Environment International 183 (2024) 108338

Contents lists available at ScienceDirect

Environment International

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

The effects of radiofrequency electromagnetic fields exposure on tinnitus, migraine and non-specific symptoms in the general and working population: A systematic review and meta-analysis on human observational studies

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ARTICLE INFO

Handling Editor: Paul Whaley

ABSTRACT

Background: Applications emitting radiofrequency electromagnetic fields (RF-EMF; 100 kHz to 300 GHz) are widely used for communication (e.g. mobile phones), in medicine (diathermy) and in industry (RF heaters).
Objectives: The objective is to systematically review the effects of longer-term or repeated local and whole human body radiofrequency electromagnetic field (RF-EMF) exposure on the occurrence of symptoms. Primary hypotheses were tinnitus, migraine and headaches in relation to RF-EMF exposure of the brain, sleep disturbances and composite symptom scores in relation to whole-body RF-EMF exposure.
Methods: Eligibility criteria: We included case-control and prospective cohort studies in the general population or workers estimating local or whole-body RF-EMF exposure for at least one week.
Information sources: We conducted a systematic literature search in various databases including Web of Science and Medline.
Risk of bias: We used the Risk of Bias (RoB) tool developed by OHAT adapted to the topic of this review.
Synthesis of results: We synthesized studies using random effects *meta*-analysis.
Results: Included studies: We included 13 papers from eight distinct cohort and one case-control studies with a total of 486,558 participants conducted exclusively in Europe. Tinnitus is addressed in three papers, migraine in one, headaches in six, sleep disturbances in five, and composite symptom scores in five papers. Only one study addressed occupational exposure.
Synthesis of results: For all five priority hypotheses, available research suggests that RF-EMF exposure below guideline values does not cause symptoms, but the evidence is very uncertain. The very low certainty evidence is due the low number of studies, possible risk of bias in some studies, inconsistencies, indirectness, and imprecision. In terms of non-priority hypotheses numerous exposure-outcome combinations were addressed in the 13 eligible papers without indication for an association related to a specific symptom or exposure source.
Discussion: Limitations of evidence: This review topic includes various challenges related to confounding control and exposure assessment. Many of these aspects are inherently present and not easy to be solved in future research. Since near-field exposure from wireless communication devices is related to lifestyle, a particular challenge is to differentiate between potential biophysical effects and other potential effects from extensive use of wireless communication devices that may compete with healthy behaviour such as sleeping or physical activity. Future research needs novel and innovative methods to differentiate between these two hypothetical mechanisms.

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https://doi.org/10.1016/j.envint.2023.108338
Received 18 May 2023; Received in revised form 1 November 2023; Accepted 19 November 2023
Available online 6 December 2023

Interpretation: This is currently the best available evidence to underpin safety of RF-EMF. There is no indication that RF-EMF below guideline values causes symptoms. However, inherent limitations of the research results in substantial uncertainty.
Other: Funding: This review was partially funded by the WHO radioprotection programme.
Registration: The protocol for this review has been registered in Prospero (reg no CRD42021239432) and published in Environment International (Röösli et al., 2021)

1. Introduction

1.1. Background

The World Health Organization (WHO) has an ongoing project to assess potential health effects of exposure to Radiofrequency electromagnetic fields (RF-EMF). To prioritize potential adverse health outcomes from exposure to these fields, WHO conducted a broad international survey amongst RF experts in 2018 (Verbeek et al., 2021). Six major topics were identified (cancer, adverse reproductive outcomes, cognitive impairment, non-specific symptoms, oxidative stress, and heat-related effects) for which WHO has commissioned systematic reviews to analyse and synthesize the available evidence. Protocols for these systematic reviews are published in a special issue of Environmental International including a protocol for the current paper focussing on tinnitus, migraine and non-specific symptoms in relation to exposure to RF-EMF investigated in human observational epidemiological studies (Röösli et al., 2021).

1.2. Description of the exposure

RF-EMF are defined as fields with frequencies from 100 kHz to 300 GHz. They are generated by a large number of equipment used in medicine (e.g. magnetic resonance imaging, diathermy, radiofrequency ablation), industry (e.g. heating and welding), domestic appliances (e.g. baby monitor, WiFi), security and navigation (e.g. radar and RFID) and especially in telecommunications (e.g. radio and TV broadcasting, mobile telephony) (Hareuveny et al., 2015; Mantiply et al., 1997; Vila et al., 2016).

A basic distinction is made between devices operating close to the body, resulting in a near-field exposure situation where RF-EMF is coupling to the body, and sources operating far away from the body, which produce a whole-body exposure from a quasi-homogeneous field (ICNIRP, 2020). The differentiation between near- and far-field depends on several factors, including the dimension of the transmitting antennas. Roughly, far-field condition is obtained if the distance between transmitter and receiver is larger than a wavelength. Typical near-field sources are mobile phones and Digital Enhanced Cordless Phone (DECT). Typical far-field sources include radio- and television masts, mobile phone base stations, DECT base stations, Wireless Local Area Network (WLAN, WiFi) access points or other people's mobile phones.

The Specific Absorption Rate (SAR in W/kg tissue weight) is the primary exposure measure of interest and if multiplied by the exposure time, it represents the absorbed RF-EMF whole-body or tissue-specific energy dose. SAR cannot easily be measured inside the human body, and therefore epidemiological studies dealing with whole-body exposure most commonly used external EMF exposure levels such as incident electrical field (V/m) or power flux density (W/m^2) to quantify exposure levels.

The output power of fixed site transmitters usually is much higher than for devices operating close to the body. However, the electric field strength decreases rapidly with distance ($\sim 1/x$), which mostly results in relatively low whole-body exposure from environmental sources in contrast to higher but highly localized exposure from devices operating close to the body (Birks et al., 2021; Cabre-Riera et al., 2020; Roser et al., 2017). In a recent dosimetry study of 1755 adults from four European countries, near-field sources contributed on average 69 % to the cumulative whole-body dose and 89 % to the brain dose (van Wel et al., 2021).

1.3. Description of the health outcomes

Some people report several types of non-specific symptoms, which they relate to exposure to RF-EMF. Due to similarities to other forms of idiopathic environmental intolerance (IEI), such as multiple chemical sensitivity, this condition is referred to as IEI attributed to EMF (IEI-EMF) (Rubin et al., 2010; WHO, 2005), although according to a systematic review of identifying criteria the most frequently used descriptive term was "hypersensitive to EMF" (Baliatsas et al., 2012b). The types of reported symptoms vary between individuals. The most commonly reported symptoms are headaches, sleep disturbances and tinnitus, among many others (Baliatsas et al., 2012a; Eltiti et al., 2007; Hillert et al., 1999; Oftedal et al., 2000; Röösli et al., 2004). Cluster analyses have not identified that specific symptom clusters are related to specific EMF exposure sources or to EMF exposure in general (Röösli et al., 2004) and the pattern of symptoms is not part of any recognized syndrome (ANSES, 2018).

Prevalence of IEI-EMF was found to vary between countries and years such as 1.5 % in Sweden (Hillert et al., 2002), 3.2 % in California (Levallois et al., 2002), 3.5 % in Austria (Schröttner and Leitgeb, 2008) and in The Netherlands (Baliatsas et al., 2015), 5 % in Switzerland (Schreier et al., 2006), about 10 % in Germany (Blettner et al., 2009), 13 % in Taiwan in 2007 (Meg Tseng et al., 2011) and 4 % in Taiwan five years later (Huang et al., 2018). In contrast, the number of people actually seeking medical help for IEI-EMF is substantially lower (Dieudonne, 2020). For instance, in a three-year environmental counselling study in the German part of Switzerland only 70 individuals per year asked for medical advice despite advertising the study to relevant stakeholder groups (Röösli et al., 2011). Some individuals with IEI-EMF report to react to EMF exposure within minutes (Baliatsas et al., 2012a; Baliatsas et al., 2012b; Röösli et al., 2004) but adverse effects may occur only after longer-term exposure or be the consequence of a delayed response. It is also conceivable that RF-EMF causes symptoms but that afflicted persons do not directly attribute them to EMF exposure. Several studies have thus addressed the association between RF-EMF exposure in the everyday environment and occurrence of symptoms in the general population without inquiring individual attribution of causal factors (Auvinen et al., 2019; Baliatsas et al., 2015; Baliatsas et al., 2016; Berg-Beckhoff et al., 2009; Frei et al., 2012; Martens et al., 2017; Mohler et al., 2012; Schoeni et al., 2017; Tettamanti et al., 2020).

1.4. Rationale for the systematic review

The World Health Organization (WHO) has an ongoing project to assess potential health effects of exposure to RF-EMF. To prioritize potential adverse health outcomes from exposure to these fields, WHO conducted a broad international survey amongst RF experts in 2018 (Verbeek et al., 2021). Six major topics were identified (cancer, adverse reproductive outcomes, cognitive impairment, non-specific symptoms, oxidative stress, and heat-related effects) for which WHO has commissioned systematic reviews to analyse and synthesize the available evidence.

In the survey amongst RF experts the topic "electromagnetic hypersensitivity" ranked as being of high relevance for considering

systematic reviews on the grounds of public concerns and the notions of IEI-EMF individuals. Possible immediate effects of RF-EMF exposure on reporting of symptoms have been evaluated in various experimental studies using a blinded, randomized design in a laboratory to apply well-controlled exposure conditions (Schmiedchen et al., 2019). These studies on acute effects are reviewed in a separate paper (Bosch-Capblanch et al., 2022).

From a practical and ethical point of view, experimental designs cannot be used to study the potential harmful effects of longer-term exposure on delayed or chronic outcomes beyond a few days or weeks. For such effects, observational epidemiological studies are most suitable. In such studies, the occurrence of symptoms in individuals is evaluated in relation to their RF-EMF exposure over a longer time period, irrespective of the individuals' attribution of symptoms to a specific cause or EMF source, respectively. A number of observational studies have evaluated such longer-term effects, but systematic reviews are scarce and mostly outdated, except for a recent systematic review on tinnitus and mobile phone use (Kacprzyk et al., 2021).

2. Objectives

The main objective of this systematic review of human observational studies is to provide a comprehensive analysis of the following PECO (Population, Exposure, Comparator, and Outcome) question:

To assess the effects of continuous or repeated local and whole human body RF-EMF exposure per-unit increase (see chapter 4) of one week or longer (E) on the occurrence of tinnitus, migraine and non-specific symptoms (O), in the general population or workers (P) and to assess whether there is an exposure–response relationship between these outcomes and RF-EMF exposure levels (C).

Thereby, we focus on the following five primary hypotheses of RF-EMF effects in the general population:

1. Tinnitus in relation to RF-EMF exposure of the brain.
2. Migraine in relation to RF-EMF exposure of the brain.
3. Headaches in relation to RF-EMF exposure of the brain.
4. Sleep disturbances in relation to whole-body RF-EMF from far-field exposure sources.
5. Composite symptom scores in relation to whole-body RF-EMF exposure.

The first three hypotheses were set, based on the ground that from a biological perspective exposures of the head for these outcomes are most relevant. Exposure from the head originates mostly from mobile and cordless (wireless) phone calls (van Wel et al., 2021). During sleep, in the absence of own device use, whole body exposure is mostly influenced by far-field sources (hypothesis 4). For composite scores, exposure to different body areas may be relevant and thus whole-body RF-EMF exposure is expected to be most critical (hypothesis 5). Note that other combinations of the PECO are also evaluated in an explorative manner according to availability of eligible studies fulfilling the inclusion criteria in terms of outcomes and exposure types.

3. Methods

The protocol of this review has been registered at Prospero (No: CRD42021239432) and an extensive protocol has been published (Röösli et al., 2021).

3.1. Eligibility criteria

3.1.1. Types of populations

We considered studies including participants of the general population (regardless of any restrictions, e.g. in terms of age or gender) as well as studies focusing on workers or persons who attribute their symptoms to EMF exposure referred to as IEI-EMF (Rubin et al., 2010; WHO, 2005), or as electromagnetic hypersensitive (EHS) individuals (Baliatsas et al., 2012b).

3.1.2. Types of exposure

3.1.2.1. Inclusion criteria. Given the public health concerns, it is of interest whether repeated high-level local exposures in the range of 1–2 W/kg under near field conditions (e.g. from a mobile phone) have different effects on health than continuous low-level whole-body exposure under far field conditions.

