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The effects of radiofrequency electromagnetic fields exposure on human self-reported symptoms: A systematic review of human experimental studies

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A R T I C L E I N F O

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A B S T R A C T

Background: The technological applications of radiofrequency electromagnetic fields (RF-EMF) have been steadily increasing since the 1950s exposing large proportions of the population. The World Health Organization (WHO) is assessing the potential health effects of exposure to RF-EMF.
Objectives: To systematically assess the effects of exposure to RF-EMF on self-reported non-specific symptoms in human subjects and to assess the accuracy of perceptions of presence or absence of RF-EMF exposure.
Methods: Eligibility criteria: experimental studies carried out in the general population and in individuals with idiopathic environmental intolerance attributed to EMF (IEI-EMF), in any language.
Information sources: Medline, Web of Science, PsycInfo, Cochrane Library, Epistemonikos, Embase and EMF portal, searched till April 2022.
Risk of Bias (ROB): we used the RoB tool developed by OHAT adapted to the topic of this review.
Synthesis of results: we synthesized studies using random effects meta-analysis and sensitivity analyses, where appropriate.
Results: Included studies: 41 studies were included, mostly cross over trials and from Europe, with a total of 2,874 participants.
Synthesis of results: considering the primary outcomes, we carried out meta-analyses of 10 exposure-outcomes pairs. All evidence suggested no or small non-significant effects of exposure on symptoms with high (three comparisons), moderate (four comparisons), low (one comparison) and very low (two comparisons) certainty of evidence. The effects (standard mean difference, where positive values indicate presence of symptom being exposed) in the general population for head exposure were (95% confidence intervals) 0.08 (−0.07 to 0.22) for headache, −0.01 (−0.22 to 0.20) for sleeping disturbances and 0.13 (−0.51 to 0.76) for composite symptoms; and for whole-body exposure: 0.09 (−0.35 to 0.54), 0.00 (−0.15 to 0.15) for sleeping disturbances and −0.05 (−0.17 to 0.07) for composite symptoms. For IEI-EMF individuals SMD ranged from −0.19 to 0.11, all of them with confidence intervals crossing the value of zero.
Further, the available evidence suggested that study volunteers could not perceive the EMF exposure status better than what is expected by chance and that IEI-EMF individuals could not determine EMF conditions better than the general population.
Discussion: Limitations of evidence: experimental conditions are substantially different from real-life situations in the duration, frequency, distance and position of the exposure. Most studies were conducted in young, healthy volunteers, who might be more resilient to RF-EMF than the general population. The outcomes of interest in this

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systematic review were symptoms, which are self-reported. The available information did not allow to assess the potential effects of exposures beyond acute exposure and in elderly or in chronically ill people. It cannot be ruled out that a real EMF effect in IEI-EMF groups is masked by a mix with insensitive subjects. However, studies on symptoms reporting and/or field perceptions did not find any evidence that there were particularly vulnerable individuals in the IEI-EMF group, although in open provocation studies, when volunteers were informed about the presence or absence of EMF exposure, such differences were consistently observed.
Interpretation: available evidence suggests that acute RF-EMF below regulatory limits does not cause symptoms and corresponding claims in the everyday life are related to perceived and not to real EMF exposure status.

1. Introduction

1.1. Background and rationale

The technological applications of radiofrequency electromagnetic fields (RF-EMF; frequencies 100 kHz to 300 GHz) have been steadily increasing since the 1950s. RF-EMF are used in medicine (e.g. magnetic resonance imaging, diathermy, radiofrequency ablation), industry (e.g. heating and welding), domestic appliances (e.g. baby monitors, WiFi), security and navigation (e.g. radar and RFID) and especially in telecommunications (e.g. radio and TV broadcasting, mobile telephony). These developments mean that large parts of the global population are now exposed to RF-EMF and more will be exposed in the future. Concerns have been raised regarding public health consequences from RF-EMF and it is therefore crucial to perform a health risk assessment to support decision-makers and to inform the general public.

The World Health Organization (WHO) has an ongoing project to assess potential health effects of exposure to RF-EMF in the general and working populations, including patients. To prioritize potential adverse health outcomes from exposure to RF-EMF, WHO conducted a broad international survey amongst RF experts in 2018 (Verbeek et al., 2021). Major topics were identified for which WHO has commissioned systematic reviews (SR). In the current paper, we present the findings of a SR on the effects of exposure to RF fields on symptoms evaluated in human experimental studies. In parallel, another SR looked at the effects of RF-EMF on symptoms evaluated in human observational studies (Röösli et al., 2024). Full details on exposures, outcomes and rationale for this SR are reported in the protocol of this SR (Bosch-Capblanch et al., 2022).

1.2. Description of the exposure

RF-EMF are defined as fields with frequencies from 100 kHz to 300 GHz. Such fields are generated by a large number of equipment both in the living environment and in workplaces. For these sources, a basic distinction is made between devices operating close to the body, resulting in near-field exposure situations 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 (Lauer et al., 2013). The main variables influencing the interaction of RF-EMF with the human body are the signal frequency, the exposure intensity, the exposure duration, the polarization of the field, the modulation of the signal and the dielectric characteristics of absorbing tissues.

1.3. Description of the health outcomes

The health outcomes to report in this review include (1) various symptoms in humans and (2) the ability of humans to perceive the presence of RF-EMF.

