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The effect of exposure to radiofrequency fields on cancer risk in the general and working population: A systematic review of human observational studies – Part I: Most researched outcomes

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Highlights

- Exposure to RF from mobile phone use likely does not increase the risk of brain cancer.
- F from broadcasting antennas or base stations likely does not increase the risk of childhood.
- cancer.
- Occupational exposure to RF may not increase the risk of brain cancer.

Abstract

Background

The objective of this review was to assess the quality and strength of the evidence provided by human observational studies for a causal association between exposure to radiofrequency electromagnetic fields (RF-EMF) and risk of the most investigated neoplastic diseases.

Methods

Eligibility criteria: We included cohort and case-control studies of neoplasia risks in relation to three types of exposure to RF-EMF: near-field, head-localized, exposure from wireless phone use (SR-A); far-field, whole body, environmental exposure from fixed-site transmitters (SR-B); near/far-field occupational exposures from use of hand-held transceivers or RF-emitting equipment in the workplace (SR-C). While no restrictions on tumour type were applied, in the current paper we focus on incidence-based studies of selected "critical" neoplasms of the central nervous system (brain, meninges, pituitary gland, acoustic nerve) and salivary gland tumours (SR-A); brain tumours and leukaemias (SR-B, SR-C). We focussed on investigations of specific neoplasms in relation to specific exposure sources (i.e. E-O pairs), noting that a single article may address multiple E-O pairs.

Information sources: Eligible studies were identified by literature searches through Medline, Embase, and EMF-Portal.

Risk-of-bias (RoB) assessment: We used a tailored version of the Office of Health Assessment and Translation (OHAT) RoB tool to evaluate each study's internal validity. At the summary RoB step, studies were classified into three tiers according to their overall potential for bias (low, moderate and high).

Data synthesis: We synthesized the study results using random effects restricted maximum likelihood (REML) models (overall and subgroup meta-analyses of dichotomous and categorical exposure variables), and weighted mixed effects models (dose–response meta-analyses of lifetime exposure intensity).

Evidence assessment: Confidence in evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.

Results

We included 63 aetiological articles, published between 1994 and 2022, with participants from 22 countries, reporting on 119 different E-O pairs. RF-EMF exposure from mobile phones (ever or regular use *vs* no or non-regular use) was not associated with an increased risk of glioma [meta-estimate of the relative risk (mRR) = 1.01, 95 % CI = 0.89–1.13), meningioma (mRR = 0.92, 95 % CI = 0.82–1.02), acoustic neuroma (mRR = 1.03, 95 % CI = 0.85–1.24), pituitary tumours (mRR = 0.81, 95 % CI = 0.61–1.06), salivary gland tumours (mRR = 0.91, 95 % CI = 0.78–1.06), or paediatric (children, adolescents and young adults) brain tumours (mRR = 1.06, 95 % CI = 0.74–1.51), with variable degree of across-study heterogeneity (I^2 = 0 %-62 %). There was no observable increase in mRRs for the most investigated neoplasms (glioma, meningioma, and acoustic neuroma) with increasing time since start (TSS) use of mobile phones, cumulative call time (CCT), or cumulative number of calls (CNC). Cordless phone use was not significantly associated with risks of glioma [mRR = 1.04, 95 % CI = 0.74–1.46; I^2 = 74 %) meningioma, (mRR = 0.91, 95 % CI = 0.70–1.18; I^2 = 59 %), or acoustic neuroma (mRR = 1.16; 95 % CI = 0.83–1.61; I^2 = 63 %). Exposure from fixed-site transmitters (broadcasting antennas or base stations) was not associated with childhood leukaemia or paediatric brain tumour risks, independently of the level of the modelled RF exposure. Glioma risk was not significantly increased following occupational RF exposure (ever *vs* never), and no differences were detected between increasing categories of modelled cumulative exposure levels.

Discussion

In the sensitivity analyses of glioma, meningioma, and acoustic neuroma risks in relation to mobile phone use (ever use, TSS, CCT, and CNC) the presented results were robust and not affected by changes in study aggregation.

In a leave-one-out meta-analyses of glioma risk in relation to mobile phone use we identified one influential study. In subsequent meta-analyses performed after excluding this study, we observed a substantial reduction in the mRR and the heterogeneity between studies, for both the contrast Ever *vs* Never (regular) use (mRR = 0.96, 95 % CI = 0.87–1.07, I^2 = 47 %), and in the analysis by increasing categories of TSS ("<5 years": mRR = 0.97, 95 % CI = 0.83–1.14, I^2 = 41 %; "5-9 years ": mRR = 0.96, 95 % CI = 0.83–1.11, I^2 = 34 %; "10+ years": mRR = 0.97, 95 % CI = 0.87–1.08, I^2 = 10 %).