Studies were included if they fulfilled all three criteria:

1. The study explicitly declares to evaluate the effects of RF-EMF exposure.
2. Exposure frequency reported or implied from the source description to be within RF-EMF range as outlined in section 1.2.
3. Exposure level measured or calculated (dosimetry) by any of the following characteristics:

i) For local exposure:
   a. The primary choice of exposure for near field sources is time-weighted average or cumulative SAR value of the brain as this represents the RF-EMF dose.
   b. Because SAR measure is rarely available, we also used other exposure surrogates such as
      i. self-reported or operator-recorded cumulative number of wireless phone calls,
      ii. cumulative duration of calls or time since start of regular wireless phone use,
      iii. or any other well-specified RF-EMF emitting source, for instance in occupational settings.

ii) For whole-body exposure we included studies that used:
   a. Time-weighted average or cumulative whole-body SAR value representing daily RF-EMF dose,
   b. whole-body exposure expressed as measured or modelled incident electric field strength (V/m), power density (W/m^2) or another metric that is convertible to these exposure metrics,
   c. surrogate exposure: studies based on geocoded distance to large broadcast or TV transmitters were included.

iii) For occupational sources of exposure:
   a. Time-weighted average or cumulative local or whole-body SAR,
   b. duration of use for local exposure or measured electric field strength or power density for whole-body exposure,
   c. reported as job exposure matrix (JEM) or implied JEM based on occupational titles such as radio or TV transmitter operators, radar workers, TETRA users (e.g. police), RF sealers/welders, dielectric heater operator, short and microwave diathermy operators, and citizens band radio users.

3.1.2.2. Exclusion criteria. We excluded studies regarding self-estimated exposure to RF-EMF in general without referring to specific sources such as mobile or cordless phones. A correlation between objective and concurrently collected self-reported data has been demonstrated for mobile phone use (Aydin et al., 2011; Mireku et al., 2018; Schüz and Johansen, 2007; Toledano et al., 2018) and is thus acceptable.

Distance metrics remain challenging as to their interpretation regarding exposure levels. Self-estimated distance to an antennae (Baliatsas et al., 2015) or perceived exposure (Martens et al. 2018) were found not to be correlated to RF-EMF exposure. Geocoded distance to mobile phone base stations had a low correlation with personal RF-EMF exposure (Frei et al., 2010), whereas geocoded distance to radio and TV transmitter was found to be moderate (Spearman: −0.46) (Hauri et al., 2014). Thus, only the latter are eligible. Self-reported distance to any antenna is not a valid exposure proxy for symptom reporting and may

pertain more to perceived exposure rather than to true exposure levels.

In principle, RF-EMF can interfere with implants such as pacemakers or cochlear implants (Sorri et al., 2006) and thus indirectly affect well-being. This interaction is well understood and avoided by proper electromagnetic compatibility testing of implants and is thus not considered in this review.

3.1.3. Types of comparators

We included studies that have compared at least two different levels of exposure intensity or duration or compare an exposed group to a non-exposed group in the two domains of exposure: exposure of the brain and/or whole-body exposure.

3.1.4. Type of outcome measures

A symptom is a physical or functional alteration that is consciously perceived and experienced as painful, incapacitating, or worrying by a given person. By definition, symptoms can only be assessed through self-reports (or self-reported to a health professional). Symptoms can be non-specific or they can be the consequences of an underlying disease and thus be medically explained. Some outcomes of this review like tinnitus and migraine are well-established diseases, and gold standard for diagnosis is an anamnesis through a health professional based on key criteria and additional examinations. For other symptoms such as headaches or sleep disturbances, it is usually not obvious without in-depth medical examinations whether there exists a medical explanation or whether they are non-specific. To the best of our knowledge, no study in this field of research has attempted to differentiate between medically explained and unexplained symptoms. Thus, these symptoms cannot be read as clinical signs of well-known diseases, but must be interpreted on their own. For this reason we label them as non-specific. Various standardized scales exist to measure non-specific symptoms. Further, in the research setting, composite symptom scales have been applied, such as the von Zerssen score (von Zerssen, 1976) or a scale targeting key symptoms mentioned in the context of IEI-EMF (Eltiti et al., 2007). We included all symptoms, no matter how serious they are. RF-EMF exposure may act as a trigger for such symptoms, or increase their severity or frequency of occurrence.

We included any non-specific symptoms as reported by participants of the study and independently whether symptoms were attributed to RF-EMF exposure or not. Actually, attribution of symptoms to a specific source is typically not addressed in epidemiological studies eligible for this review. We considered tinnitus, migraine, headache, sleep quality measures, and composite symptom scores as the main outcomes of this review. Other non-specific symptoms (e.g. fatigue, exhaustion, nervousness) were included as well.

3.1.5. Types of studies

3.1.5.1. Inclusion criteria. Only observational studies with a longitudinal design are eligible for inclusion. These are cohort and case-control studies. A cohort study is defined as a study where there are two or more groups exposed to different levels of RF-EMF or no exposure that are followed over time to assess the occurrence of the outcome in question.

Case-control studies depend on identifying cases (so need a diagnostic procedure or otherwise clear case definition). For symptoms with a high prevalence and that vary over time, the case-control study design is not a preferred choice and such studies are not included. If the outcome occurs rarely and is persistent, which in the scope of this review is the case for tinnitus and migraine, case-control studies are an appropriate design. Therefore, for tinnitus and migraine, we included cohort and case-control studies. For all other outcomes, we only consider cohort studies.

3.1.5.2. Exclusion criteria. We excluded:

- cross-sectional studies because there is a lack of temporality in these studies, which makes it difficult to establish causal effects and confounding,
- studies that did not consider any confounder in their analysis,
- studies of patients receiving medical treatment with RF-EMF emitting devices,
- panel studies that study acute and short-term effects only. A panel study is a special case of a cohort study that typically includes more frequent follow-up measurements (e.g. using a symptom diary) and thus considers mostly effects occurring within a relatively short time of a few hours to a few days. For such acute effects, observational studies are suboptimal as they cannot control blinding of exposure and thus may be vulnerable to well established nocebo effects (Brascher et al., 2017; Schmiedchen et al., 2019; Van den Bergh et al., 2017).

A special case are field trials. Similar to observational studies, such studies are done in the everyday environment of study participants. However, if they follow an experimental approach, e.g. by turning on and off a mobile phone base station (Danker-Hopfe et al., 2010), such studies qualify for a review on human experimental studies (Bosch-Capblanch et al., 2022).

3.1.5.3. Years considered. Any year of publication that is recorded in the scientific databases was considered.

3.1.5.4. Publication language. We included studies written in any language. Articles in languages other than the ones spoken by the reviewers (English, German, Spanish, Catalan, French and Portuguese) were discussed with collaborators in the network of authors' institutions proficient in those languages. However, considering that title and abstract of non-English articles published in peer-reviewed journals are in English, only English terms were used to search the publication databases.

3.1.5.5. Publication types. We included studies reported as peer-reviewed publications.

3.1.6. Types of effect measures

For dichotomous outcomes, we used the relative risk (RR) as the measure of the effect. We also considered Odds Ratios (OR) and Hazard Ratios (HR). For continuous outcomes, we used mean differences as the effect size. Since the same symptoms were measured with different scales, we used standardized mean differences as the effect size. Effect measures of analyses based on exposure categories are expressed per unit increase of corresponding exposure measures, based on a *meta*-regression described in chapter 3.6.

3.2. Information sources and search strategy

Eligible studies were identified by literature searches in the databases Medline, Web of Science, PsycInfo, Cochrane Library, Epistemonikos and Embase. Each database strategy is tailored to the characteristics of each platform together with encompassing its controlled language (index) features, where appropriate, and using a combination of title, abstract and author keywords. To obtain a vigilance balance between sensitivity and specificity the search strategy combined the three elements i) different terms describing RF-EMF exposure, ii) different terms for relevant study designs, iii) different terms for the outcome of interest. The search strategy was published in Appendix A of Röösli et al. (2021). We have also consulted the EMF-Portal, a dedicated database of the scientific literature on the health effects of exposure to electromagnetic fields (https://www.emf-portal.org/en) and the search was supplemented by checks of the reference lists of previous systematic reviews. The software Endnote was used to manage the bibliography.

The search was conducted on 22 April 2021 and repeated on 7 April 2022. On 13 February 2023, we have checked the EMF-Portal and the BERENIS literature database for any eligible study that may have appeared since the last literature search, which was not the case.

3.3. Paper selection

First, the relevance of the identified papers was checked based on titles and abstracts, conducted by two reviewers (SD, HJ). The full texts of the remaining papers were independently assessed by the same reviewers for inclusion. Studies excluded in this step are listed in supplementary file 1 including reasons for exclusion. Cross-sectional studies that fulfilled the inclusion criteria except the longitudinal design criteria are hallmarked in this list, as well as all included articles.

In all steps, any disagreements between the two reviewers were resolved by discussion with MR acting as a third reviewer, if no consensus was reached.

3.4. Data extraction

For each included study, bibliographic information including description of the study methods and the study sample and study results were extracted based on a predefined form (see Appendix B in Röösli et al. (2021)). Two reviewers worked independently to extract quantitative and other key data. Possible disagreements between reviewers were resolved by discussion including a third reviewer.

In terms of exposure–response data, all information that was provided in a paper was extracted for further syntheses of the results. If several analyses were done for the same outcome, we have extracted effect estimates labelled as primary results by the author or if this information was missing, the most comprehensive confounding adjustment.

If there was more than one article per study, we used the original paper (i.e. the first publication), while findings reported in subsequent articles based on the same individual data were only extracted if relevant or if comprising a more comprehensive sample or addressing a type of eligible population, exposure or outcome not addressed in the original paper.

If data necessary for the analysis were missing from the articles, we asked the corresponding author for additional information.

3.5. Risk of bias assessment

For evaluating the internal validity, we conducted a risk-of-bias assessment using the "Risk of Bias Rating Tool for Human and Animal Studies" developed by the NTP Office of Health Assessment and Translation (OHAT) (NTP, 2015; Rooney et al., 2014), which was modified for the specific exposure and outcomes considered in this review and originally published as Appendix C in the protocol of this systematic review (Röösli et al., (2021). Adaptions were informed by topic knowledge of the review team, discussions with other WHO review teams, ROBINS-I (Sterne et al., 2016) and COSTER (Whaley et al., 2020) (see supplementary file 2). We only considered domains relevant for cohort and case-control studies as suggested by OHAT, which left us with the following eight questions: Selection/participation bias, confounding, attrition/exclusion bias, exposure assessment errors, outcome assessment errors, selective reporting, and other biases, which includes the two sub-questions related appropriate statistical methods, and reverse causality. Reverse causality may occur if IEI-EMF individuals take measures to reduce their RF-EMF exposure when developing symptoms (Röösli et al., 2010). If not adequately considered in the longitudinal design, this would downward bias the effect estimates towards a false protective effect of RF-EMF, because change of symptoms score would be negatively correlated with exposure status.

Risk of bias was evaluated independently by SD and HJ for each paper separately and for each type of outcome, each type of exposure, each type of exposure assessment method and type of population. In terms of inconsistency a consensus was reached among SD, HJ and MR. The answer format definitely low risk of bias (++), probably low risk of bias (+), probably high risk of bias (- or not reported "NR"), or definitely high risk of bias (–) was used. For each study result that was considered to be at probably or definitively high risk of bias, the reviewer also judged the direction of the bias (or combined biases) for the corresponding effect estimate. This includes the following four answer formats: false positive risk (i.e. overestimation of harmful effect), bias towards absence of an association (underestimation of harmful effect), false protective finding (i.e. favours beneficial effect) and unpredictable.

As suggested by the OHAT handbook, we apply a 3-Tier system for synthesizing study findings when risks of bias vary across studies or across different analyses from the same study. A Tier 1 study result must be rated as "definitely low" or "probably low" risk of bias for all three key domains (i.e. confounding, exposure and outcome assessment) AND have no other critical bias identified. For near-field exposure studies Tier 1 studies need to have applied any kind of analytic strategy to differentiate between device usage and RF-EMF exposure as outlined in chapter 3.5. A Tier 3 study result must be rated as "definitely high" or "probably high" risk of bias for key domains. A Tier 2 study result meets neither the criteria for 1st or 3rd Tiers (NTP, 2019).

3.6. Synthesis methods

For the five primary symptoms, we performed a random-effects *meta*-analysis if at least two study results were available, which were comparable in terms of exposure source. Only one eligible study on migraine was available and thus no *meta*-analysis was conducted for this symptom. Some cohort studies used several analyses approaches. In this case priority was given to cohort analysis compared to other approaches such as change analyses. For all *meta*-analyses, we used random-effect methods weighted with inverse variance weighting.

For tinnitus, a *meta*-analysis of RR was conducted whereas for headache, sleep and symptom score SMD (standardized mean difference) was *meta*-analyzed. For studies reporting score changes, SMD was obtained by standardizing the effect estimates with the standard deviation. For studies that reported odds ratio or relative risks, SMD was obtained following the method proposed by Chinn (2000). To do so, we assigned a single exposure value to each exposure category.

