Environment International 187 (2024) 108664

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Response to the Letter to the Editor regarding "Mobile phone use and brain tumour risk — COSMOS, a prospective cohort study"

ARTICLE INFO

Handling Editor: Mark Nieuwenhuijsen
Keywords
Cell phones
Radiofrequency fields
Electromagnetic fields
Non-ionizing radiation
Brain neoplasms
Cohort study

We thank Dr. Kundi for his interest in our study (Feychting et al., 2024). We take this opportunity to clarify some design features and to endorse the conclusions of our study.

First, we wish to take note of a basic epidemiological concept, namely to distinguish between exposure time and follow-up (or risk) time. The follow-up time in a cohort study is the period during which incident cases of the studied disease are registered. This need not be the entire time from potential tumour initiation until diagnosis, as information about individual exposure histories can be collected when the cohort is established, before cohort participants have been diagnosed with the studied disease; this includes information on past exposure so that cumulative exposure over the entire exposure time becomes available, which is more than 20 years for the early mobile phone users in COSMOS. Then the cohort is followed prospectively to identify various health outcomes. This is a well-established method used in numerous prospective cohort studies. One well-known example is the cohort of British doctors established in 1951, which collected smoking histories on 40,564 medical doctors (Doll and Hill, 1954). Doll and colleagues could already within three years demonstrate a higher lung cancer mortality among smokers.

As we reported, COSMOS participants gave detailed information about their current and historical mobile phone use in the baseline questionnaire, covering the entire time period from the day they first started to use a mobile phone. Handheld mobile phones were introduced in 1987; thus, the longest latency possible was ~ 30 years, and 30.5 % of the COSMOS study population had used a mobile phone 15 years or longer (Feychting et al., 2024).

Cancer development is a multistage process that encompasses tumour initiation, promotion, malignant conversion and progression (Dean and Moitra, 2018; Weston and Harris, 2003). This process involves a sequence of molecular changes that may eventually manifest in clinically detectable cancer. A number of mutational events occur during this process which can be caused by various agents, some of which may have the potential to initiate cancer, while others act as promotors or progressors.

The mechanism by which non-thermal levels of non-ionizing radiation such as radiofrequency electromagnetic fields (RF-EMF) would affect cancer development, if any, is unknown (Roosli et al., 2019). The energy absorbed in tissues from non-ionizing radiation is too weak to break chemical bonds and is not believed to directly cause DNA damage (Challis, 2005). Thus, RF-EMF is unlikely to be an initiator of tumourigenesis. Kundi argues that it would not be possible to observe an increased risk of brain tumours in the COSMOS study because brain tumours have too long latencies, using ionizing radiation as an example. Ionizing radiation is a known cancer initiator, as the absorbed energy is high enough to ionize molecules and damage DNA (Berrington de Gonzáles et al., 2018). It is more relevant, however, to discuss latencies or induction periods associated with different exposures, as these will vary depending on the mechanism by which the exposure affects cancer development (Rothman and Greenland, 1998). For ionizing radiation, higher brain tumour incidence is indeed observed several decades after exposure, for example among atomic bomb survivors (Brenner et al., 2020) and persons who received radiation treatment for tinea capitis as children (Sadetzki et al., 2005). However, many carcinogens known to cause DNA damage may also act as promotors and progressors, and a higher cancer incidence among people exposed to a specific agent may be evident within a few years after first exposure. Ionizing radiation is a good example as it also acts as a promotor (Berrington de Gonzáles et al., 2018). This is, for example, evident in a study of ionizing radiation from computed tomography (CT) scans during childhood and adolescence, where the highest excess relative risk (ERR) for brain cancer was observed 5 to < 10 years after exposure (ERR/100 mGy = 1.84; 95 % CI 0.78–3.76) (Hauptmann et al., 2023). A study of tinea capitis patients found an excess relative risk (ERR) for malignant brain tumours of 2.94

DOI of original article: https://doi.org/10.1016/j.envint.2024.108552.

https://doi.org/10.1016/j.envint.2024.108664
Received 9 April 2024; Accepted 15 April 2024
Available online 21 April 2024

(95 % CI 0.39–13.95) per Gy with less than 20 years latency (Sadetzki et al., 2005) and observed raised risks also for longer latencies. Studies of Japanese atomic bomb survivors found an increased risk of leukaemia within a few years after exposure, whereas an increase in the incidence of solid tumours was evident after less than 15 years (Little, 2009). Kundi's arguments about too short exposure time in COSMOS and the claim about a very long latency for brain tumours are not correct.

Notably, one rationale of starting COSMOS was that some previous case-control studies reported associations between cumulative mobile phone use and especially glioma risk, after much shorter latencies than COSMOS now has been able to address (Baan et al., 2011), raising concerns as to whether protective measures were necessary. These studies had maximum exposure durations of ~ 15 years. The main value of COSMOS is the use of a study design that overcomes the well-known limitations of the case-control studies due to differential recall bias, and considerably extending the exposure duration as compared to previous studies. With an improved study design, no increased brain tumour risks were observed.

As we discuss in the article, the main current limitation of our study, which will diminish with time, is the limited statistical power, especially for acoustic neuroma but also for meningioma (Feychting et al., 2024). Additional updates of the COSMOS cohort linkages to the cancer registers are warranted to increase statistical power, allow analyses of longer latencies, and study potential carcinogenic effects from newer generations of mobile technologies.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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