Some people report several types of non-specific symptoms such as headache or sleep disturbances, 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) (WHO, 2005), although according to a SR on IEI criteria, the most frequently used descriptive term was “hypersensitive to EMF” (Baliatsas et al., 2012b). We will consider all sorts of population in our selection criteria.

Given that many of those attributing symptoms to EMF exposure report that they can perceive the RF-EMF during and shortly after exposure (e.g. Röösli et al., 2004), it is also useful to consider studies that report the ability to perceive or sense RF-EMF (from now on called EMF perceptions). It is also important to clarify whether individuals with IEI-EMF are able to perceive RF-EMF more accurately than individuals without IEI-EMF.

1.4. Rationale to carry out this systematic review

Several literature reviews have been carried out to assess whether RF-EMF levels below regulatory limits may cause symptoms or may be perceived by volunteers with and without IEI-EMF. However, available reviews on these human volunteer studies are outdated (Rubin et al., 2010; Röösli, 2008; Augner et al., 2012), restricted to mobile phone base stations (Klaps et al., 2016), focusing on individuals with IEI-EMF (Schmiedchen et al., 2019) or children (Bodewein et al., 2022) or had important limitations (Farashi et al., 2022; Jalilian et al., 2022). Thus, a comprehensive systematic review of human experimental studies on various non-specific symptoms of RF-EMF is lacking.

1.5. Objectives

Our aim is to assess the evidence on the relation between short term exposure to RF-EMF and acute symptoms, attributable to a physical mechanism related to the exposure, beyond a nocebo effect; and whether the presence of RF-EMF exposure below the levels of the ICNIRP guidelines can be perceived.

We used the Participants, Exposure, Comparator and Outcome (PECO) framework to formulate the systematic review research questions (Morgan et al., 2018):

- in volunteers with IEI-EMF and without IEI-EMF (P), is exposure to RF-EMF (E), as compared to no or lower exposure levels (C), related to immediate effects on symptoms (O)?
- in volunteers with IEI-EMF and without IEI-EMF (P), are different exposure levels to RF-EMF (E, C) related to the intensity of self-reported symptoms (O)?
- can volunteers with IEI-EMF and without IEI-EMF (P), exposed to sham or real RMF (E), accurately perceive (O) the presence of EMF?

2. Methods

The review was carried out following the recommendations in the WHO Handbook for Guideline Development (WHO, 2014) and COSTER (Recommendations for the conduct of SRs in toxicology and environmental health research) (Whaley et al., 2020). We present here a summary of the methods, which are fully developed elsewhere (Bosch-Capblanch et al., 2022).

2.1. Eligibility criteria

In terms of participants, we included people of any age, gender, occupation or socio-economic condition, with and without IEI-EMF.

For the exposures, we included all studies that have applied electric, magnetic or electromagnetic fields in the frequency range of 100 kHz to 300 GHz, including both near-field and far-field exposures. We included studies that had at least participants or researchers blinded to the exposure condition. We based our overall estimates only on the studies that have blinded participants to the exposure situation because, such a design reduces potential nocebo effects. For any study to be eligible, at least one type of exposure estimate should be present, as described in the full protocol.

We excluded studies that have applied exposure signals with more than 10% of the total signal energy outside the considered frequency range 100 kHz–300 GHz. We did not exclude studies on the grounds of the intensity or duration of exposure. We excluded studies reporting exposure effects on implants such as pacemakers or cochlear implants (Sorri et al., 2006).

In terms of comparators, we included studies with at least one active exposure condition and one control condition that may be either sham exposure or another RF-EMF exposure.

We considered two types of outcomes: symptoms and EMF perceptions. We considered symptoms commonly reported, such as headache, sleep quality measures and composite symptom scores, as the main outcomes of this review. To assess the accuracy of RF-EMF exposure perception, we scrutinised perception outcomes in the included studies reporting symptoms.

In terms of study designs, we included parallel or cross-over trials, conducted either in laboratories or at any other location, such as in homes or workplaces.

We did not limit our searches by timeframe or language. We only considered published, peer-reviewed studies.

2.2. Information sources and search strategy

Eligible studies were identified by literature searches in the following databases: Medline, Web of Science, PsycInfo, Cochrane Library, Epistemonikos and Embase and consulted the EMF portal, searched up to April 2022. Each database strategy was tailored to its specific search syntax. Search strategies can be found in the protocol (Bosch-Capblanch et al., 2022) and in supplementary material 1.

2.3. Selection and data collection processes

After the retrieval of references, we identified and discarded duplicates. First, the relevance of identified papers was checked on the basis of titles and abstracts, to discard animal studies or studies obviously out of the scope of this review. The full text of relevant references was obtained to assess whether they fulfiled all the inclusion criteria, independently by two reviewers (EE, CMO). If there were disagreements on the decisions made, these were resolved by consensus between the two reviewers, and with a third reviewer (XBC or MR), if necessary. If a certain study was described in more than one article with complementary results, we used the results as reported in all available articles and referred to it as a single study. If a single document reported several studies, we individually considered each one of the studies separately.

Several reviewers independently extracted and recorded the relevant data of each eligible study (EE, CMO, XBC, CAU). We anticipated that if any of the authors of the review were an author of an included study, we would have excluded that author from key tasks. Discrepancies were solved by checking the source. If disagreement occurred between the reviewers, a third reviewer (XBC) carried out the final check with the full text. The list of items extracted can be found in the full protocol.