Step 1 *meta*-analysis: Many studies used categorized exposure values for their analysis. Thus, if studies have not reported linear-exposure response trends, we calculated first within each study for each outcome and exposure combination the linear exposure–response trends per unit increase of exposure following the methods of Orsini et al. (2006). Indicator for RF-EMF exposure of the brain is wireless phone use and unit of exposure was set to 100 min call duration per week. Indicator for whole-body exposure was measured or modelled electric field strength and unit of exposure for analysis was 1 V/m. For closed categories, the geometric mean of the upper and lower bounds of the exposure categories was used; for the (uppermost and lowest) open-ended categories, we assigned an estimated median value as proposed by (Il'yasova et al., 2005).

Step 2 *meta*-analysis: Subsequently, the exposure–response trends from each study were *meta*-analysed across studies together with the estimated confidence intervals using random effects and inverse variance weighting. With this approach, we assumed a linear exposure–response relationship. Given the limited number of studies, we refrained from exploring non-linear relationships. However, in sensitivity analyses we conducted *meta*-analyses of the original categorical estimates to search for indications of non-linearity, which was not the case.

In each *meta*-analysis, we did not combine results from completely or partially overlapping populations. We conducted separate analyses for exposure surrogates related to the brain (operator recorded mobile phone use, self-reported mobile and cordless phone use) and for

exposure surrogates representing whole-body exposure (total personal exposure, fixed site transmitters or mobile phone base stations).

Subgroup analyses and assessment of heterogeneity

We evaluated heterogeneity of the findings according to the PECO elements and quantified the statistical heterogeneity between studies with the tau-square measure and calculated 80 % prediction intervals (IntHout et al., 2016), where the number of studies for various subgroups permits. A prediction interval is defined as the interval within which the effect size of a new study would fall if this study was selected at random from the same population of the studies already included in the *meta*-analysis. We intended to group results according to the types of populations (adults, children, adolescents, IEI-EMF, or workers) but too few estimates were obtained for the same outcome-exposure combination from different populations. Similarly, intended separate analyses for various types of far-field exposure varying in terms of frequency and modulation were not feasible for the thin study base. In the synthesis, we focussed on consistency across various subtypes of exposures (mobile vs. cordless phone or various whole-body exposure surrogates), different exposure assessment methods (self-reported vs. database/operator or measurements vs. modelled). For other aspects of heterogeneity mentioned in the protocol (data analysis approaches, type of exposure–response analysis) the small number of studies prevented from such checks.

We identified a few studies that addressed both, self-reported and objectively calculated far field exposure. Previous research has shown negligible correlation between these two measures (Frei et al., 2010; Martens et al., 2017). Thus, for these studies we summarized the findings separately for both types of exposure measure. We hypothesized that absence of link with objective exposure while observing a link with self-reported exposure could be indicative for bias, although not a proof for absence of true association.

3.7. Certainty assessment

The certainty rating for each set of PECO considered sufficiently similar to be combined was done according to the procedure of the OHAT handbook (NTP 2019). Initial certainty rating started with "moderate" (score 3), since some extent of bias cannot be excluded by design in observational research of RF-EMF effects on symptoms. The following five factors were used for downgrading the quality of the body of evidence from observational studies by one or two levels for each set of PECO (details see Appendix D in Röösli et al. (2021)).

1. Risk of bias across studies for each outcome (not likely, serious, very serious): No downgrading was conducted if most information is from Tier 1 studies with low risk of bias for all key domains. Downgrading by one unit (serious risk of bias) is done if Tier 2 and Tier 3 studies had a notable influence on the result of the meta-analysis. Downgrading by two units (very serious risk of bias) is done if the proportion of information from Tier 3 studies at high risk of bias for all key domains is sufficient to affect the interpretation of results.

2. Inconsistency of results between studies (none, serious): To make a judgement about the amount of heterogeneity that would be a reason for concern and a reason to downgrade if it cannot be explained by study characteristics, we considered heterogeneity test and the PI. If significant heterogeneity across studies were found, it was evaluated whether this could be explained by methodological factors. If not, evidence was downgraded if heterogeneity cannot be explained. The certainty of the body of evidence is downgraded with one level. If the 80 % PI overlaps with the null value (RR = 1), it means that studies show both beneficial and harmful effects of exposure and the certainty of the body of evidence is downgraded with one level. Also, if the 80 % PI for a specific *meta*-analysis of RRs is considerably wider than the confidence interval (for example double the size), then there is reason for concern about heterogeneity.

We did also downgrade if results for comparable exposure sources (e.g. mobile vs. cordless phones or mobile phone base stations vs. other far-field exposure sources) are not consistent, when taking into account the level of exposure.

If only two or less exposure–response results are available for a specific outcome and type of exposure, certainty of evidence was downgraded by one item.

3. Indirectness of evidence in the studies (none, serious): If there had been considerable differences between the characteristics of those exposed to electromagnetic fields in the real world and the characteristics of those evaluated in the studies, we had downgraded the quality of the evidence by one level.

According to the OHAT handbook, indirectness refers to the population under study. However, in the framework of this review, we also consider indirectness in terms of the exposure metric. It has to be emphasized that effects on symptoms from mobile phones and other electronic communication media can be unrelated to EMF exposure. This includes sleep disturbance from incoming calls and text messages during night (Foerster et al., 2019) or psychological and somatic arousal through media content (Cain and Gradisar, 2010). Further, it has been postulated that electronic media use may result in less physical activity (Edelson et al., 2016), higher night time eating (Cha et al., 2018), higher BMI (Fatima and Mamun, 2015), or media addiction (Roser et al., 2016; Samaha and Hawi, 2016). Since it is virtually impossible to monitor emitted RF-EMF exposure from devices continuously in a population based study, there exists an indirectness between what the reviewed studies attempt to address (RF-EMF) and what is actually addressed (a mixture of RF-EMF and co-exposures from media use). Some studies have developed further specific strategies to deal with this type of confounding and to differentiate between associations related to usage and associations related to RF-EMF dose. Mobile phones and to some extent also other devices have an efficient power control (Gati et al., 2009; Persson et al., 2012; Popovic et al., 2019). Depending on the network settings, signal quality and the type of usage, output power of mobile phones can vary with a factor of one million (Mazloum et al., 2019). Some studies have used such information and considered the average output power of mobile phone calls in the GSM and UMTS network, to achieve an exposure surrogate, which better represents EMF dose than just usage (Auvinen et al., 2019). Other studies used negative exposure control variables such as number of text messages, which is virtually not correlated to RF-EMF exposure, to compare associations of different usage proxies (Schoeni et al., 2017). Such information is considered in the assessment of indirectness.

4. Imprecision (none, serious): We had downgraded the evidence if the upper limit of the confidence interval of a relative risk is > 2 in a non-significant effect estimate. For a significant effect estimate, downgrading is done if the upper limit of the confidence estimate divided by the point estimate is > 1.5. An analogue rule was applied to the SMD and prediction interval. Imprecision was defined if the upper limit of the confidence interval was found to be > 1 SD for a non-significant effect estimate or if the upper limit of SMD divided by SMD was > 1.5 for a significant effect estimate.

5. Publication bias detected in a body of evidence (none, serious): Given the small number of studies we could not evaluate publication bias and did not consider this item for downgrading.

The following three factors were used for upgrading the certainty in the quality of evidence of observational studies (Appendix D in Röösli et al. (2021)):

1. Large magnitude of effect (small, large, very large): We rated a pooled significant relative risk of > 2 or < 0.5 as of high magnitude and > 5 or < 0.2 as of very high magnitude and would upgrade the certainty of the evidence quality by one or two units, respectively. For score changes, we consider an effect > 0.5*SMD as of high magnitude (very high magnitude 2*SMD).

2. Exposure Response gradient (no, yes): Exposure-response gradient is considered to be consistent, if a test for trends across exposure categories is found to be significant (step 1 *meta*-analysis). Depending on the original data, number of categories should be between four and six when

performing a test for trend. When evaluating the exposure–response gradient we may also consider other aspects of exposure than intensity such as exposure duration.

3. Residual confounding (towards null, not likely): If all plausible confounding would shift the risk estimates towards the null and still there would be a significant association, we upgraded the certainty of the body of evidence by one level. The effect of residual confounding was also indirectly assessed in studies on local exposure that attempted to differentiate between usage and RF-EMF dose as described above in chapter 3.5. If the conclusions from these studies support RF-EMF as an explanation for observed associations, this would increase our certainty in an observed association by one unit (opposite procedure as explained above when downgrading due to risk of bias).

4. Results

4.1. Study selection

Fig. 1 depicts the study selection process. In the literature search 4458 papers were identified, complemented with additional 21 papers identified from other sources (supplementary file 1). After removing duplicates and screening title and abstracts 256 papers remained for full-text evaluation. Thereof 243 were excluded for various reasons, which are shown in the table "excl after full text check" of supplementary file 1. The most common reasons were that EMF exposure was not noted as an aim of the study (n = 139), outcome did not fulfil inclusion criteria (n = 23) and cross-sectional study design (n = 23). The papers which were solely excluded because of the cross-sectional design are shown in table "cross-sectional as excl crit" in supplementary file 1. The final completeness check of newly published papers on 13th February 2023 did not reveal any eligible paper but 3 cross-sectional studies on the topic, which also ticked other exclusion criteria.

4.2. Study characteristics

Table 1 gives an overview about the included studies. In total, 13 papers have fulfilled the inclusion criteria. One study was conducted in workers (Elliott et al., 2019), one paper describes an analysis restricted to IEI-EMF persons (Röösli et al., 2010), one paper an analysis restricted to adult cases of multiple sclerosis (Harbo Poulsen et al., 2012) and the remaining papers dealt with adults (n = 8) or adolescents (n = 2) from the general population. All papers except one case-control study on tinnitus (Hutter et al., 2010) are based on a prospective cohort design, where the incidence of symptoms was evaluated in a population sample that was free of the corresponding symptom at baseline. The sample size of the cohorts ranges from 425 adolescents (Schoeni et al., 2016) to 420,095 adults in a nationwide cohort study from Denmark (Schüz et al., 2009). Tinnitus is addressed in three papers, migraine in one paper,

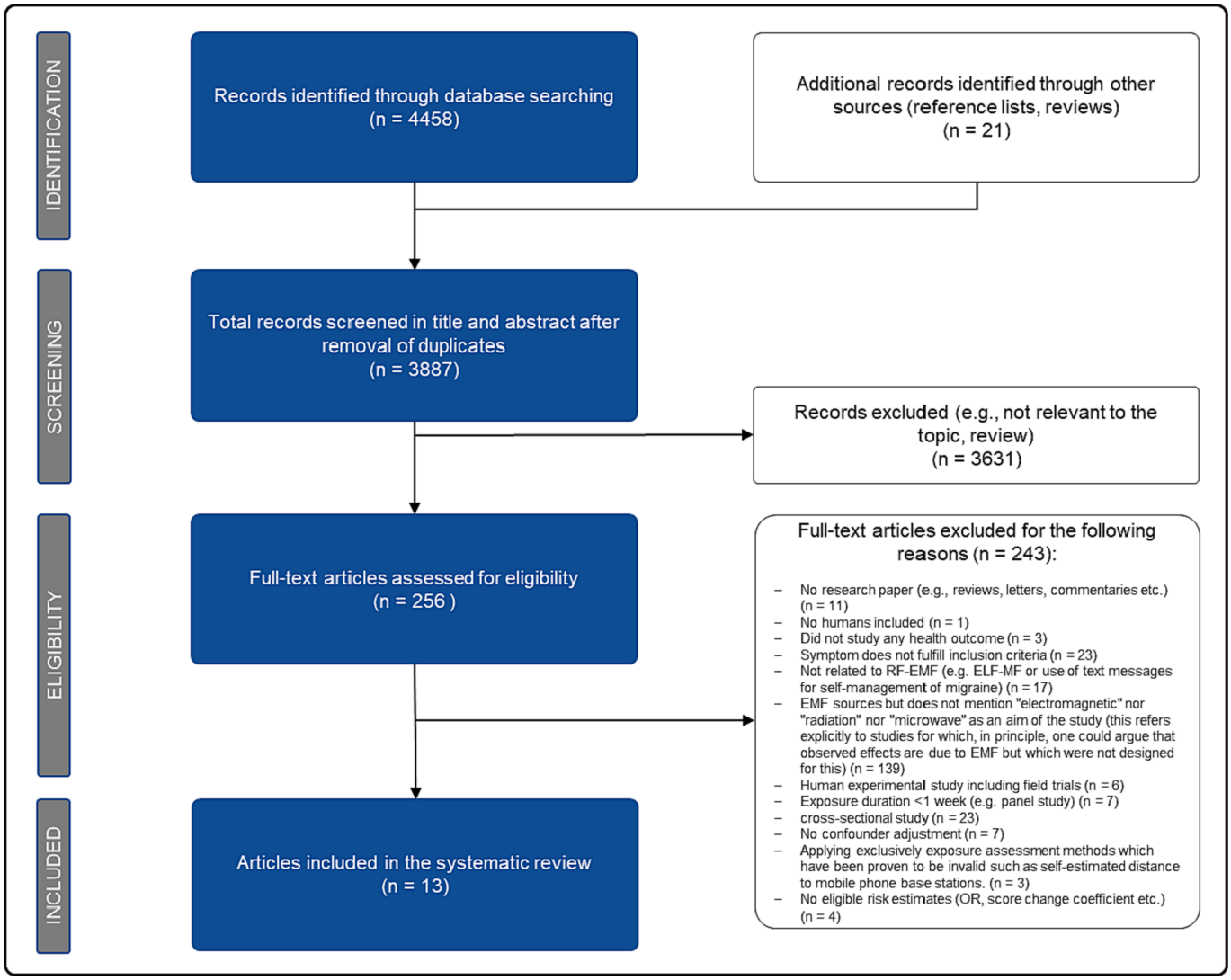

Fig. 1. Flow diagram of literature search, eligibility and inclusion process. Adapted from Moher et al.(2009).

