Note that although the study's results were mixed, the only significant increase in risk (for one form of cancer) was among those with an extremely high lifetime use of cell phones -- at least 1,640 hours.

Review

The results of the largest-ever study of cell phones and cancer seems to be best summed up as "implausible" and, after a decade of waiting, they seem likely to inflame the debate rather than laying it to rest.

The so-called Interphone study -- involving 14 research centers in 13 countries and nearly 13,000 cases and controls -- found no overall increase of risk for glioma and meningioma associated with using a cell phone, according to Elisabeth Cardis, PhD, of the Centre for Research in Environmental Epidemiology in Barcelona, and colleagues.

But at the very highest level of reported use -- a level described as "implausible" by the researchers -- there was a significant increase in the risk of glioma, they reported online in the *International Journal of Epidemiology*.

On the other hand, odds ratios for most other analyses tended to be less than unity and many were statistically significant, suggesting that somehow cell phone use was protecting against cancer.

The researchers also dismissed the apparent protective effect as implausible.

"Rather than focus on the most extreme values," Cadis and colleagues wrote, "the interpretation should rest on the overall balance of evidence."

If there were no association between brain cancer and cell phone use, they noted, research should produce an "approximately symmetric pattern" of negative and positive odds ratios. Instead, they found a "disproportionately high" number of odds ratios less than unity and a small number of elevated odds ratios.

The "skewed distribution could be due to a bias or to a true effect," they said.

Most studies to date have shown little or no effect of cell phone use on the risk of cancer, but that hasn't stopped the research effort. (See New Study Looks at Long-Term Effects of Cell Phones)

And it seems likely that more studies are in the offing. The Interphone collaborators concluded that their findings are severely limited by "biases and errors" and suggested that -- in the face of increasing cell phone use -- more research is needed.

But, they said, "new studies should, in general, only be done if they can substantially reduce or eliminate selection bias, obtain detailed and high-quality exposure information over the full period of use and offer sufficient statistical power to detect comparatively small effects in people with heavy or long continued exposure."

The Interphone study was begun by the International Agency for Research on Cancer after feasibility studies in the late 1990s showed such a large case-control study would be both feasible and informative.

The researchers enrolled 2,425 meningioma cases, 2,765 glioma cases, and 7,658 controls, matched for age, sex, and region of residence. They were interviewed about their cell phone use during the previous 10 years, either in person or by proxy if they were too ill to be interviewed.

For the analysis, a person who had ever averaged at least one call per week for a period of at least six months was defined to be a regular cell phone user at least for that period. The reference group included those who had never used a cell phone and those whose use was never enough to qualify them as regular users.

Cardis and colleagues analyzed the cohort using exposure variables including ever having been a regular user, time in years since first regular use, cumulative number of calls, and cumulative duration of calls.

They found, among other things:

- A reduced odds ratio for glioma (OR 0.81, 95% CI 0.70 to 0.94) and meningioma (OR 0.79, 95% CI 0.68 to 0.91) associated with ever having been a regular cell phone user.
- No elevated risk for glioma or meningioma 10 years or more after first phone use. Odds ratios in both cases had 95% confidence intervals that crossed unity.
- Odds ratios were less than unity for all deciles of lifetime number of phone calls and nine of the deciles of cumulative call time.
- In the 10th decile of recalled cumulative call time -- at least 1,640 hours -- the odds ratio was 1.40 for glioma (with a 95% CI 1.03 to 1.89) and 1.15 for meningioma (but the 95% confidence interval ranged from 0.81 to 1.62).
- Odds ratios for glioma tended to be greater in the temporal lobe than elsewhere, but with wide confidence intervals.
- Odds ratios for glioma tended to be greater in patients who reported usual phone use on the same side of the head as their tumor than on the opposite side.

The apparent protective effect of cell phone use for regular users may reflect

participation bias or "other methodological limitations," the researchers said.

The findings seem likely to heat up the debate over the issue. Indeed, even one member of the research team -- Jack Siemiatycki, PhD, of the University of Montreal -- is reported to be critical of one aspect of the study.

Tough but inconsistent ethics rules, Siemiatycki told Canada's *National Post*, limited how many people took part and likely skewed the type of participants. On the other hand, he told the paper, the results imply that most cell phone users should not be concerned about brain cancer.

In the published study, the researchers also noted that they were "constrained by the requirements of ethical review committees and facing the population's increasing reluctance to participate in interview studies."

Of eligible participants, they said, 78% among meningioma cases, 64% among glioma cases, and 53% among controls agreed to take part. The proportions "raise the possibility of selection bias," they said, especially since a shorter interview among some of those who refused to take part in the full study showed a lower level of cell phone use.

The study had overall funding of about 19.2 million euros, including 5.5 million euros from industry sources. Some 3.5 million euros were contributed through the International Union against Cancer) and most of the rest came indirectly to individual research centers from mobile phone operators and manufacturers, through taxes and fees collected by government agencies. The European Commission provided 3.74 million euros and national and local agencies in participating countries -- such as the Australian National Health and Medical Research Council and the Canadian Institutes of Health Research -- provided a total of 9.9 million euros.

Cardis did not report any conflicts.

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