2.4. Risk of bias assessment

For evaluating the internal validity, we conducted a Risk of Bias (ROB) assessment using the "ROB 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 adapted for the specific exposures and outcomes considered in this review. We only considered domains relevant to "Human Controlled Trials". In the ROB form (supplementary material 2), all instructions from the original OHAT document (NTP, 2015) are typed in black. All adaptions to the form, which were informed by the review team and discussions with other WHO review teams and COSTER (Whaley et al., 2020), are typed in blue for easier recognition. Studies were assessed across six domains with eight different questions, with detailed criteria elaborated for each domain in the ROB instructions. The following issues were considered: randomisation of exposure level, allocation concealment, blinding, attrition level, exposure characterisation, outcome assessment and reporting, funding sources and other sources of bias.

Using the instructions guide, ROB was assessed at outcome level and therefore studies reporting on several outcomes had the corresponding ROB assessments. Following the OHAT ROB classification, ROB were reported as definitely low ROB (++), probably low ROB (+), probably high ROB (− or not reported "NR"), or definitely high ROB (−−) for each criteria. ROB may result into a false positive risk (i.e. overestimation of harmful effect), bias towards absence of an association (i.e. underestimation of harmful effect), false protective finding (i.e. favours beneficial effect) or unpredictable effect.

As suggested by the OHAT handbook, we applied a 3-tier system for later synthesizing study findings when ROB vary across studies or across different analyses from the same study. The tier approach was based on the following three key criteria:

1. Can we be confident about the random and concealment of allocation of subjects (instead of "did the study design or analysis account for important confounding and modifying variables?", applied to observational studies).
2. Can we be confident in the exposure characterization?
3. Can we be confident in the outcome assessment?

A Tier 1 study result must be rated as "definitely low" or "probably low" ROB for key criteria and have no other critical bias identified. A Tier 3 study result must be rated as "definitely high" or "probably high" ROB for key elements. A Tier 2 study result meets neither the criteria for 1st or 3rd Tiers (NTP, 2019).

Funding source and disclosure of conflict of interest is not a specific domain in the OHAT ROB tool, but we collected such information during data extraction.

If there were more than five studies in a given meta-analysis, publication bias was assessed applying Egger's test to the included studies.

2.5. Effect measures and synthesis methods

Exposure quantifications using the incident electric field, magnetic field or the power density were converted into whole-body average SAR. We did this by applying the correspondence between the ICNIRP, 2020 basic restrictions (whole-body average SAR) and the reference levels (i.e. incident power density, incident electric field and incident magnetic field)for whole-body exposure.

Symptoms reported using discrete or continuous outcomes were reported using Standardised Mean Differences (SMD). For dichotomous outcomes, OR have been converted into SMD following Chinn, 2000. We carried sub-group analyses stratifying by people with and without IEI-EMF and by head and whole-body exposure, as these two factors were considered as a source of heterogeneity.

The relationship between exposure levels and outcomes was explored using meta-regression, separately by head and whole body exposure. We considered four groups of studies, using combinations of head and whole-body exposure in the general population and in IEI-EMF individuals. The dependant variable was the estimated effect as SMD and the moderator was the exposure level of the exposed groups.

The number of events reported in the findings and shown in the forest plots correspond to the number of ratings in each group, which may be higher than the number of individuals enrolled, if there were more than one rating per individual.

If symptoms had been recorded at different points in time, we used the assessment that measured the largest severity or, if no severity reported, the assessment closest to the end of exposure in the meta-analysis. Where the same study reported several outcomes of the same type (e.g. pain in several areas of the head or different measures of sleep disturbances) we selected only one to be included in the estimation of effects and documented these choices.

If data necessary for analysis were missing from the articles, we asked the authors to provide them. If only effect sizes were available and were consistent with SMD, we used these as reported in the studies and their 95% confidence intervals.

For EMF perceptions, for dichotomous ratings we report the number of correct ratings, as well as false-positive and false-negative recordings. For each study and each exposure level, we calculate the sensitivity, specificity and receiver operating characteristic (ROC) curve. If perception was expressed with a discrete or continuous variable (e.g. perception of the 'intensity' of exposure) we estimated mean differences. Some studies did not report sensitivity and specificity but only the overall correct answer rates for true and sham conditions combined. Thus, we also calculated the ratio between the number of observed correct ratings and the number of expected correct ratings by chance (O/E), taking into account the underlying testing design, as described in Röösli, 2008. The number of expected correct hits was obtained by multiplying the number of trials with the probability of a chance hit. The probability of a chance hit is unclear if the number of sham and real exposure sessions are not identical, given the preference of IEE-EMF individuals to report presence of field and the preference of the general population to rate absence of field (Nam et al., 2009). To account for this, the expected hits were calculated based on the observed marginal distribution of a two by two table showing all four combinations of real and perceived exposure status. A value of 1 for the O/E corresponds to a pure chance rating. Confidence intervals (95%) of O/E perception were calculated on the basis of a binomial distribution.

For symptoms and the O/E ratios, we used random-effects model meta-analyses, using R (rma with DerSimonian-Laird estimator, R Core Team, 2020). For EMF perception, we used random effect meta-analysis to pool study specific sensitivity and specificity rating and to obtain a pooled ROC curve (Nyaga and Arbyn, 2022). To test whether O/E ratio, sensitivity and specificity of the RF-EMF perception differ between IEI-EMF and general population samples, we added the corresponding information as a covariate into the model.