Table 1
Description of included papers.

Study			Participants		Exposure					Comparator	Outcomes
Reference	**Design**	**Country/ Time period (baseline to follow-up)**	**Human: Adults/ Patients/ Children Animal: Species mean age (range), gender proportions**	**Number (participation rate)**	**Localisation**	**Frequency bands**	**Source type**	**Exposure unit /assessment method**	**Level (mean (range) or categories), Duration**	**Either lowest category or increase per exposure No Expo/1 Unit Lower Exposure**	**Type (*primary outcomes in italics*)**
Auvinen, 2019	Cohort	Sweden, Finland (2008/10 to 2013/14)	Adults (general population) Mean age: 44.8 years Female ratio: 55.5 %	Baseline: 40,472 (9.9 %) Follow-up: 24,259 (59.9 %)	Head	GSM 900 & 1800 MHz, UMTS 900 & 2100 MHz	Mobile phone	Average weekly call time (minutes), operator-recorded	50-74th percentile (78–175 min per week) 75-89th percentile (175–276 min per week) 90-100th percentile (>276 min per week)	Lowest 50 % (<78 min per week)	*Headache, tinnitus,* hearing loss
Baliatsas, 2016	Cohort	Netherlands (2004 to 2011)	Adults (general population, and IEI-EMF) Mean age: 57.4 years Female ratio: 51.6 %	Baseline: 1965 (33.1 %) Follow-up: 1069 (54.4 %)	Whole-body	GSM 900 & 1800 MHz, UMTS	Mobile phone base stations	Average residential exposure (V/m), modelled	T0: 0.109 V/m (SD: 0.23) T1: 0.121 V/m (SD: 0.22)	Increase per V/m	Total NSS EMF-relevant NSS Fatigue/tiredness Digestive&metabolic/ nutritional Ear symptoms Cardiovascular symptoms Muscuskeletal symptoms Neurological symptoms Psychological symptoms Respiratory symptoms Skin symptoms Number of NSS Ear symptoms
Elliott, 2019	Cohort	United Kingdom (2008/15 to 2018)	Adults (workers) Mean age: 40.5 years Female ratio: 35.3 %	32,102 (60.4 %)	Head	TETRA 380–395 MHz	Mobile phones	Average monthly call duration from use of personal radios in the year prior to enrolment, calculated based on self-reports and objective network operator data	Median personal radio use (year prior to enrolment): 29.7 min per month (interquartile range 7.5, 64.7) among users	Users vs. non-users, doubling of minutes of use among users	Sickness absence Infectious diseases Mental and behavioural Nervous system *Headache* Respiratory system Flu and cold Digestive system Musculoskeletal system Genitourinary system Symptoms, signs, abnormal laboratory findings Abdominal pain Nausea and vomiting Injury, poisoning, other consequences of external causes

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Table 1 (*continued*)

Study			Participants		Exposure					Comparator	Outcomes
Reference	**Design**	**Country/ Time period (baseline to follow-up)**	**Human: Adults/ Patients/ Children Animal: Species mean age (range), gender proportions**	**Number (participation rate)**	**Localisation**	**Frequency bands**	**Source type**	**Exposure unit /assessment method**	**Level (mean (range) or categories), Duration**	**Either lowest category or increase per exposure No Expo/1 Unit Lower Exposure**	**Type (*primary outcomes in italics*)**
											Factors influencing health status and contact with health services Miscellaneous
Frei, 2012	Cohort	Switzerland (2008 to 2009)	Adults (general population) Mean age: 47 years Female ratio: 60.4 %	Baseline: 1375 (36.5 %) Follow-up: 1122 (81.6 %)	Head, whole-body	GSM/UMTS: 900, 1800, 2100 MHz DECT: 1800 MHz WLAN: 2.45 GHz Various broadcast: 88–862 MHz (from Bürgi et al. 2010)	Far-field: - total personal exposure - fixed site transmitters; Near-field: - mobile phone, - cordless phone	Self-reported exposure, Operator data (mobile phone use) Modelled total personal exposure	Cohort analysis: 50th-90th percentile, >90th percentile Change analysis: decrease, no change, increase (participants with 20 % largest decrease and increase compared to remaining 60 % with smaller or no change of exposure between baseline and follow-up)	Cohort analysis: <50th percentile (RF-EMF: 0.12 mW/m^2) Change analysis: increase	*Somatic complaints (von Zerssen)* *Headache (HIT-6)* *Tinnitus*
Harbo Poulsen, 2012	Cohort	Denmark (1987/95 to 2004)	Adult cases of multiple sclerosis Mean age: unclear Female ratio: 67 %	5058 cases of multiple sclerosis (100 %, selected from population registry)	Head	GSM 900/ 1800 (based on timing)	Mobile phone	Holding a private mobile phone subscription (based on network operator records)	Range: <1 to > 10 years of subscription	Non-subscribers	Vertigo Fatigue Cerebellar symptoms Diplopia Optic neuritis Pyramidal dysfunction Sensory symptoms Sphincter control Other/Unstated symptoms
Hutter, 2010	Case-control	Austria (recruitment: 2003/04)	Adults (general population) Mean age: 42.5 years Female ratio: 46 %	100 cases (96 %), 100 controls (93 %)	Head	GSM 900/ 1800 (based on timing)	Mobile phone	Self-reported mobile phone use (based on WHO Interphone questionnaire)	Ever use <10 min/day ≥10 min/day <160 h cumulative use ≥160 h cumulative use <4000 calls ≥4000 calls <1y of mobile phone	Never use	*Chronic tinnitus lasting for longer than 3 months, diagnosed at the Ear-Nose-Throat Department of the Medical University of Vienna, Austria*

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Table 1 (*continued*)

Study			Participants		Exposure					Comparator	Outcomes
Reference	**Design**	**Country/ Time period (baseline to follow-up)**	**Human: Adults/ Patients/ Children Animal: Species mean age (range), gender proportions**	**Number (participation rate)**	**Localisation**	**Frequency bands**	**Source type**	**Exposure unit /assessment method**	**Level (mean (range) or categories), Duration**	**Either lowest category or increase per exposure No Expo/1 Unit Lower Exposure**	**Type (*primary outcomes in italics*)**
									use 1–3 years ≥4 years		
Martens, 2017	Cohort	Netherlands (2010/11 to 2013/14)	Adults (general population) Mean age: 50.2 years Female ratio: 56 %	Baseline (T0): 3992 (26.9 % of a full cohort invited to participate) Follow-up (T1): 2228 (55.8 %) Follow-up (T2): 1740 (43.6 %)	Whole-body	GSM 900 & 1800 MHz, UMTS	Mobile phone base stations	Residential far-field exposure (mW/m^2), modelled using a 3-dimensional geospatial model (NISMap) Perceived exposure (scale of 0–6; 0 = not at all; 6 = very much)	Top decile (cut-off: 0.050 mW/m^2) vs remainder	Cut-off: 0.050 mW/m^2	*Symptom score (self-reported) (Four-Dimensional Symptom Questionnaire (4DSQ-S) consisting of 16 nonspecific somatic symptoms)* *Sleep Index score (self-reported) (Sleep Scale of the Medical Outcomes Study (MOS))*
Mohler, 2012	Cohort	Switzerland (2008 to 2009)	Adults (general population) Mean age: 47 years Female ratio: 61 %	Baseline: 1375 (36.5 %) Follow-up: 1125 (81.8 %) Eligible for analysis (no shift work): 955	Head, whole-body	GSM/UMTS: 900, 1800, 2100 MHz DECT: 1800 MHz WLAN: 2.45 GHz Various broadcast: 88–862 MHz (from Bürgi et al. 2010)	Far-field: total personal exposure, fixed site transmitters, night-time EMF; Near-field: mobile phone, cordless phone	Self-reported exposure (mobile & cordless phone use), Operator data (mobile phone use), modelled far-field environmental EMF	Cohort analysis: 50th-90th percentile, >90th percentile Change analysis: decrease, no change, increase (participants with 20 % largest decrease and increase compared to remaining 60 % with smaller or no change of exposure between baseline and follow-up)	Cohort analysis: <50th percentile (RF-EMF: 0.11 mW/m^2) Change analysis: increase	Daytime sleepiness (seven items of the Epworth Sleepiness Scale) *Sleep disturbances (sleep disturbance score, four standardized questions from the Swiss Health Survey 2007)*
Röösli, 2010	Cohort	Switzerland (2008 to 2009)	Adults with IEI-EMF Mean age: 45.4 years Female ratio: 65 %	130 individuals who participated at baseline and follow-up (see Frei et al., 2012)	Head, whole-body	GSM/UMTS: 900, 1800, 2100 MHz DECT: 1800 MHz WLAN: 2.45 GHz Various broadcast: 88–862 MHz (from Bürgi	Far-field: total personal exposure, fixed site transmitters, night-time EMF; Near-field: mobile phone, cordless phone	Self-reported exposure (mobile & cordless phone use), Operator data (mobile phone use), modelled far-field environmental EMF	Cohort analysis: 50th-90th percentile, >90th percentile Change analysis: decrease, no change, increase (participants with 20 % largest decrease and increase compared to remaining 60 %	Cohort analysis ≤ median: RF-EMF: 0.11 mW/m^2 (estimated) Change analysis: increase	*Somatic complaints (von Zerssen)* *Headache (HIT-6 score)** *Daytime sleepiness (seven items of Epworth Sleepiness Scale)** *Sleep disturbances (sleep disturbance score, four standardized questions*

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Table 1 (*continued*)

Study			Participants		Exposure					Comparator	Outcomes
Reference	**Design**	**Country/ Time period (baseline to follow-up)**	**Human: Adults/ Patients/ Children Animal: Species mean age (range), gender proportions**	**Number (participation rate)**	**Localisation**	**Frequency bands**	**Source type**	**Exposure unit /assessment method**	**Level (mean (range) or categories), Duration**	**Either lowest category or increase per exposure** **No Expo/1 Unit Lower Exposure**	**Type (*primary outcomes in italics*)**
						et al. 2010)			with smaller or no change of exposure between baseline and follow-up)		*from the Swiss Health Survey 2007)**
Schoeni, 2016	Cohort	Switzerland (2012/2013 to 2013/2014)	Adolescents Mean age: 15 years Female ratio: 59.8 %	Baseline: 439 (36.8 %) Follow-up: 425 (96.8 %)	Whole-body	GSM/UMTS: 900, 1800, 2100 MHz DECT: 1800 MHz WLAN: 2.45 GHz Various broadcast: 88–862 MHz (from Roser et al. 2015**)	Exposure from fixed site transmitters (broadcasting and mobile phone base stations)	Modelled (geospatial propagation model), at home and school	Cohort analyses: exposure below median, 50th to 75th percentile, top 25th percentile Change analyses: study participants with an increase in exposure (>0 μW/m^2) were compared to the remaining study participants who did not experience an exposure increase between baseline and follow-up (reference)	Cohort analyses: ≤median Change analysis: no increase	*Headache (HIT-6 score)* *Tiredness*, lack of energy, lack of concentration and rapid exhaustibility (four-point Likert scale) *Physical well-being (Kidscreen-52 questionnaire)*
Schoeni, 2017	Cohort	Switzerland (2012/2013 to 2013/2014)	Adolescents Mean age: 15 years Female ratio: 59.8 %	Baseline: 439 (36.8 %) Follow-up: 425 (96.8 %)	Whole-body and brain		Wireless communication devices (calls, text, and data transmission)	Wireless communication device use assessed by questionnaires 53 % of participants consented to provide operator recorded mobile phone use data Modelled whole-body and brain dose	Interquartile increase in exposure Whole sample: Duration gaming [min/d], self-reported Number of texts sent [x/d], self-reported Duration data traffic on mobile phone [min/d], self-reported Duration cordless phone calls [min/d], self-reported Duration mobile phone calls [min/d], self-reported Brain dose [mJ/kg/d] Whole-body dose	Increase per IQR of use in min/day or per IQR of dose in mJ/kg/d	*Headache (HIT-6 score)* *Tiredness*, lack of energy, lack of concentration and rapid exhaustibility (four-point Likert scale) *Physical well-being (Kidscreen-52 questionnaire)*

