

Response

We thank Hardell et al. and Doré et al. for their interest in our work. Hardell et al. raise several questions about our study. The scientific question about whether mobile phone use is associated with brain tumors has been addressed by several epidemiological studies of various designs, such as case-control, cohort, and secular time trend studies, all of which have strengths and weaknesses. Because of the ubiquitous exposure, however, the presence or absence of an association will ultimately be confirmed by secular trend studies, such as ours. Indeed, if mobile phone use causes brain tumors, the effect of this association will necessarily be reflected in the time trends eventually because of the very high prevalence of mobile phone use. Conversely, the lack of a marked change in the time trends, at any point in time, would constitute evidence against such an effect. A prerequisite, however, is high-quality cancer registration on a sufficiently large population, such as what exists in the Nordic countries.

Although case-control studies are regarded as the most effective design for studying the etiology of rare diseases, they are prone to biases and errors. In the context of mobile phone use and brain tumors, validation studies demonstrated a selection bias (1) as well as both large random and systematic errors in the reporting of exposure (2,3) because of the difficulty of accurately remembering past mobile phone use.

Hardell et al. claim that “the impact of this low prevalence [of 14.2 % prevalence of mobile phone use in 1993] on the incidence of brain tumors would be small, if not zero.” However, the prevalence among the entire population is misleading because mobile phones were adopted at a difference pace by various age and sex subgroups. Among men aged 40–59 years, the reported prevalence of use was 7% in 1989 and reached 28% in 1993 [data from 2155 general population control subjects aged 20–79 years in the four Nordic INTERPHONE studies (4,5)]. If the risk of gliomas associated with mobile phone use doubled after 10 years of use as reported in Hardell et al. (6) or increased even more as reported in Hardell et al. (7), the incidence rate in this subgroup should have increased by approximately 20% or

more between 1999 and 2003; in fact, it remained stable during this time period. The risks reported in these publications are therefore incompatible with the observed secular trends. Increased risks reported for shorter-term use in the same studies are obviously in even stronger contrast with the observed incidence time trends.

Hardell et al. also argue that a consistent pattern of increased risk has been reported for gliomas in two meta-analyses (8,9). Meta-analyses, however, directly depend on the quality of the included studies, which may vary.

The quality of the Nordic Cancer registries is generally considered to be high. In the Swedish cancer registry, underreporting of nervous system tumors was mainly found among persons aged 70 years or older (10); among persons younger than 70 years, including our focus group of men aged 40–59 years, registry completeness reached 94.5% in 1998 for Sweden. In the Finnish cancer registry, between 1985 and 1988, the completeness for malignant central nervous system tumors (ie, gliomas, essentially) was 98.6% (11). Furthermore, only changes in registry completeness over time would affect the time trends.

When we started this project, cancer registry data were available only up to 2003 for all four countries. We agree that further analyses covering more recent incidence data are needed.

The NORDCAN dataset mentioned by Hardell et al. is based on the same cancer registry data that we used, but it does not provide as detailed a classification as our analyses. NORDCAN groups all nervous system tumors, including brain and spine, whereas we specifically investigated the two largest histological subtypes, glioma and meningioma.

As Hardell et al. rightly point out, the induction period between an exposure and the diagnosis of a cancer is unknown and could be long. Hence, we would like to reiterate our conclusions: our findings do not alleviate concerns about increased risks of glioma and meningioma among small segments of the population, particularly very intensive mobile phone users, nor about induction periods longer than 5–10 years. Our results are consistent with no association (5,12,13), with evidence against a substantial risk increase as in the Danish cohort study (14), and with the possibility

of a small risk increase for glioma (5), but are in sharp contrast with the levels of increased risks as reported in the studies by Hardell et al.

We agree with Doré et al. that the temporal area of the brain is the most heavily exposed site (15) and that incidence time trends concentrating on this anatomical location would be informative. Unfortunately, brain tumor anatomical location has not been recorded consistently over the years in the cancer registries; for example, a large and varying proportion of cases have been coded as “brain, unspecified location.” Before undertaking such specific analyses, an evaluation of the quality of the information on anatomical location in cancer registries would be required.

ISABELLE DELTOUR
CHRISTOFFER JOHANSEN
ANSSI AUVINEN
MARIA FEYCHTING
LARS KLAEBOE
JOACHIM SCHÜZ

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Notes

Affiliations of authors: Department of Biostatistics and Epidemiology (ID, JS) and Department of Psychosocial Cancer Research (CJ), Institute of Cancer Epidemiology, Danish Cancer Society, Copenhagen, Denmark; Department of Epidemiology, Tampere School of Public Health, University of Tampere, Tampere, Finland (AA); Research and Environmental Surveillance, Radiation and Nuclear Safety Authority, Helsinki, Finland (AA); Unit of Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden (MF); Norwegian Radiation Protection Authority, Østera's, Norway and Cancer Registry of Norway, Oslo, Norway (LK).

Correspondence to: Isabelle Deltour, PhD, Department of Biostatistics and Epidemiology, Institute of Cancer Epidemiology, Danish Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen, Denmark (e-mail: deltour@cancer.dk).

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