Because we re-estimated the effects of exposure and could not take into account individual correlations existing in cross-over trials, we carried out sensitivity analyses repeating the meta-analyses of the primary outcomes re-calculating the SE (Higgins et al., 2019) of the effect using a correlation of 0.5 (Follmann et al., 1992 as cited in Fu et al., 2013) for cross-over trials.

2.6. Assessment of the certainty of the evidence

We used an elaborated GRADE approach (Morgan et al., 2016) to assess the certainty of the evidence for exposure-outcome combinations. The initial level of certainty of evidence was determined by the study design ('high' for RCT). The certainty of evidence was downgraded depending on the following criteria: ROB of the underlying study, inconsistency, indirectness, imprecision and publication bias. No upgrading was considered, since this review only included randomised and cross-over trials.

The certainty of evidence was assessed for each outcome. The overall confidence in the association between each outcome and type of exposure was rated from high to very low.

In general, we considered as 'no effect' of exposure when the overall SMD was smaller than 0.2 and the 95% confidence interval of the SMD contained the value zero.

2.7. Reporting

We used the PRISMA guidelines for the reporting of SRs to report the findings of our review (Page et al., 2021) and PRISMA-abstract for the abstract (Beller et al., 2013). We also included the Summary of Findings table by PECO, reflecting each primary outcome.

3. Results

3.1. Study selection and excluded studies

We retrieved a total of 8,908 citations, of which we scrutinised for relevance 7,439, after discarding duplicated. Of these, 106 were considered as relevant and the full text examined. Of those, 41 were included and 65 were excluded. Fig. 1 shows the flow of studies. The citations of included studies can be found in supplementary material 3 and the list of excluded studies and reasons for exclusion can be found in Table S.4 in supplementary material 4.

3.2. Study characteristics

The characteristics of included studies can be found in Table 1 (with footnotes in Table S.3 in supplementary material 3). Included studies were published in the years between 1998 and 2022 in the following countries (number, percentage): Germany (7, 17.07%), United Kingdom (7, 17.07%), Sweden (5, 12.2%), Hungary (3, 7.32%), Korea (3, 7.32%), Denmark (2, 4.88%), Finland (2, 4.88%), Italy (2, 4.88%), Japan (2, 4.88%), Norway (2, 4.88%), Switzerland (2, 4.88%), and once each (2.44%) the following: Australia, Netherlands, Slovakia and Taiwan. 38 (93%) studies were cross-over trials and 3 (7%) parallel group trials.

Across all studies, there were 2,874 participants (mean 74 per study). Most of the participants were recruited purposively (in 37 studies, 90%) and only randomly selected from a large group in 4 studies (10%). In terms of age groups (number, percentage), there were adults (25, 61%), young adults (12, 29%), other or not explicitly defined age groups (3, 7%) and elderly (1, 2%). Six studies (15%) had only males and 2 study (5%) only females; the rest did not specify or had no gender selection.

In terms of exposures (number, percentage), most studies used near field exposure (32, 78%), followed far-field (8, 20%) and mixed (1, 2%) exposures. The near field devices included mobile phones (15, 37%), base stations (7, 17%), total near field exposures (2, 5%) or other sources (17, 41%). Studies involved head (31, 76%) and the whole body (10, 24%) exposures.

30 studies expressed exposure in terms of SAR, mostly referring to near field exposure, ranging from 0.01 W/Kg to 6.0 W/Kg (median 1.4 W/Kg, mean 1.6 W/Kg). These values were below the basic restriction for occupational exposure (10 W/Kg) and mostly below the values for the general population (2 W/Kg) (ICNIRP, 2020). Eight studies expressed far field exposure with values ranging from 1.0 V/m to 19.4 V/m (median 1.9 V/m; mean: 6.4 V/m).

30 studies reported symptoms and 23 perceptions; 12 of those reported both symptoms and perceptions. A large variety of symptoms were reported. We recoded similar outcomes into common categories. These are the numbers an percentages of the outcome categories: Headache (13, 11.02%), Composite (12, 10.17%), Fatigue (10, 8.47%), Sleeping disturbances (9, 7.63%), Temperature changes (9, 7.63%), Pain (6, 5.08%), Anxiety (4, 3.39%), Arousal (4, 3.39%), Concentration (4, 3.39%), Discomfort (4, 3.39%), Itching (4, 3.39%), Nausea (4, 3.39%), Relaxation (4, 3.39%), Tension (4, 3.39%), Dizziness (3, 2.54%), Feeling low-spirited (3, 2.54%), Skin reddening (3, 2.54%), Vertigo (3, 2.54%), Vision problems (3, 2.54%), Face swollen (2, 1.69%), Skin other (2, 1.69%), Stress (2, 1.69%), and once each (0.85%) the following: Feeling bored, Feeling stressed, Feeling worried, Palpitations, Swollen face and