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Table 1 (*continued*)

Study			Participants		Exposure					Comparator	Outcomes
Reference	**Design**	**Country/ Time period (baseline to follow-up)**	**Human: Adults/ Patients/ Children Animal: Species mean age (range), gender proportions**	**Number (participation rate)**	**Localisation**	**Frequency bands**	**Source type**	**Exposure unit /assessment method**	**Level (mean (range) or categories), Duration**	**Either lowest category or increase per exposure No Expo/1 Unit Lower Exposure**	**Type (*primary outcomes in italics*)**
									[mJ/kg/d] Sample with operator data: Volume data traffic on mobile phone [MB/d], operator recorded Duration mobile phone calls [min/d], operator recorded Number of SMS sent [x/d], operator recorded Brain dose [mJ/kg/d] Whole-body dose [mJ/kg/d]		
Schüz, 2009	Cohort	Denmark 1982/1995 to 2003	Adult mobile phone subscribers (general population) Mean age: ≥39.1 years Female ratio: 15 %	Baseline: 420,095 (58.1 % of all subscriptions)	Head	N/A	Mobile phone	Mobile phone subscriptions in Denmark during the period 1982–1995, without corporate subscriptions	Latency (years since first subscription to a mobile phone): 1 1–4 5–9 ≥10	No subscription	*Migraine* Vertigo
Tettamanti, 2020	Cohort	Sweden, Finland (2008/10 to 2013/14)	Adults (general population) Mean age: 44.8 years Female ratio: 55 %	Baseline: 40,472 (9.9 %) Follow-up: 24,169 (59.7 %)	Head	GSM 900 & 1800 MHz, UMTS 900 & 2100 MHz	Mobile phone	Average weekly call time (minutes), operator-recorded	50th-74th percentile (72–163 min per week) 75th-89th percentile (164–257 min per week) ≥90th percentile (≥258 min)	<50th percentile (<72 min per week)	*Sleep disturbance* Sleep adequacy Daytime somnolence Sleep latency Insomnia (Medical Outcome Study (MOS) sleep questionnaire)

headaches in six papers, sleep disturbances including fatigue in five papers, and composite symptom scores in five papers. In six papers exclusively RF-EMF exposure of the brain is described (e.g. from mobile phone use), in three papers exclusively whole-body exposure (e.g. from fixed site transmitters) and in four papers both types of exposure are addressed.

Supplementary file 3 ("Effect estimates use in *meta*-analysis") provides a table of all effect estimates of the four primary outcomes that have been used for the *meta*-analysis. It contains the original study results (effect size and 95 % confidence interval [CI]) as originally published (relative risks, odds ratio, score changes), and the derived SMD's including CI (headaches, sleep disturbances, composite scores) or relative risks (tinnitus) as well as the linear exposure response coefficients from the step 1 *meta*-analysis.

4.3. Risk of bias in studies

Fig. 2 shows a heat map of the risk of bias analyses for all primary hypotheses used in the *meta*-analysis per each type of outcome, type of exposure, type of exposure assessment method and type of population. Supplementary file 4 shows the reasoning of our judgement for all eight risk of bias domains of all studies including those not considered for the *meta*-analysis. About half of the assessed outcome-exposure-population combinations had low probability for risk of bias and belonged to the Tier 1 studies. In terms of the key domain "outcome assessment" probably high risk of bias was attributed to studies on tinnitus that did not have access to clinical diagnosis. In terms of exposure assessment, all studies addressing exclusively far-field exposure were considered of probable high risk of bias as they did not demonstrate that brain or whole body exposure contribution from far-field was substantially

Outcome	Exposure	Exposure assessment method	Population	Reference	Selection/participation bias	Confounding*	Attrition/exclusion bias	Exposure assessment errors*	Outcome assessment errors*	Selective reporting	Appropriate statistical methods	Reverse causality	Quality category (1st tier / 2nd tier / 3rd tier)
Headache	Cordless phone	Self-reported	general, adult	Frei et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Cordless phone	Self-reported	general, adolescents	Schoeni et al. 2017	+	+	+	+	+	+	+	+	Tier 1
	Fixed-site transmitters	Modelled	general, adult	Frei et al. 2012	+	+	+	–	+	+	+	+	Tier 3
	Fixed-site transmitters	Modelled	general, adolescents	Schoeni et al. 2016	+	+	+	–	+	+	+	+	Tier 3
	Mobile phone	Operator-recorded	general, adult	Auvinen et al. 2019	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Operator-recorded	general, adult	Frei et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Operator-recorded	general, adolescents	Schoeni et al. 2017	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Self-reported	general, adult	Frei et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Self-reported	general, adolescents	Schoeni et al. 2017	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Self-reported & operator-recorded	workers	Elliott et al. 2019	+	–	+	+	++	+	+	+	Tier 3
	Mobile phone data traffic	Operator-recorded	general, adolescents	Schoeni et al. 2017	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone data traffic	Self-reported	general, adolescents	Schoeni et al. 2017	+	+	+	–	+	+	+	+	Tier 3
	Total personal exposure	Modelled	general, adult	Frei et al. 2012	+	+	+	–	+	+	+	+	Tier 3
Migraine	Mobile phone subscription	Operator-recorded	general, adult	Schüz et al. 2009	++	–	+	–	++	+	+	–	Tier 3
Tinnitus	Cordless phone	Self-reported	general, adult	Frei et al. 2012	+	+	+	+	–	+	+	+	Tier 3
	Fixed-site transmitters	Modelled	general, adult	Frei et al. 2012	+	+	+	–	–	+	+	+	Tier 3
	Mobile phone	Operator-recorded	general, adult	Auvinen et al. 2019	+	+	+	+	–	+	+	+	Tier 3
	Mobile phone	Operator-recorded	general, adult	Frei et al. 2012	+	+	+	+	–	+	+	+	Tier 3
	Mobile phone	Self-reported	general, adult	Frei et al. 2012	+	+	+	+	–	+	+	+	Tier 3
	Mobile phone	Self-reported	general, adult	Hutter et al. 2010	+	–	+	–	++	+	+	–	Tier 3
	Total personal exposure	Modelled	general, adult	Frei et al. 2012	+	+	+	–	–	+	+	+	Tier 3
Sleep disturbances	Base station	Modelled	general, adolescents	Schoeni et al. 2016	+	+	+	–	+	+	+	+	Tier 3
	Base station	Modelled	general, adult	Martens et al. 2017	+	+	+	–	+	+	+	+	Tier 3
	Broadcast	Modelled	general, adolescents	Schoeni et al. 2016	+	+	+	–	+	+	+	+	Tier 3
	Cordless phone	Self-reported	general, adult	Mohler et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Fixed-site transmitters	Modelled	general, adult	Mohler et al. 2012	+	+	+	–	+	+	+	+	Tier 3
	Fixed-site transmitters	Modelled	general, adolescents	Schoeni et al. 2016	+	+	+	–	+	+	+	+	Tier 3
	Mobile phone	Operator-recorded	general, adult	Mohler et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Operator-recorded	general, adult	Tettamanti et al. 2020	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Self-reported	general, adult	Mohler et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Total far field (night time)	Modelled	general, adult	Mohler et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Total far field	Modelled	general, adult	Mohler et al. 2012	+	+	+	–	+	+	+	+	Tier 3
Composite symptom scores	Base station	Modelled	general, adolescents	Schoeni et al. 2016	+	+	+	–	+	+	+	+	Tier 3
	Base station	Modelled	general, adult	Martens et al. 2017	+	+	+	–	+	+	+	+	Tier 3
	Base station	Modelled	general, adult	Baliatsas et al. 2017	+	+	+	–	++	+	+	+	Tier 3
	Broadcast	Modelled	general, adolescents	Schoeni et al. 2016	+	+	+	–	+	+	+	+	Tier 3
	Cordless phone	Self-reported	general, adolescents	Schoeni et al. 2017	+	+	+	+	+	+	+	+	Tier 1
	Cordless phone	Self-reported	general, adult	Frei et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Fixed-site transmitters	Modelled	general, adolescents	Schoeni et al. 2016	+	+	+	–	+	+	+	+	Tier 3
	Fixed-site transmitters	Modelled	general, adult	Frei et al. 2012	+	+	+	–	+	+	+	+	Tier 3
	Mobile phone	Operator-recorded	general, adolescents	Schoeni et al. 2017	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Operator-recorded	general, adult	Frei et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Self-reported	general, adolescents	Schoeni et al. 2017	+	+	+	+	+	+	+	+	Tier 1
	Mobile phone	Self-reported	general, adult	Frei et al. 2012	+	+	+	+	+	+	+	+	Tier 1
	Total personal exposure	Modelled	general, adult	Frei et al. 2012	+	+	+	–	+	+	+	+	Tier 3

Fig. 2. Risk of bias for all primary hypotheses used in the *meta*-analysis per each type of outcome, type of exposure, type of exposure assessment method and type of population. * Three key domains of the risk of bias. "++": Definitely low risk of bias, "+": Probably low risk of bias, "-": Probably high risk of bias, "–": Definitely high risk of bias.

higher than from devices operating close to body. For three studies confounding adjustment was found to be critical.

4.4. Results for the PECOs

A. Review of priority PECO 1: Tinnitus in relation to RF-EMF exposure of the brain

Fig. 3 depicts the *meta*-analysis for tinnitus in relation to exposure of the brain using the best available information from each study. Three studies were available: a prospective cohort study of 24,259 adults with four years of follow-up (Auvinen et al., 2019), a prospective cohort study of 1122 adults with one year of follow-up (Frei et al., 2012) and a case-control study with 100 cases and 100 controls (Hutter et al., 2010). Pooled relative risk was 1.43 (95 %-CI: 0.94 to 2.18) per 100 min wireless phone call time per week. The 80 % prediction interval was very wide (0.42 to 4.91) and there was substantial heterogeneity between the studies ($p < 0.001$) (Table 2). In Figure S1 of Supplementary file 5, pooled estimates stratified by exposure source are shown, which show some variability although not statistically significant ($p = 0.13$). Risk of bias, inconsistency, indirectness and imprecision resulted in downgrading of the evidence quality (Supplementary file 6, Table S1). Thus, certainty in the observed absence of association was *very low* (Table 3).

B. Review of priority PECO 2: Migraine in relation to RF-EMF exposure of the brain

Only one large cohort study addressed the risk for migraine in relation to mobile phone subscription (Schüz et al., 2009). Relative risk was found to be 1.2 (95 %-CI: 1.1 to 1.3) for mobile phone subscribers compared to non-subscribers. Substantial risk of bias, indirectness and inconsistency resulted in downgrading of the evidence quality (Supplementary file 6, Table S2). Thus, certainty in the observed association was *very low* (Table 3).

C. Review of priority PECO 3: Headaches in relation to RF-EMF exposure of the brain

Fig. 4 depicts the *meta*-analysis for headaches in relation to exposure of the brain using the best available information from each study. Four studies were available: a prospective cohort study of 24,259 adults with four years of follow-up (Auvinen et al., 2019), a prospective cohort study of 32,102 workers adults with a maximum follow-up of ten years addressing occupational mobile phone use (Elliott et al., 2019), a prospective cohort study of 1122 adults with one year of follow-up (Frei et al., 2012) and a prospective cohort study of 425 adolescents with one year of follow-up (Schoeni et al., 2017). Pooled change in SMD was −0.64 (95 %-CI: −2.38 to 1.10) per 100 min wireless phone call time per week and the 80 % prediction interval ranged from −3.91 to 2.64 (Table 4). There was substantial heterogeneity between the studies ($p < 0.001$) (Table 4) but not between type of exposure ($p = 0.37$) although large differences in precision (Supplementary file 5, Figure S2). Inconsistency, indirectness and imprecision resulted in downgrading of the evidence quality (Supplementary file 6, Table S3). Thus, certainty in the observed absence of association was *very low* (Table 3).

