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TI - 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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AB - 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)Â =Â 1.01, 95Â % CIÂ =Â 0.89-1.13), meningioma (mRRÂ =Â 0.92, 95Â % CIÂ =Â 0.82-1.02), acoustic neuroma (mRRÂ =Â 1.03, 95Â % CIÂ =Â 0.85-1.24), pituitary tumours (mRRÂ =Â 0.81, 95Â % CIÂ =Â 0.61-1.06), salivary gland tumours (mRRÂ =Â 0.91, 95Â % CIÂ =Â 0.78-1.06), or paediatric (children, adolescents and young adults) brain tumours (mRRÂ =Â 1.06, 95Â % CIÂ =Â 0.74-1.51), with variable degree of across-study heterogeneity (I(2)Â =Â 0Â %-62Â %). 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 [mRRÂ =Â 1.04, 95Â % CIÂ =Â 0.74-1.46; I(2)Â =Â 74Â %) meningioma, (mRRÂ =Â 0.91, 95Â % CIÂ =Â 0.70-1.18; I(2)Â =Â 59Â %), or acoustic neuroma (mRRÂ =Â 1.16; 95Â % CIÂ =Â 0.83-1.61; I(2)Â =Â 63Â %). 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 (mRRÂ =Â 0.96, 95Â % CIÂ =Â 0.87-1.07, I(2)Â =Â 47Â %), and in the analysis by increasing categories of TSS ("<5 years": mRRÂ =Â 0.97, 95Â % CIÂ =Â 0.83-1.14, I(2)Â =Â 41Â %; "5-9Â years ": mRRÂ =Â 0.96, 95Â % CIÂ =Â 0.83-1.11, I(2)Â =Â 34Â %; "10+ years": mRRÂ =Â 0.97, 95Â % CIÂ =Â 0.87-1.08, I(2)Â =Â 10Â %). 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 (49Â % tier-1 and 51Â % 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)Â =Â 77Â % and 76Â %), was explained by the summary RoB-tier. In the tier-1 study subgroup, the mRRs (95Â % CI; I(2)) in long-term (10+ years) users were 0.95 (0.85-1.05; 5.5Â %) for glioma, and 1.00 (0.78-1.29; 35Â %) 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 estimatesÂ >Â 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 (95Â % CIÂ =Â 0.86-1.05)], and the degree of heterogeneity across studies (I(2)Â =Â 3.6Â %). 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
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OTO - NOTNLM
OT - Acoustic neuroma
OT - Base stations
OT - Brain cancer
OT - Broadcast transmitters
OT - Case-control studies

OT - Childhood cancer
OT - Cohort studies
OT - Cordless phones
OT - Epidemiology
OT - Glioma
OT - Leukaemia
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COIS- 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 â€˜blindâ€™, with the client being unidentified. Susanna Lagorio
      was principal investigator (April 2019 â€“ March 2020) of the research project
      â€œBRiC 2018/06 - Systematic reviews of exposure to radiofrequency fields and
      cancerâ€□, supported by the Italian Workersâ€™ 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 RÃ¶Ã¶sliâ€™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 â€œMobile phone and radiationâ€ 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
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