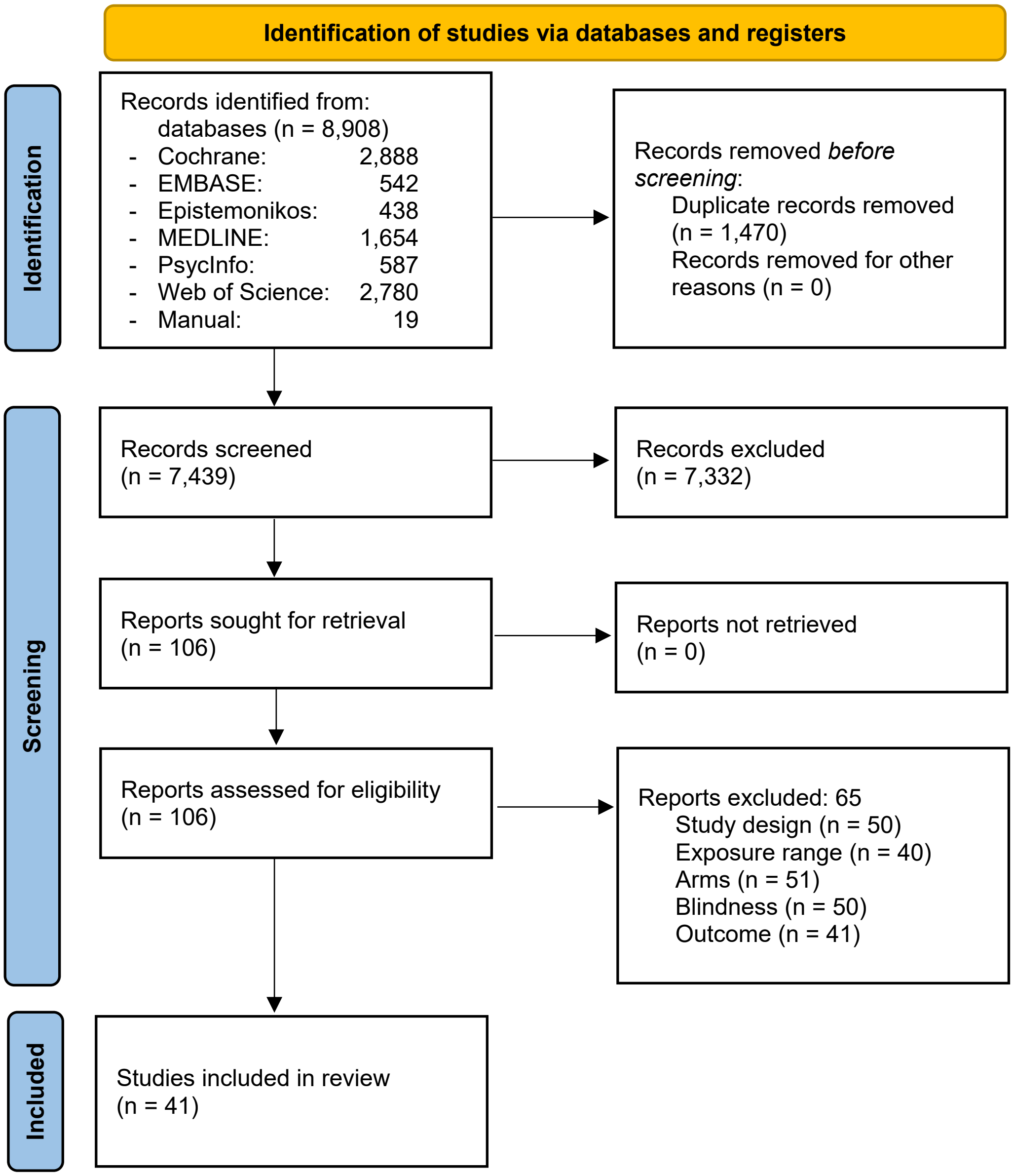

Fig. 1. Flow diagram of studies considered in this review.

Throbbing.

Outcomes related to sleeping quality or disturbances included a great variety of outcomes, such as awakening, sleep onset, sleep duration, easy of raising, sleep efficiency, time in bed, sleep duration, among others, all of them subjective. In studies reporting several sleep outcomes we selected the ones that were better related to overall sleep quality. We transformed outcomes measures to ensure that higher values in the SMD meant less sleep quality or more sleep disturbances.

Some studies reporting perceptions reported separate estimates for IEI-EMF and general population samples, different population groups (e.g. adults, teenagers) or providing results from more than one experiment.

3.3. Risk of Bias in included studies

The summary ROB assessment across all included studies is shown in Fig. 2. A graphical representation of ROB of primary outcomes accompany the forest plots depicting the results of the meta-analyses in Figs. 3–12. The explanations of the ROB assessments by study are reported in Table S.5 (supplementary material 5). The ROB of the effects of exposure in secondary outcomes are shown in the right side of Tables 11 and 12 in the supplementary material 6.

Forteen studies (34%) were classified in Tier-1 and 27 as Tier-2 (66%). No study was classified as Tier 3. Tier-1 studies were: Dorn et al., 2014; Furubayashi et al., 2009; Hillert et al., 2008; Huang et al., 2022; Nakatani-Enomoto et al., 2013; Regel et al., 2006; Riddervold et al., 2008; Riddervold et al., 2010; Rubin et al., 2011; Schmid et al., 2012; Vecsei et al., 2013 Vecsei et al., 2018; Verrender et al., 2018a; Wallace et al., 2012.

The criteria with higher proportions of judgments as 'very low' ROB were the completeness in the reporting of primary outcomes in 40 studies (91%), followed by attrition in 34 studies (83%) and characterisation of exposures in 32 studies (78%); and in much lower proportions, definitely low ROB was found in the randomisation of exposure (9 studies, 22%), mostly due to unclear/lack of counterbalancing, concealment of allocation (rated as 'low' in cross-over trials) and blindness (both in 7 studies, 17%) and in the assessment of outcomes (2 studies, 5%).