D. Review of priority PECO 4: sleep disturbances in relation to whole body RF-EMF exposure from far-field exposure sources.

Fig. 5 depicts the *meta*-analysis for sleep disturbances in relation to far-field exposure sources using the best available information from each study. Three studies were available: a prospective cohort study of 3992 adults with up to three years of follow-up (Martens et al., 2017), a prospective cohort study of 955 adults with one year of follow-up (Mohler et al., 2012) and a prospective cohort study of 425 adolescents with one year of follow-up (Schoeni et al., 2016). Pooled change in SMD was 1.51 (95 %-CI: −2.00 to 5.03) per 1 V/m of exposure. There was substantial heterogeneity between the studies ($p < 0.001$) (Table 5). In Figure S3 of Supplementary file 5 a pooled estimate for RF-EMF from fixed site transmitter is presented (whereas in Fig. 5 estimated nighttime personal exposure was taken from Mohler et al. (2012)), which changed the pooled estimate only slightly. Risk of bias, inconsistency and imprecision resulted in downgrading of the evidence quality (Supplementary 6, Table S4). Thus, certainty in the observed absence of association was *very low* (Table 3).

E. Review of priority PECO 5: Composite symptom scores in relation to whole-body RF-EMF exposure.

Fig. 6 depicts the *meta*-analysis for non-specific symptoms in relation to whole-body RF-EMF exposure using the best available information from each study. Four studies were available: a prospective cohort study of 1965 adults with seven years of follow-up (Baliatsas et al., 2016), a prospective cohort study of 1122 adults with one year of follow-up (Frei et al., 2012), a prospective cohort study of 3992 adults with up to three years of follow-up (Martens et al., 2017), and a prospective cohort study of 425 adolescents with one year of follow-up (Schoeni et al., 2016). Pooled change in SMD was 1.13 (95 %-CI: −0.94 to 3.20) per 1 V/m of exposure and the 80 % prediction interval ranged from −3.32 to 5.58 (Table 5). There was substantial heterogeneity between the studies ($p < 0.001$) (Table 5). In Figure S4 of Supplementary file 5 a pooled estimate for RF-EMF from fixed site transmitter is presented (whereas in Fig. 6 estimated personal whole-body exposure was taken from Frei et al. (2012)), which changed the pooled estimate only slightly. Risk of bias, inconsistency and imprecision resulted in downgrading of the evidence quality (Supplementary file 6, Table S5). Thus, certainty in the observed absence of association was *very low* (Table 3).

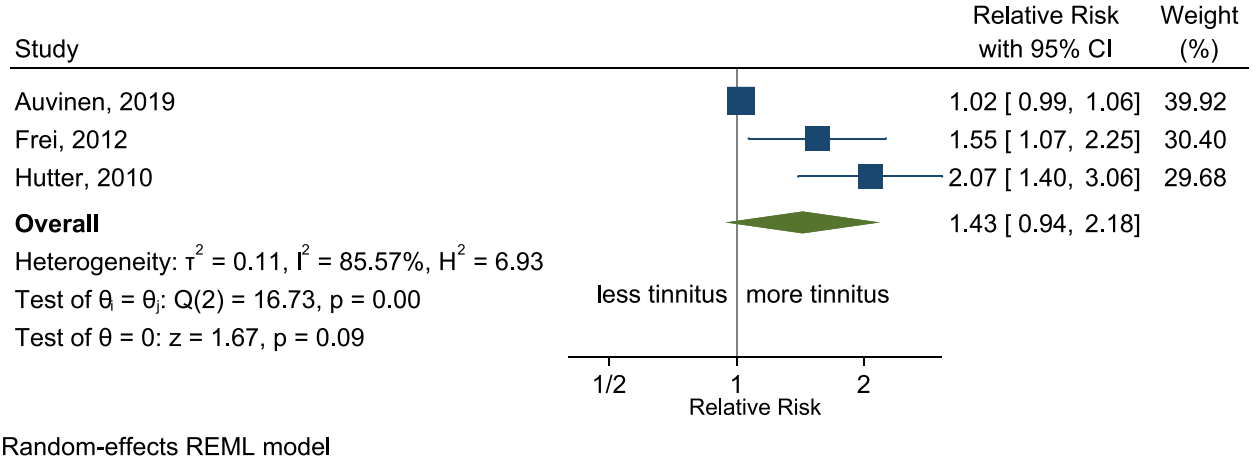

Fig. 3. Meta-analysis of PECO 1: Tinnitus in relation to exposure of the brain using best available evidence from each study*: relative risk per 100 min wireless phone usage per week. *Best estimate from each study selected with the following priority: *operator recorded mobile phone use, self-reported mobile phone use, self-reported cordless phone.

Table 2
Overview on the pooled evidence for tinnitus and migraine in relation to exposure of the brain: relative risk (RR) per 100 min wireless phone usage per week.

Outcome	Type of exposure	No of studies	I^2 [%]	T^2	p for heterogeneity	RR (95 % CI)	80 %-Prediction interval	Risk of bias[$]
Tinnitus	Operator recorded mobile phone use	2	78.6	0.068	0.031	1.21 (0.81 to 1.77)	not defined	Tier 3
	Self-reported mobile phone use	2	92.7	0.267	<0.001	1.38 (0.66 to 2.99)	not defined	Tier 3
	Self-reported cordless phone use	1	–	–	–	0.36 (0.12 to 1.14)	not defined	Tier 3
	Any brain exposure source*	3	85.6	0.115	<0.001	1.43 (0.94 to 2.18)	0.42 to 4.91	Tier 3
Migraine	Operator recorded MP subscription	1	–		–	1.2 (1.1 to 1.3)	not defined	Tier 3

*Best estimate from each study selected with the following priority: operator recorded mobile phone use, self-reported mobile phone use, self-reported cordless phone use.
[$] Refers to the lowest Tier that contributed to this estimate.

F. Review of other PECOs.

Numerous other exposure response associations have been published in the 13 eligible studies. In terms of priority outcomes, associations with secondary exposure measures are shown in supplementary file 5 (see also Table 4 and 5). Figure S5 (Supplementary file 5) shows that SMD for headaches changes by −0.17 (95 %-CI: −0.30 to −0.03) per 1 V/m increase in whole-body exposure based on two studies. Figure S6 shows that SMD for sleep disturbances changes by 2.01 (95 %-CI: −2.95 to 6.97) per 100 min weekly wireless phone usage increase in brain exposure based on three studies. Figure S7 (Supplementary file 5) shows that SMD for composite symptom scores changes by 0.01 (95 %-CI: −0.07 to 0.09) per 100 min weekly wireless phone usage increase in brain exposure based on three studies. Only one study addressed tinnitus in relation to far-field sources, which does not indicate an association (Frei et al., 2012). No study addressed migraine in relation to far-field RF-EMF exposure.

Numerous non-priority outcomes were addressed in the 13 eligible studies. However, the number of comparable studies in terms of exposure source and type of outcome was not sufficient to conduct a *meta*-analysis to obtain summary estimates. A heat map was thus created to visualize findings of all these non-priority symptoms that have been addressed in the 13 papers (Supplementary file 7). Most exposure–response associations were not significant. The significant estimates go in both directions, increase and decrease of symptom severity.

G. Comparison of objectively collected with self-estimated far-field exposure:

Two studies have compared associations of symptom scores, headaches or sleep disturbance score for modelled far-field and self-perceived exposure (Fig. 7). Whereas these symptoms were not associated with modelled far-field exposure, association with self-perceived exposure was highly significant. Correspondingly difference between the estimates of the two groups of studies was also highly significant ($p < 0.001$).

5. Discussion

Summary of the evidence and interpretation of the results

Numerous combinations of outcomes and types of RF-EMF exposure were addressed in 13 eligible papers in this review. For all five priority hypotheses, we found very low certainty evidence that RF-EMF exposure is associated with the various primary outcomes. The low certainty evidence is due to the low number of studies, possible risk of bias in some studies, inconsistencies, indirectness, and imprecision. In terms of non-priority hypotheses numerous exposure-outcome combinations were addressed in the 13 eligible papers without indication for an association related to a specific symptom or exposure source.

5.1. Limitations in the evidence

There are substantial limitations in the available research on this topic. We could include only one to four papers per each of the five primary outcomes in the *meta*-analysis. We envisaged that an analysis of consistency across various study characteristics such as types of exposure, exposure assessment methods or population characteristics is informative for drawing causal inference and identify bias. However, with this small study sample, corresponding evaluation was limited and affected by single study results.

Indirectness of the exposure surrogate is of concern for observational studies on near field exposure. In these studies, mobile phone use, considered as an RF-EMF exposure surrogate for the brain, is accompanied with many potential risk and protective factors for the outcomes of interest. It is virtually impossible to elucidate how these different aspects of mobile phone use interact with each other and what is the resulting effect. Conceptually, we considered this aspect in this review as indirectness but it may also be conceptualized as latent variables related to wireless communication devices use that act as confounders by indication or are causing reverse causality. The latter may even be relevant for longitudinal studies given the relative short follow-up period in most available studies. Given that mostly lack of associations was observed, there may be concern that risk from RF-EMF is masked by positive confounding, a kind of healthy communicator effect analogous to healthy worker effects. One strategy to address this limitation is to compare similar usage patterns which involves different amounts of exposure. In two papers (Auvinen et al., 2019; Tettamanti et al., 2020), a comparison between Global System for Mobile Communications (GSM) and Universal Mobile Telecommunications Service (UMTS) mobile phone call duration was made, since the latter involves substantially less output power on average (Gati et al., 2009; Persson et al., 2012; Popovic et al., 2019). These two papers did not find indications that level of RF-EMF exposure is critical for development of symptoms. Another study used negative exposure control variables such as number of text messages, which is virtually not correlated to RF-EMF exposure, to compare associations of different usage proxies (Schoeni et al., 2017). Also with this approach no indication was found that wireless phone use involving substantial RF-EMF exposure is more critical than usage that involves little exposure.

Studies related to far-field exposure are less vulnerable to confounding from lifestyle factors. However, in these studies the exposure of interest may be marginal compared to total absorbed RF-EMF exposure. Typically, near-field sources are the main contributors to whole-body exposure (van Wel et al., 2021) and the strength of the mobile phone base station signal is inversely correlated with the output power of mobile phones (Mazloum et al., 2019). Thus, it is conceivable that in a collective of moderate to heavy mobile phone users, level of exposure from mobile phone base station is not well correlated or even negatively correlated with whole-body exposure. None of the available studies have

Table 3
Overview of the evidence rating for the five primary hypotheses (for details see Suppementary file 5).

Outcome	Type of exposure	Start rating	Factors decreasing confidence				Factors increasing confidence			Overall certainty of evidence
			Risk of bias	Inconsi-stency	Indirectness	Imprecision	Publication bias	Strength of association	Exposure-response gradient	Residual confounding	
Tinnitus	Brain	3 (moderate)	−2	−1	−1	−1	0	0	0	0	<0 (very low)
Migraine	Brain	3 (moderate)	−2	−1	−1	0	0	0	0	0	<0 (very low)
Headache	Brain	3 (moderate)	0	−1	−1	−1	0	0	0	0	0 (very low)
Sleep disturbances	Whole-body	3 (moderate)	−1	−1	0	−1	0	0	0	0	0 (very low)
Composite symptoms	Whole-body	3 (moderate)	−1	−1	0	−1	0	0	0	0	0 (very low)

considered near-field exposure in their analysis, which gave them a probable high risk of bias rating in the exposure assessment domain.

Another limitation is the fact that the outcomes of this review are primarily self-reported symptoms, including any bodily sensation or a feeling or change in well-being, which is obtained by a written questionnaire or personal interview. Several individual and socio-cultural factors may affect such self-reporting. However, some variation in self-reporting does not imply a bias, if not related to exposure status. A particular challenge in this field is that both, outcome and exposure (e.g. duration of mobile phone use), may be self-reported. By definition, participants are thus aware of their exposure status and this may affect their outcome reporting. To evaluate this aspect, we have conducted a sensitivity analysis of two papers, which considered both, self-estimated EMF exposure and modelled far-field exposure (Frei et al., 2012; Martens et al., 2017). In these studies (Fig. 7), we found substantial evidence that people who are convinced to be highly exposed also report more symptoms, which is, at least partly, compatible to the cognitive or attributive explanatory hypotheses for symptom development in the context of RF-EMF exposure (Dieudonne, 2020). The cognitive hypothesis assumes that occurrence of symptoms results from the belief in EMF harmfulness, promoting nocebo responses to perceived EMF exposure. According to the attributive hypothesis individuals suffering from pre-existing conditions search for an explanation and discover EMF as a potential cause resulting in being convinced to be exposed to EMF. For these reasons we have not considered effect estimates of studies that used self-estimated exposure to RF-EMF in general for certainty assessment. In principle, this aspect could also be critical for studies relying on self-reported RF-EMF surrogates like wireless phone use. However, we did not find strong indications for systematic differences between self-reported and operator recorded mobile phone use (e.g. Figure S1 and S2), as long as self-reported usage is prospectively collected as done in the included cohort studies.