There was limited variation across studies in RoB for the priority domains (selection/attrition, exposure and outcome information), with the number of studies evenly classified as at low and moderate risk of bias (49 % tier-1 and 51 % tier-2), and no studies classified as at high risk of bias (tier-3). The impact of the biases on the

study results (amount and direction) proved difficult to predict, and the RoB tool was inherently unable to account for the effect of competing biases. However, the sensitivity meta-analyses stratified on bias-tier, showed that the heterogeneity observed in our main meta-analyses across studies of glioma and acoustic neuroma in the upper TSS stratum (I^2 = 77 % and 76 %), was explained by the summary RoB-tier. In the tier-1 study subgroup, the mRRs (95 % CI; I^2) in long-term (10+ years) users were 0.95 (0.85–1.05; 5.5 %) for glioma, and 1.00 (0.78–1.29; 35 %) for acoustic neuroma.

The time-trend simulation studies, evaluated as complementary evidence in line with a triangulation approach for external validity, were consistent in showing that the increased risks observed in some case-control studies were incompatible with the actual incidence rates of glioma/brain cancer observed in several countries and over long periods. Three of these simulation studies consistently reported that RR estimates > 1.5 with a 10+ years induction period were definitely implausible, and could be used to set a “credibility benchmark”. In the sensitivity meta-analyses of glioma risk in the upper category of TSS excluding five studies reporting implausible effect sizes, we observed strong reductions in both the mRR [mRR of 0.95 (95 % CI = 0.86–1.05)], and the degree of heterogeneity across studies (I^2 = 3.6 %).

Conclusions

Consistently with the published protocol, our final conclusions were formulated separately for each exposure-outcome combination, and primarily based on the line of evidence with the highest confidence, taking into account the ranking of RF sources by exposure level as inferred from dosimetric studies, and the external coherence with findings from time-trend simulation studies (limited to glioma in relation to mobile phone use).

For near field RF-EMF exposure to the head from mobile phone use, there was moderate certainty evidence that it likely does not increase the risk of glioma, meningioma, acoustic neuroma, pituitary tumours, and salivary gland tumours in adults, or of paediatric brain tumours.

For near field RF-EMF exposure to the head from cordless phone use, there was low certainty evidence that it may not increase the risk of glioma, meningioma or acoustic neuroma.

For whole-body far-field RF-EMF exposure from fixed-site transmitters (broadcasting antennas or base stations), there was moderate certainty evidence that it likely does not increase childhood leukaemia risk and low certainty evidence that it may not increase the risk of paediatric brain tumours. There were no studies eligible for

inclusion investigating RF-EMF exposure from fixed-site transmitters and critical tumours in adults.

For occupational RF-EMF exposure, there was low certainty evidence that it may not increase the risk of brain cancer/glioma, but there were no included studies of leukemias (the second critical outcome in SR-C).

The evidence rating regarding paediatric brain tumours in relation to environmental RF exposure from fixed-site transmitters should be interpreted with caution, due to the small number of studies. Similar interpretative cautions apply to the evidence rating of the relation between glioma/brain cancer and occupational RF exposure, due to differences in exposure sources and metrics across the few included studies.

Other

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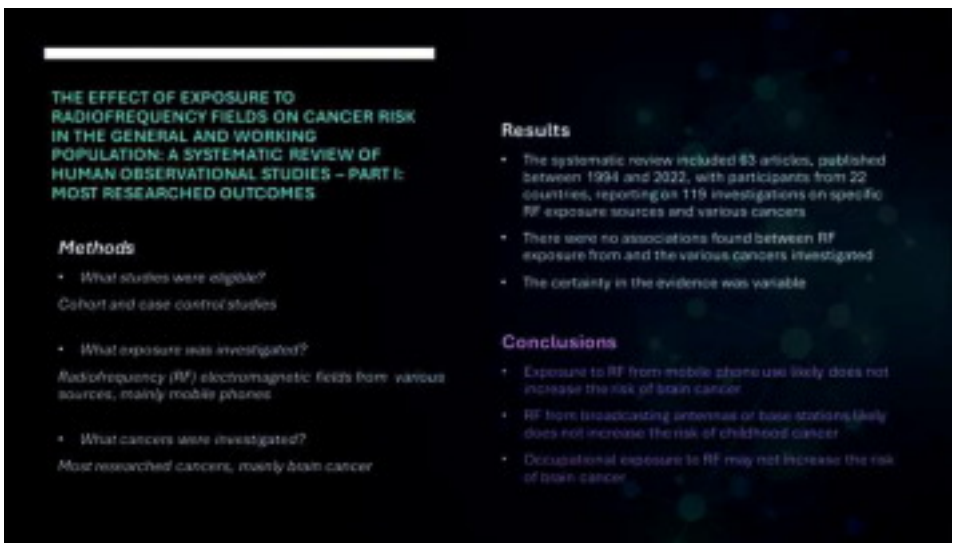
Graphical abstract



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Keywords

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