Almost all studies had exclusive public funding except fives studies with a mix of funding sources, one study had industry funding and

Table 1
Characteristics of included studies.

Item	Reference	Study design	Country	Participants	Type of participants	Sample size	Exposure type	Exposure value [1]	Body part	Outcomes
1	Bamiou 2008	Cross-over trial	United Kingdom	Adults	General population	30	Near - Mobile phone	1.3 W/kg	Head	Perception
2	Borbély 1999	Cross-over trial	Germany	Young adults (only male)	General population	24	Near - Other	NA	Head (30 cm)	Sleeping disturbances
3	Burgess 2016	Cross-over trial	United Kingdom	Adults	General population	221	Near - Mobile phone	1.3 W/kg	Head	Perception
4	Choi 2014	Cross-over trial	Korea	Young adults and adolescents	General population	52	Near - Mobile phone	1.57 W/kg	Head (3 mm)	Headache and other
5	Cinel 2008	Cross-over trial	United Kingdom	Adults	General population	496	Near - Mobile phone	1.4 W/kg	Head	Headache and other
6	Curcio 2009	Cross-over trial	Italy	Young adults (only female)	General population	15	Near - Mobile phone	0.5 W/kg	Head (1.5 cm)	Headache and other
7	Danker-Hopfe 2010	Cross-over trial	Germany	Adults	General population	397	Far - Base station	NA	Whole body	Sleeping disturbances
8	Danker-Hopfe 2011	Cross-over trial	Germany	Young adults (only male)	General population	30	Near - Mobile phone	2 W/Kg	Head	Sleeping disturbances
9	Danker-Hopfe 2020	Cross-over trial	Germany	Elderly	General population	60	Near - Other	6 W/kg	Head	Sleeping disturbances
10	Dorn 2014	Cross-over trial	Germany	Adults (only male)	General population	15	Near - Other	6 W/kg	Head (35 mm)	Temperature
11	Eltiti 2007	Cross-over trial	United Kingdom	Adults	IEI-EMF only and General population	NA	Far - Base station	1.94 V/m	Whole body (5 m)	Variety
12	Fritzer 2007	Parallel group	Germany	Adults (only male)	General population	20	Near - Other	1 W/kg	Head (30 cm)	Sleeping disturbances
13	Furubayashi 2009	Cross-over trial	Japan	Adults (only female)	IEI-EMF only and General population	54	Far - Base station	0.01 W/kg	Whole body (3 m)	Perception
14	Hietanen 2002	Cross-over trial	Finland	Adults	IEI-EMF only	20	Near - Mobile phone	NA	Head (1–5 cm)	Perception
15	Hillert 2008	Cross-over trial	Sweden	Adults	IEI-EMF only and General population	71‘	Near - Other	1.4 W/kg	Head	Headache and other
16	Huang 2022	Cross-over trial	Taiwan	Adults	IEI-EMF only and General population	150	Far - Base station	19.41 V/m	Whole body (50 cm)	Perception and Headache and Composite
17	Johansson 2008	Cross-over trial	Sweden	Young adults	Patients with atopic dermatitis	30	Near - Total near field	1 W/kg	Head (8.5 cm)	Composite
18	Kwon 2012	Cross-over trial	Korea	Adults	IEI-EMF only and General population	37	Near - Mobile phone	1.57 W/Kg	Head (3 mm)	Perception
19	Lowden 2011	Cross-over trial	Sweden	Adults	General population	48	Near - Other	1.4 W/kg	Head	Sleeping disturbances
20	Lowden 2019	Cross-over trial	Sweden	Young adults	General population	18	Near - Other	1.6 W/kg	Head	Headache and other
21	Misek 2018	Parallel group	Slovakia	Young adults	General population	46	Near - Total near field	NA	Head (30 cm)	Perception and Composite
22	Nakatani-Enomoto 2013	Cross-over trial	Japan	Adults	General population	19	Near - Mobile phone	1.52 W/kg	Head (15 mm)	Sleeping disturbances and Perception
23	Nam 2009	Cross-over trial	Korea	Young adults	IEI-EMF only and General population	37	Near - Mobile phone	1.22 W/Kg	Head	Perception
24	Nieto-Hernandez 2011	Cross-over trial	United Kingdom	Adults	IEI-EMF only and General population	120	Near - Mobile phone	1.3 W/kg	Head (few mm)	Headache and other
25	Oftedal 2007	Cross-over trial	Norway	Adults	IEI-EMF only	17	Near - Other	0.8 W/kg	Head (8.5 cm)	Perception and Pain and Headache and Composite
26	Parazzini 2007	Cross-over trial	Italy	Young adults	General population	26	Near - Mobile phone	Target organ in 10.5 to 13.5 cm of	Head	Temperature and Perception

(continued on next page)

Table 1 (*continued*)