We specified in the protocol to separately evaluate studies on IEI-EMF to evaluate potential particularly vulnerable subgroups of the population. Although it is appealing to evaluate whether vulnerable subgroups exist, there is also an inherent challenge involved with self-attribution of symptoms to EMF. It is well established that IEI-EMF individuals take measures to reduce their RF-EMF exposure when developing symptoms (Röösli et al., 2010). In principle, this could produce a bias towards a false protective effect of RF-EMF. Two studies have conducted separate subgroup analyses of IEI-EMF individuals. These studies were not similar enough to be pooled in a *meta*-analysis. Whereas (Röösli et al., 2010) did not find major differences compared to the general population, (Baliatsas et al., 2016) found for a minority of all analyzed symptoms associations for IEI-EMF individuals but not for the general sample. However, in the latter study IEI-EMF status was obtained at follow-up, which results in a high risk for recall bias. Since IEI-EMF was found to be a relatively transient condition (Röösli et al., 2010; Traini et al., 2023), it is well conceivable that this findings can be explained by the cognitive or attributive hypotheses.

High heterogeneity may reflect real differences (e.g. in terms of exposure or population vulnerability) or results from methodological bias. Heterogeneity was evaluated in different manners. First, we considered heterogeneity of studies that addressed the same type of exposure. For all four primary hypotheses, where more than one study was available, significant heterogeneity was observed. Second we compared heterogeneity between groups of studies that addressed similar exposure surrogates. For instance one would expect similar results for self-reported cordless and mobile phone use as well as operator recorded mobile phone use given the similarity in the exposure conditions. For tinnitus and headache pooled effect estimates for these three types of exposure were noticeably different, although not reaching statistical significance given the low numbers of studies per type of exposure (Figure S1 and S2). Given the similar exposure situations in all the European countries and the relatively similar populations, methodological explanations such as confounding or differences in exposure

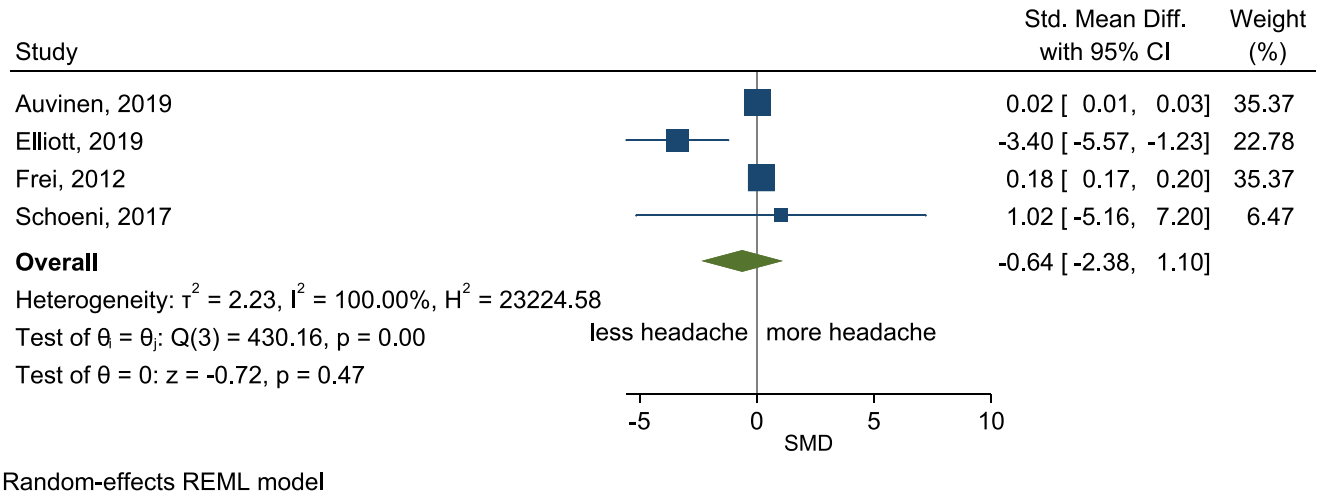

Fig. 4. Meta-analysis of PECO 3: headache in relation to exposure of the brain using best available evidence from each study*: SMD per 100 min wireless phone usage per week. *Best estimate from each study selected with the following priority: *operator recorded mobile phone use, self-reported mobile phone use, self-reported cordless phone use.

Table 4
Overview on the pooled evidence for headaches, sleep disturbances and symptom score in relation to exposure of the brain: standardized mean difference (SMD) per 100 min wireless phone usage per week.

Outcome	Type of exposure	No of studies	I^2 [%]	T^2	p for heterogeneity	SMD (95 % CI)	80 %-Prediction interval	Risk of bias[$]
Headaches	Operator recorded mobile phone use	3	99.5	0.013	<0.001	0.10 (-0.06 to 0.26)	−0.33 to 0.54	Tier 1
	Self-reported mobile phone use	3	94.7	3.447	0.003	−0.71 (-2.93 to 1.52)	−7.40 to 5.99	Tier 3
	Self-reported cordless phone use	2	0.0	0.000	0.346	−0.00 (-0.01 to 0.00)	not defined	Tier 1
	Any brain exposure source*	4	100.0	2.226	<0.001	−0.64 (-2.38 to 1.10)	−3.91 to 2.64	Tier 3
Sleep disturbances[&]	Operator recorded mobile phone use	3	100.0	15.720	0.042	2.01 (-2.95 to 6.97)	−12.47 to 16.48	Tier 1
	Self-reported mobile phone use	3	0.0	0.000	0.561	−0.005 (-0.010 to 0.001)	−0.014 to 0.004	Tier 1
	Self-reported cordless phone use	2	12.7	0.118	0.285	0.19 (-0.47 to 0.84)	not defined	Tier 1
	Any brain exposure source*	3	100.0	15.720	0.042	2.01 (2.95 to 6.97)	−12.47 to 16.48	Tier 1
Symptom score	Operator recorded mobile phone use	2	0.0	0.000	0.344	0.007 (-0.073 to 0.086)	not defined	Tier 1
	Self-reported mobile phone use	2	46.4	0.075	0.172	0.09 (-0.38 to 0.56)	not defined	Tier 1
	Self-reported cordless phone use	2	0.0	0.000	0.684	0.001 (-0.011 to 0.013)	not defined	Tier 1
	Any brain exposure source*	2	0.0	0.000	0.344	0.007 (-0.073 to 0.086)	not defined	Tier 1

* Best estimate from each study selected with the following priority: operator recorded MP, self-reported MP, self-reported cordless phone.
[&] Includes tiredness from Schoeni as a proxy for sleep problems.
[$] Refers to the lowest Tier that contributed to this estimate.

assessment methods seem more plausible than different vulnerabilities group.

All cohort studies estimated RF-EMF exposure at baseline for a follow-up period of one to several years. Still little is known about how stable individual RF-EMF exposure is over time. A recent study in an adolescent cohort found that within two years Pearson correlation for brain dose was 0.31 and for whole-body dose 0.31 (Eeftens et al., 2023). Such a weak correlation may result in substantial exposure misclassification, which is expected to bias effect estimates to null if there were an association. To avoid this type of bias, a few studies have thus additionally considered both, exposure at baseline and follow-up to estimate cumulative exposure and partly also conducted change analyses, i.e. whether symptoms changed according to change of exposure between baseline and follow-up. There were no noticeable differences for such analyses. Note, in principle such approaches could be affected by reverse causality, meaning that occurrence of symptoms may result in changes of RF-EMF exposure (e.g. by changing use of wireless communication devices).

A limitation for the certainty assessment is the low number of available studies for specific outcome-exposure pairs, which often varied in terms of the outcome scales or data analysis. We had to convert relative risks to SMD and derive exposure–response associations from categorical analysis using *meta*-regression. Thereby, we assumed linear exposure response association in the absence of any other evidence for the exposure–response curve.

Various biological mechanisms in the low RF-EMF exposure range below guideline values are controversially discussed (Barnes and Greenebaum, 2020). It is beyond the scope of this paper to

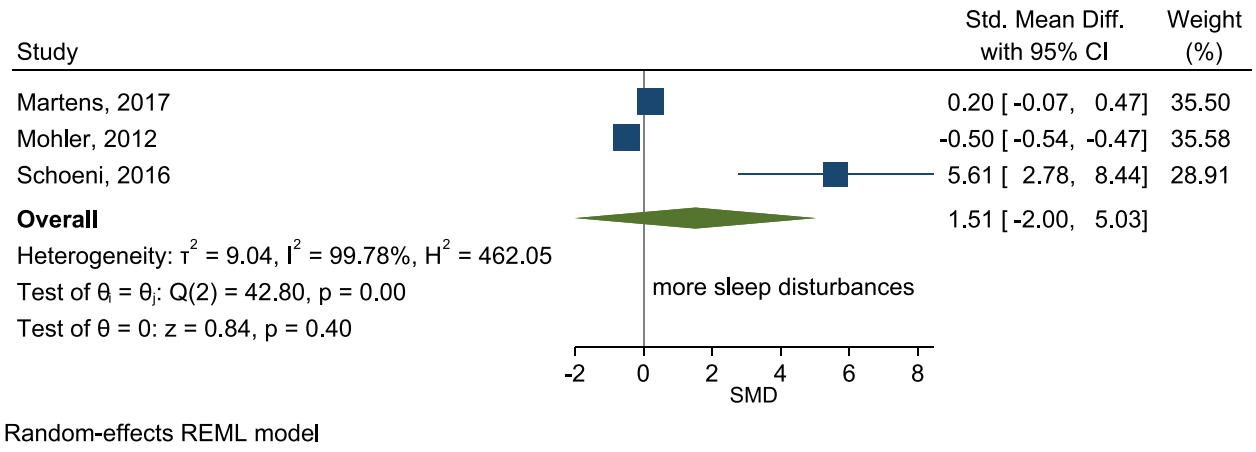

Fig. 5. Meta-analysis of PECO 4: sleep disturbances in relation to whole-body exposure using best available evidence from each study*: SMD per 1 V/m. *Best estimate from each study selected with the following priority: *all sources during night-time, all types fixed site transmitters, mobile phone base stations.

Table 5
Overview on the pooled evidence for headaches, sleep disturbances and symptom score in relation to whole-body exposure: standardized mean difference (SMD) per 1 V/m.

Outcome	Type of exposure	No of studies	I^2 [%]	T^2	p for heterogeneity	SMD (95 % CI)	80 %-Prediction interval	Risk of bias[$]
Headache	Total personal exposure	1	–		–	−0.16 (-1.06 to 0.73)	not defined	Tier 3
	Fixed site transmitters	2	47.6	1.188	0.167	0.20 (-1.68 to 2.07)	not defined	Tier 3
	Any whole-body exposure source*	2	0.0	0.000	0.408	−0.17 (-0.304 to −0.028)	not defined	Tier 3
Sleep disturbances[&]	Total personal exposure night	1	–		–	−0.50 (-0.71 to −0.29)		Tier 1
	Fixed site transmitters[&]	3	99.7	8.290	<0.001	1.61 (-1.76 to 4.99)	−8.71 to 11.94	Tier 3
	pooled*	3	99.8	9.040	<0.001	1.51 (-2.00 to 5.03)	−9.26 to 12.29	Tier 3
Symptom score	Total personal exposure	1	–		–	0.02 (-2.15 to 2.18)	not defined	Tier 3
	Fixed site transmitters[&&]	4	99.9	4.504	<0.001	1.11 (-0.97 to 3.19)	−3.37 to 5.59	Tier 3
	pooled*	4	99.7	4.445	<0.001	1.13 (-0.94 to 3.23)	−3.32 to 5.58	Tier 3

* Best estimate from each study selected with the following priority: operator recorded mobile phone use, self-reported mobile phone use, self-reported cordless phone use.
[&] Includes tiredness from Schoeni as a proxy for sleep problems.
[$] Refers to the lowest Tier that contributed to this estimate.

