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Response to the letter from Di Ciaula et al

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1. Introduction

Re: Di Ciaula et al. Exposure to radiofrequency electromagnetic fields and risk of cancer: epidemiology is not enough!

We thank the authors for their comments and the opportunity to clarify the points raised related to our systematic review.

The conclusion of our systematic review are based on the best available human evidence at the time of the review, with moderate certainty, near field RF-EMF exposure to the head from mobile phone use likely does not increase the risk of glioma, meningioma, acoustic neuroma, pituitary tumours, and salivary gland tumours in adults, or of paediatric brain tumours. We are aware that absence of evidence does not definitively equate to evidence of absence; however, we can only review and *meta*-analyse the available data and evidence, which predominantly came from case-control studies which by design have some limitations with retrospective exposure assessment when exploring causal relationships (hence, moderate certainty) and we acknowledge this in the Discussion (see 5.2. Limitations in the evidence).

Di Ciaula et al. state that high body mass index, alcohol consumption and dietary habits are risk factors for glioblastoma and argue that they could act as confounders. Indeed, only a few studies in our review have considered such potential confounders. These studies did not find any evidence for such confounding (See Annex 5, table S7.1 and S7.2 for details). Most important, to act as confounder, the above-mentioned factors have to be related to mobile phone use as well. For body mass index and alcohol consumption, some positive correlations with mobile phone use have been observed (e.g. Schuz et al 2022). This implies, original studies that have not adjusted for these factors are more likely to overestimate the association between mobile phone use and cancer. Consequently, the observed absence of association in our *meta*-analysis cannot be explained by lack of control for these confounding factors in the original studies. If there would be residual confounding from these factors, it would rather result in an overestimation than to an underestimation of the observed cancer risk from mobile phone use in our systematic review.

Regarding the inclusion of a comprehensive discussion on animal experimental studies we were clear in our protocol and manuscript that the review was on human studies and did not include animals. Another systematic review on animal studies and cancer is currently in progress [see the published protocol (Mevissen et al. 2022)]. The current systematic review is one of ten commissioned by the World Health Organization (WHO) (https://www.sciencedirect.com/special-issue/109J1SL7CXT). The WHO will use the results from all the systematic reviews and look at all the evidence to assess the health effects of RF-EMF exposure.

We agree that exposure status at a population-level has changed over the past decade and that mobile phone use is now ubiquitous in all developed and most developing countries with different networks in operation and we highlight this in the manuscript with the ongoing cohort studies that will provide some of the first evidence on this. Our paper discusses ongoing and future research in section '5.5. Implications for research' and we mention the need for validation studies. Population-based prospective cohort studies in children and adults are currently underway as mentioned. Previous studies do not indicate any substantial risk for this age group (Bodewein et al, 2022). Nevertheless, our paper acknowledges and highlights these studies (see section 6.3. New relevant studies issued after the literature search end date), and we encourage researchers to initiate further prospective cohort studies with harmonised exposure assessment and study designs to reduce methodological and statistical heterogeneity when comparing findings between these studies. Beyond this we believe it would be inappropriate and outside the scope of this review to call for the precautionary approach on the use of wireless technology.

2. Support

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Ken Karipidis as part of his employment is involved in the provision of advice to the Australian Commonwealth Government, Australian States and Territories and the general public on the risks and health effects of exposure to ionising and non-ionising radiation. He is also a member of the International Commission on Non-Ionizing Radiation Protection where he contributes in the development and dissemination of science-based advice on limiting exposure to non-ionizing radiation. Mark Elwood has given expert advice on topics in electromagnetic fields and health, and on the objective interpretation of epidemiological and other scientific information, over many years to individuals and groups, including government ministries, environmental regulators, community groups, commercial organisations, and formal inquiries by government and professional groups including parliamentary and legal proceedings. Some of this work has been financially supported, by universities, health care organisations, research bodies, or by government, professional or commercial groups. Some work has been reported 'blind', with the client being unidentified. Susanna Lagorio was principal investigator (April 2019 – March 2020) of the research project "BRiC 2018/06 - Systematic reviews of exposure to radiofrequency fields and cancer", supported by the Italian Workers' Compensation Authority, a public no-profit entity (grant code I85B19000120005). Her employment duties involved provision of advice on health hazards from exposure to RF-EMF to the Italian Ministry of Health and Higher Health Council (she retired on August 1st, 2023). Martin Röösli's research is entirely funded by public entities or not for profit foundations. He has served as advisor on potential health effects of exposure to non-ionizing radiation to several national and international public advisory and research steering groups, including the World Health Organization, the International Agency for Research on Cancer, the International Commission on Non-Ionizing Radiation Protection, the Swiss Government (member of the working group "Mobile phone and radiation" and chair of the expert group BERENIS), the German Radiation Protection Commission (member of the committee Non-ionizing Radiation (A6) and member of the working group 5G (A630)) and the Independent Expert Group of the Swedish Radiation Safety Authority. From 2011 to 2018, M.R. was an unpaid member of the foundation board of the Swiss Research Foundation for Electricity and Mobile Communication, a non-profit research foundation at ETH Zurich. Neither industry nor nongovernmental organizations are represented on the scientific board of the foundation. Chris Brzozek as part of his employment is involved in the provision of advice to the Australian Commonwealth Government, Australian States and Territories and the general public on the risks and health effects of exposure to ionising and non-ionising radiation. The other authors declare that they have no known conflicts of interest].

Data availability

Data will be made available on request.

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