Item	Reference	Study design	Country	Participants	Type of participants	Sample size	Exposure type	Exposure value [1]	Body part	Outcomes
								deepness: 0.02 W/Kg		
27	Radon 1998	Individualised cross-over trial	Germany	Other or unclear	General population	11	Other	9.51 V/m	Whole body	Perception
28	Regel 2006	Cross-over trial	Switzerland	Adults	IEI-EMF only and General population	128	Far - Base station	10 V/m (whole body SAR: 0.62 mW/Kg)	Whole body (2 m)	Perception and Composite
29	Riddervold 2008	Cross-over trial	Denmark	Adolescents	General population	80	Far - Base station	1 V/m	Whole body (2.8 m)	Headache and Concentration
30	Riddervold 2010	Cross-over trial	Denmark	Adults (only male)	General population	54	Near - Other	2 W/kg	Head	Perception
31	Rubin 2006	Cross-over trial	United Kingdom	Adults	IEI-EMF only and General population	131	Near - Mobile phone	1.4 W/kg	Head (few mm)	Perception
32	Schmid 2012	Cross-over trial	Switzerland	Young adults (only male)	General population	30	Near - Other	2 W/kg	Head (115 mm)	Sleeping disturbances
33	Stovner 2008	Cross-over trial	Norway	Adults	General population	17	Near - Other	1 W/kg	Head (8.5 cm)	Headache
34	Tahvanainen 2004	Cross-over trial	Finland	Adults	General population	32	Near - Mobile phone	1.58 W/kg	Head	Temperature
35	vanMoorselaar 2017	Individualised cross-over trial	Netherlands	Adults	General population	42	Far - Other	Individualized according to open provocation test (0.2 to 6 V/m)	Whole body	Perception
36	Vecsei 2013	Cross-over trial	Hungary	Young adults	General population	22	Near - Other	0.73 W/kg	Head	Pain
37	Vecsei 2018a	Cross-over trial	Hungary	Young adults	General population	60	Near - Mobile phone	1.8 W/kg	Head (7 mm)	Perception
38	Vecsei 2018b	Cross-over trial	Hungary	Adults	General population	18	Near - Other	1.8 W/kg	Head (7 mm)	Pain
39	Verrender 2018	Individualised cross-over trial	Australia	Young adults	General population	44	Far - Other	10.63 V/m	Whole body (30 cm)	Perception and Composite
40	Wallace 2010	Cross-over trial	United Kingdom	Adults	IEI-EMF only and General population	183	Far - Base station	1.94 V/m	Whole body (4.95 m)	Variety
41	Wilén 2006	Cross-over trial	Sweden	Adults	IEI-EMF only	40	Near - Other	0.8 W/kg	Head (8.5 cm)	Composite

[1] If more than value, only the largest one is shown in this table.
[2] Reported in the study as power flux density.

another two for which we could not elicit the funding sources.

Note that, in relation to the assessment of outcome measurements, Likert or Visual Analogues Scales (VAS) were considered as well established methods. Furthermore, the fact that we focused on studies assessing short term effects of exposure, we did not detect differences between exposure arms in loss of follow up or blindness in the measurement of outcomes, while all participants are equally exposed in cross-over trials.

We analysed publication bias in those exposure-outcomes pairs that had five or more data points; in all cases there was no evidence of publication bias (p values of Egger test > 0.05): head exposure related to headache in the general population ($p = 0.87$) and related to sleeping disturbances ($p = 0.63$).

3.4. *Effects of the exposure*

In this section we report the results related to symptoms by PECO, first for the general population, then for IEI-EMF subjects. We report the primary outcomes considered for this systematic review (i.e. headache, sleep disturbances and composite symptoms). These main outcomes alongside the effect estimates of individual secondary outcomes are reported in Tables 1–10 in supplemental material 6. The rationale for the selection of outcomes is documented in Table S.7 in supplemental material 7. Note that all effects are reported using SMD; therefore, the original values of outcomes in each study cannot be simply subtracted in order to obtain the shown SMD.

Table 2 is the summary of findings table for the primary outcomes of this review: we evaluated the effects in the following combinations of participants, exposure and outcomes: general population and IEI-EMF individuals, near and far-field exposure, and in headache, sleeping disturbances and composite symptoms. This would be 12 exposures, but we could not find studies on the effects of exposure on sleeping disturbances in IEI-EMF individuals. Hence, 10 comparisons were found and shown.

All the effects, expressed in SMD, were less than 0.2, suggesting small or no effect, and statistically non-significant. In terms of direction, six of them suggest that the exposure groups worsened the symptoms (SMD $>$ 0) and the contrary in the other four.

The certainty of evidence (number of comparisons) was ‘very low’ (2 comparisons), ‘low’ (1), ‘moderate’ (4) and ‘high’ (3). In six comparisons the ROB had some concerns because there was no predominance of Tier-1 in the included studies in those comparisons. The GRADE assessment of specific comparisons, with explanations, are documented in Table S.8 in supplemental material 8.