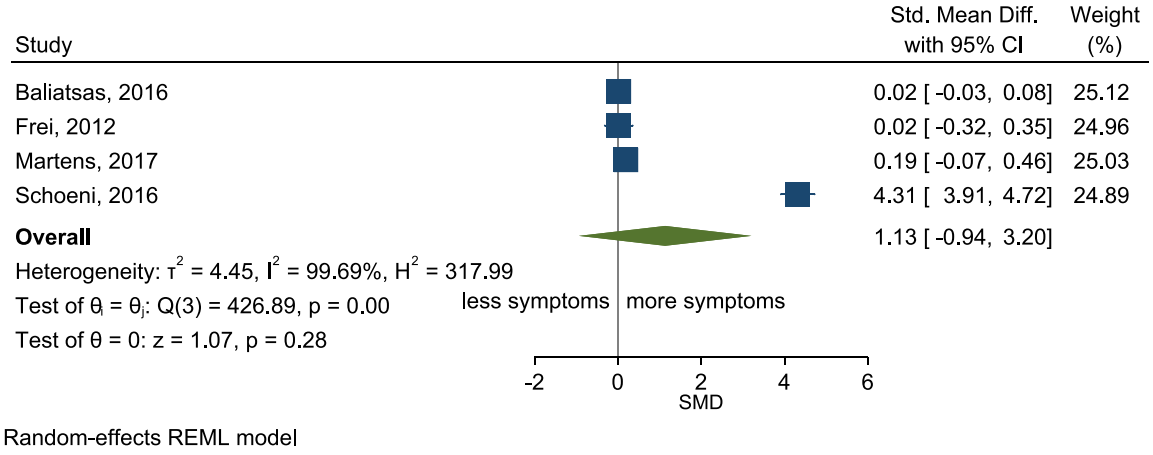

Fig. 6. Meta-analysis of PECO 5: Composite symptom scores in relation to whole-body RF-EMF exposure using best available evidence from each study*: SMD per 1 V/m. *Best estimate from each study selected with the following priority: *all sources, all types fixed site transmitters, mobile phone base stations.

systematically review every potential biological mechanisms, but to the best of our knowledge, none of them could plausibly cause or prevent non-specific symptoms, in line with the lack of associations observed in this review. It is well established that very high levels of RF-EMF exposure can cause excessive tissue heating resulting in pain and thermal damage (ICNIRP, 2020). Further, RF-EMF exposure can cause pain or tissue damage indirectly via contact currents. This can happen if a person touches a conducting object, which results in a current flow through the body. Another well understood mechanism is microwave hearing from highly pulsed RF-EMF levels originating, for instance, from

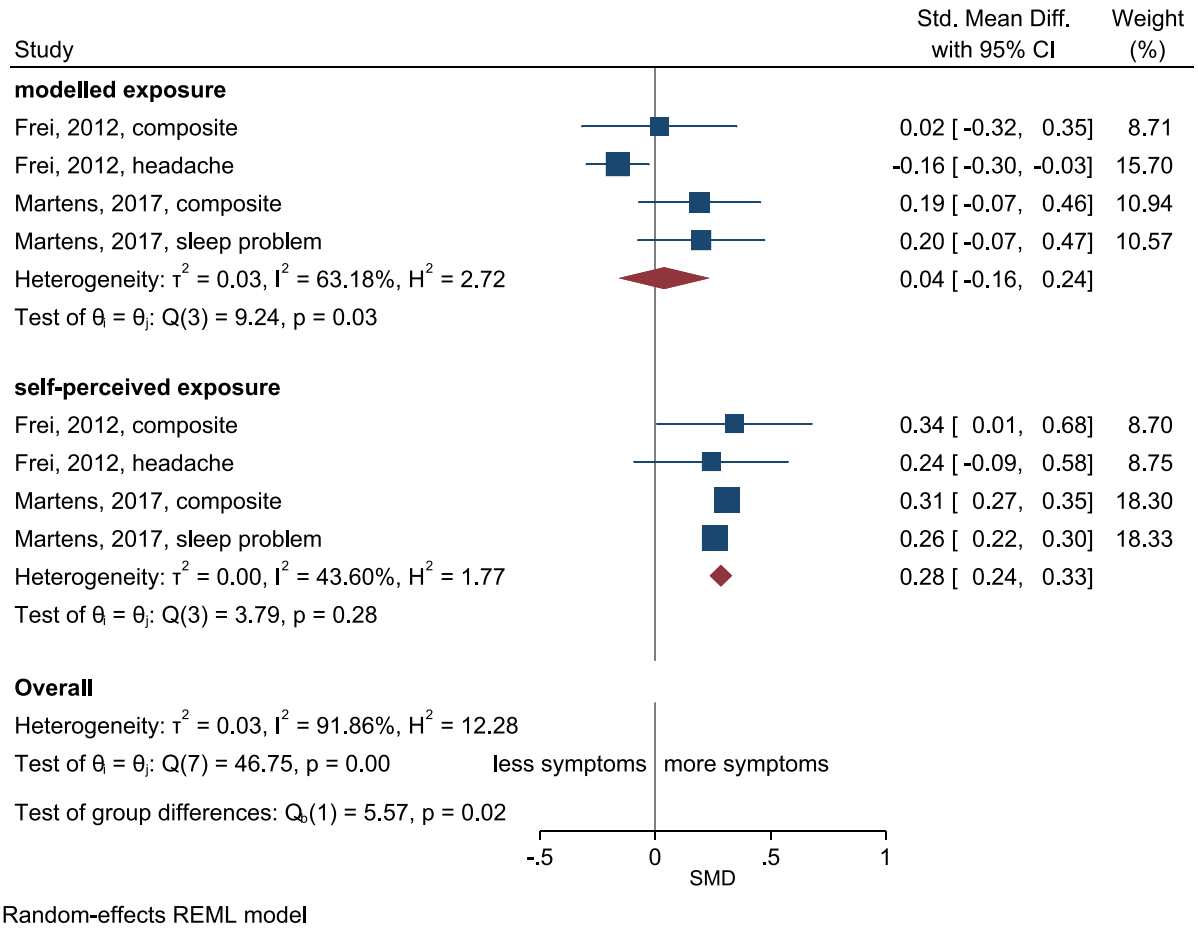

Fig. 7. Comparison of studies addressing non-specific symptoms in relation to modelled exposure and self-perceived exposure: SMD per 1 V/m (modelled exposure) or for people that consider themselves to be highly exposed.

radar systems (Frey, 1962). Such pulses result in a thermoelastic expansion of the auditory system, which produce audible clicks or buzzing. In the therapy setting, radiofrequency ablation is applied for pain management (Orhurhu et al., 2019) and has been suggested to be helpful for treatment of obstructive apnoea syndrome and related sleep disturbances (Baba et al., 2015). For all these well characterized phenomena, the guideline values are well protective. Further, the lack of a specific symptom pattern in relation to RF-EMF exposure may also be considered as indirect evidence that no specific biological pathway exists in the low exposure range, further supporting the observed empirical results of this review.

A particular challenge is the explorative manner of most of the papers involved. In the absence of a known biological mechanism, numerous symptoms have been included in the reviewed papers, and some papers used various approaches to analyse the data. For the *meta*-analysis we have relied on the exposure–response association that was declared to be the primary analysis. If nothing was declared, primary analysis was decided based on how prominent results were presented. It was beyond the capacity of this review to address all associations and the number of similar approaches for systematic evaluation of different approaches was mostly too small. Nevertheless, we conducted many sensitivity analyses and did not find that results of this review were critically affected by the choice of specific effect estimates.

Typical far-field exposures in the reviewed studies were around 0.1 to 0.2 V/m and exceeding 1 V/m only for a very small proportion of study participants. This is in line what was found in environmental (Huss et al., 2021; Jalilian et al., 2019; Sagar et al., 2018) and personal measurement studies (Birks et al., 2018; Ramirez-Vazquez et al., 2023; Schmutz et al., 2022). Thus, these studies do not provide any certainty evidence for the range of the ICNIRP guideline values varying between 27 and 87 V/m in the radio frequency range (ICNIRP, 2020). In terms of devices used close to the body, maximum output power has not changed in the last few decades. However, typical or average output power has substantially reduced in the last few decades due to densification of the network and replacement of the 2G network with 3G and 4G (Joshi et al., 2017; Kühn and Kuster, 2013; Paramananda et al., 2017). Thus, older studies may be more informative for potential effects close to the guideline values of near-field exposure.

5.2. *Limitations in the review process*

We included one case-control study on tinnitus and did not convert the OR into a RR due to lack of reliable incidence data for the study population. However, impact is considered to be minor since observed OR of 2.070 would change to 2.055 based on a transformation assuming an incidence of 0.01 (Jarach et al., 2022).

Given the small number of studies with high heterogeneity, we noticed that pooled effect estimates and particularly confidence intervals were relatively sensitive to various methodological choices, which all may be considered to be justified like definition of study weights or estimation algorithms. The two stage *meta*-analysis approach is also expected to be a source of uncertainty.

Assessing risk of bias from confounding and from exposure assessment is a particular challenge in this field. It is unclear what are critical confounders and thus we only considered studies of probable high risk of bias if they missed very basic confounders such as age, gender, markers of socioeconomic position or distress (the latter only for near-field sources). Most studies have considered many more confounders but

even then it is virtually impossible to rule out confounding. Thus, we were convinced that indirectness is a better concept to describe the challenges of using wireless device use as a proxy for RF-EMF exposure of the brain.

In the protocol time-weighted average or cumulative SAR value of the brain or whole-body was declared to be the primary choice of exposure. However, such a measure was only presented in one study and thus we could not work with this exposure measure but had to rely on other markers of exposure.

5.3. Implications for research

In this review, eight of nine studies were of a prospective cohort design, which is in general the most reliable epidemiological study design. Nevertheless, the review shows that for this specific highly challenging research question substantial challenges related to exposure assessment, confounding control and reverse causality remain. This is inherent to the topic because the main RF-EMF exposure source on population level, which is wireless device usage, is related to many aspects of lifestyle and thus to various potential non-EMF protective and risk factors such as sleep deprivation or lack of physical activity. In order to differentiate between biophysical effects and other potential non-EMF effects in future research, a critical aspect would be to prospectively quantify RF-EMF exposure from near field sources instead of only considering simple proxies like self-reported usage. Future research should address concurrently both exposure sources, near and far field sources. Only research, which uses novel and innovative methods to extract potential RF-EMF from other effects, and which is based on a distinct hypothesis about involved biological pathways relevant for symptom development will help to further clarify open questions. As long as no better approaches will become available, no better evidence will be generated.

5.4. Other information

5.4.1. Registration and protocol

The protocol for this review has been registered in Prospero (reg no CRD42021239432, https://www.crd.york.ac.uk/prospero/display_record.php?RecordID = 239432) and published in Environment International (Röösli et al., 2021).

There are a few differences between the protocol and the review. Because of the low number of eligible studies, we have done less subgroup analyses than foreseen in terms of population groups, subtype of exposures, analysis methods and risk of bias. For the non-priority effect estimates we have developed a heat map to visualize the findings, which was not part of the original protocol.

We had declared in the protocol to evaluate potential bias but we have not specifically foreseen to be able to compare results of studies addressing both, self-estimated and objectively obtained EMF exposure. Such a comparison was considered to be useful for estimating risk of bias in studies relying on self-estimated EMF exposure.

We have extended the definition of indirectness in the certainty assessment beyond a comparison of those exposed in the studies with those exposed in the real world. We also considered the difference of the exposure circumstances in the study in relation to the research question that focussed on potential RF-EMF effects.

6. Conclusions

Overall, mostly absence of associations between various outcomes and RF-EMF exposure proxies were found with substantial heterogeneity between studies suggesting that RF-EMF exposure below guideline values does not cause tinnitus, migraine or any non-specific symptoms. Since the review topic includes various inherent challenges related to confounding control and exposure assessment, the evidence was judged to be very uncertain.

Support

This project was funded by the World Health Organization (RAD 2020/1048990–0; EHC-RAD 2020/994772–0) and by intramural funds of the Swiss Tropical and Public Health Institute. A strict oversight was exercised by the WHO Secretariat to ensure that all commissioned systematic reviews were planned according to a harmonized and good practice standard. WHO provided the basis for the protocol and methodological support throughout the review process.

CRediT authorship contribution statement

Martin Röösli: methodology, supervision, formal analysis, writing-original draft, funding acquisition; **Stefan Dongus:** data extraction, data curation, risk of bias, writing - review & editing; **Hamed Jalilian:** data extraction, risk of bias, writing - review & editing; **John Eyers:** Literature search, **Ekpereonne Esu:** writing - review & editing; **Chioma Moses Oringanje:** writing - review & editing; **Martin Meremikwu:** writing - review & editing; **Xavier Bosch-Capblanch:** methodology, writing - review & editing, funding acquisition.

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. Martin Röösli's research is entirely funded by public or not-for-profit foundations. He has served as advisor to a number of national and international public advisory and research steering groups concerning the potential health effects of exposure to nonionizing radiation, 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.

Data availability

Data will be made available on request.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.108338.

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