



Bundesamt
für Strahlenschutz

Spotlight on EMF Research

Spotlight on “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” by Karipidis et al. in Environment International (2024)

Category [radiofrequency, review]

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Competence Centre for Electromagnetic Fields (KEMF)

1 Putting the paper into context by the BfS

The World Health Organization (WHO) has initiated an ongoing project to systematically assess the potential health effects of exposure to radiofrequency electromagnetic fields (RF-EMF). To this end, in 2018, the WHO conducted a comprehensive international survey among RF-EMF experts to prioritize the potential health effects according to their importance [2]. Key topics were identified for which the WHO has commissioned systematic reviews. More information on the WHO systematic reviews in general can be found in this *Spotlight on EMF Research* article (Apr/2024 no.2 [3]).

The use of technology emitting RF-EMF has grown consistently since the 1950s, with applications spanning medicine, industry, households, the military, and, notably, telecommunications. Concerns about the potential health effects of mobile phone technology emerged in the late 1990s and early 2000s as mobile phones became widely used by the general public. Without hands-free systems, phone use in those days resulted in relatively high exposure to the head. Consequently, scientific focus primarily centred on a possible link between mobile phone use and head tumours, such as gliomas, meningiomas, and acoustic neuromas. This led to the initiation of several epidemiological studies to explore the potential long-term effects of mobile phones on brain tumour risk.

The systematic review at hand by Karipidis et al. [1] assesses the influence of RF-EMF exposure on cancer risk in the general and working population, based on human observational studies and part of the WHO commissioned systematic review series. The most researched cancer outcomes in this research field are reported, namely neoplasms of the central nervous system, the salivary gland, and leukaemia. In a second paper [4] from the same study group, less researched cancer outcomes are reported, including, e.g., lymphohematopoietic system tumours, thyroid cancer and oral cavity/pharynx cancer and will be addressed in a separate *Spotlight on EMF Research* article.

2 Results and conclusions from the perspective of Karipidis et al.

The objective of the systematic review and meta-analysis by Karipidis et al. [1] is the assessment of quality and strength of the evidence for an association between exposure to RF-EMF and the risk of cancer in human observational studies.

The authors published a protocol [5] before the start of the work on the systematic review. In their protocol, they outline all methods used throughout the systematic review and meta-analysis. In short, the authors followed the WHO approach to guideline development [6], followed the COSTER (conduct of systematic reviews in toxicology and environmental health research) [7] recommendation and reported the findings in accordance to the PRISMA guidelines [8]. For assessing the Risk of Bias (RoB) they followed the method developed by the National Toxicology Program – Office of Health Assessment and Translation (OHAT) [9]. For this, the authors set up tailored bias rating instructions and answer options forms that were published alongside the paper and performed a pre-pilot among all assessors.

The RoB assessment was performed on exposure-outcome level by two assessors individually. Bias domains were confounding, selection bias, attrition/exclusion/missing data bias, confidence in the exposure characterization, confidence in the outcome assessment, selective reporting and appropriateness of statistical assessment. For the OHAT's three level tiering of the quality of individual studies "selection/attrition bias", and "exposure/outcome information bias" were defined as the key-domains. Tier-1 studies are studies with definitely or probably low risk of bias for all key-domains and most of the other items, while tier-3 studies are studies with definitely or probably high risk of bias for all key-domains and most of the other items. Tier-2 studies are those studies not meeting the above criteria for Tier-1 or Tier-3 studies.

The systematic review includes three **PECO (Population, Exposure, Comparator, Outcome)** statements used for defining the eligibility criteria. There is one PECO statement on RF-EMF **Exposure (E)** from wireless phone use, including mobile or cordless phones (SR-A), one on RF-EMF exposure from environmental sources, such as radio-television transmitters or base stations (SR-B) and one on occupational exposure to RF-EMF, such

as professional use of hand-held transceivers or RF-emitting equipment in the workplace (SR-C). Regarding the **Population (P)** SR-A and SR-B include members of the general population, while SR-C is on workers. There were no restrictions on sex, age or any other individual characteristic. The existence of a **Comparator (C)** group of unexposed or less exposed individuals was required to be included in the systematic review. Similar to the Exposure (E) element of the PECO scheme, the **Outcome (O)** differs between SR-A, SR-B and SR-C. For SR-A glioma/brain cancers in adults, paediatric brain tumours, meningioma, acoustic neuroma, pituitary gland tumours and salivary gland tumours were included. In SR-B childhood leukaemia, paediatric brain tumours, glioma/brain cancer in adults and leukaemia in adults were investigated. SR-C focused on glioma/brain cancer and leukaemia.

The authors included cohort studies, case-control studies, and nested case-control studies published in peer-reviewed journals, applying no restriction on publication date or language. Comparative studies such as ecological studies and cross-sectional studies were excluded.

For the overall confidence in evidence assessment, the OHAT Grade approach was used for SR-A, SR-B and SR-C separately. The confidence levels were classified as High, Moderate, Low, or Very Low. The assessment process involved three steps: 1) assigning an initial “moderate” rating to studies, 2) adjusting the rating based on factors like inconsistency or bias, and 3) assessing confidence across multiple exposure types and outcomes. Limited to glioma in relation to mobile phone use, the external coherence with findings from time-trend simulation studies was checked.

In total, 5,060 articles were identified. Throughout the deduplication process, title/abstract screening and the full-text screening, non-relevant articles were excluded, leaving 63 articles for inclusion in the systematic review. The articles were published between 1994 and 2022 with participants from 22 countries, reporting on 119 different exposure-outcome pairs (studies). Among those 63 articles 82 studies were part of SR-A, investigating the risk for selected tumours in the head region (paediatric brain tumour, glioma, meningioma, acoustic neuroma, pituitary gland tumours and salivary gland tumours) in relation to mobile phone use. Another 23 studies reported use of cordless phones for a number of the above-mentioned brain tumours. For SR-B 10 studies on risk of childhood leukaemia and paediatric brain tumours were included. For SR-C only 3 relevant studies of brain cancer/glioma risk were identified.

Of all included studies, 49% were classified as tier-1 studies with a low risk of bias. 51% were rated tier-2 and no study was rated tier-3. At the individual study level, the most critical issue was the key-domain exposure characterization and the susceptibility to selection bias. Outcome assessment and statistical methods were rated as low risk of bias for almost all included studies. The main findings are summarized in Table 1.

In short, no statistically significant increase in risk for glioma, meningioma, acoustic neuroma, pituitary tumours, salivary gland tumours, or paediatric brain tumours associated with mobile phone use (SR-A) was identified for the main analyses of *ever use* compared to *never use*. Additional analyses of potential associations with mobile phone use duration or number of calls support these findings. Similarly, no statistically significant increased risk of glioma, meningioma, or acoustic neuroma was observed for the use of cordless phones (SR-A). For fixed-site transmitters, namely exposure from broadcasting antennas or base stations, no statistically significant association with childhood leukaemia or paediatric brain tumour risk (SR-B) was observed. Regarding occupational exposure, no statistically significant increase in glioma risk was observed (SR-C). In addition, published time-trend simulation studies indicated that increases in glioma or brain cancer risk observed in some studies were inconsistent with actual incidence trends.

Karipidis et al. conclude, that from the available observational studies there is moderate certainty evidence, that 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. For cordless phone use, there was low certainty evidence that it may not increase the risk for glioma, meningioma or acoustic neuroma. For far-field whole-body exposure from fixed-site transmitters and childhood leukaemia, there was moderate certainty that it likely does not increase the risk and low certainty for paediatric brain tumours. For occupational exposure, RF-EMF may not increase the risk of brain cancer, however the number of studies on this aspect is limited. Overall, the study found no statistically significant increased risk for any of the analysed cancer outcomes associated with RF-EMF exposure.

3 Comments by the BfS

For the publication presented here, BfS employees have participated as authors. As a result, we are refraining from providing a detailed evaluation and commentary on the content and significance of this publication.

Outcome Cancer subtype	No. of studies / Exposed cases (n)	Exposure metric	Effect, meta Relative Risk (mRR) (95 % KI)	Statistically significant effects	Certainty of the evidence
Results of SR-A of studies on RF-EMF exposure from wireless phone use (Near-field personal exposure to the head)					
Glioma	3 Cohort, 10 Case-control n = 4,200	Mobile phone Ever vs. never use	1.01 (0.89-1.13)	No	Moderate
	3 Case-control n > 1,022*	Cordless phone Ever vs. never use	1.04 (0.74-1.46)	No	Low
Meningioma	3 Cohort, 7 Case-control n = 2,990	Mobile phone Ever vs. never use	0.92 (0.82-1.02)	No	Moderate
	3 Case-control n > 1,089*	Cordless phone Ever vs. never use	0.91 (0.70-1.18)	No	Moderate
Acoustic neuroma	2 Cohort, 9 Case-control n = 1,614	Mobile phone Ever vs. never use	1.03 (0.85-1.24)	No	Moderate
	4 Case-control n > 716*	Cordless phone Ever vs. never use	1.16 (0.83-1.61)	No	Low
Pituitary tumour	1 Cohort, 4 Case-control n > 466*	Mobile phone Ever vs. never use	1.16 (0.83-1.61)	No	Moderate
Salivary gland tumour	1 Cohort, 9 Case-control n = 611	Mobile phone Ever vs. never use	0.91 (0.78-1.06)	No	Moderate
Paediatric brain tumour	3 Case-control n = 733	Mobile phone Ever vs. never use	1.06 (0.74-1.51)	No	Moderate
Results of SR-B of studies on RF-EMF exposure from environmental sources (Far-field whole-body exposure from fixed-site transmitters)					
Paediatric brain tumour	1 Cohort, 3 Case-control n = 1,056	Exposed vs. unexposed	0.97 (0.73-1.29)	No	Low
Childhood leukaemia	1 Cohort, 4 Case-control n = 2,219	Exposed vs. unexposed	0.93 (0.85-1.03)	No	Moderate
Results of SR-C of studies on occupational exposure to RF-EMF (Near-field/far-field)					
Glioma	3 Case-control n = 313	Exposed vs. unexposed	1.06 (0.72-1.54)	No	Low

* No information on exposed cases in one study

Table 1: Summary of the results.

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