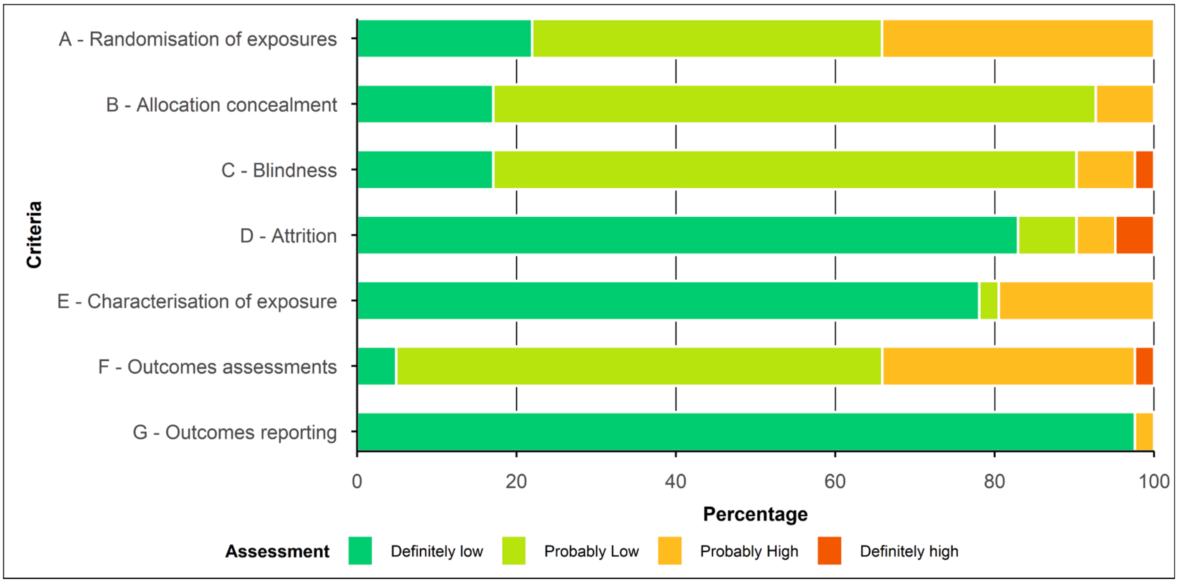

Fig. 2. Summary risk of bias across all included studies.

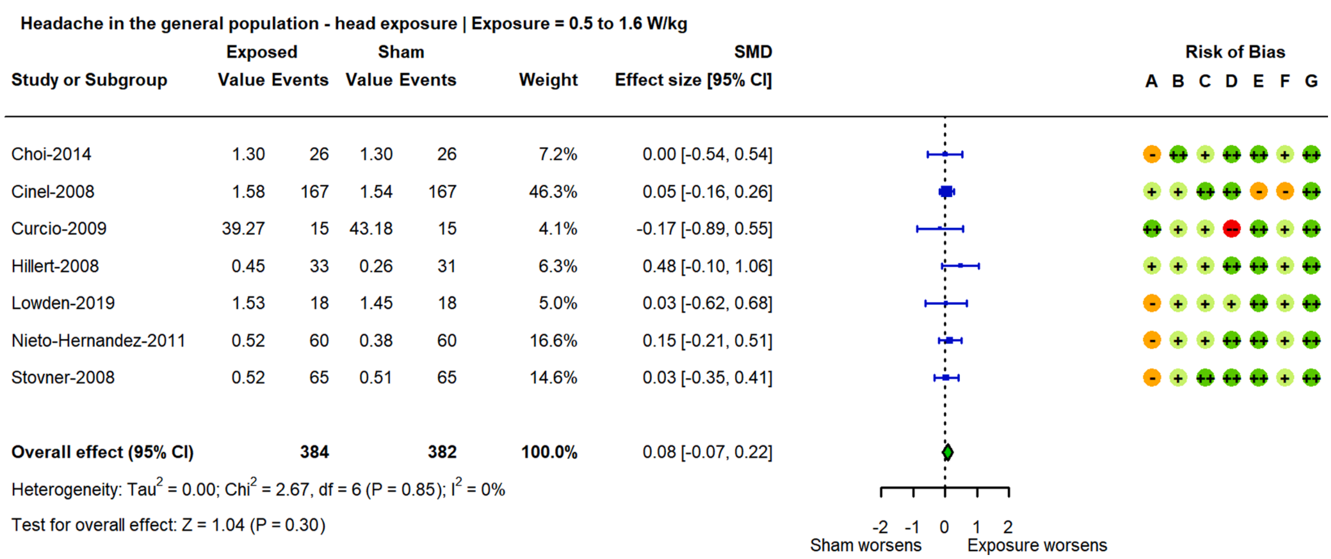

Fig. 3. Forest plot of the effects of EMF exposure to head exposures on headache in the general population.

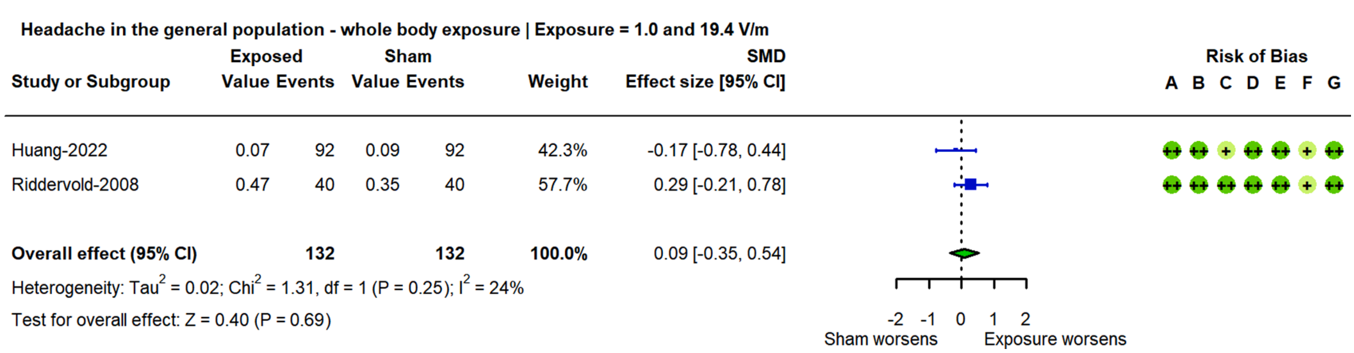

Fig. 4. Forest plot of the effects of EMF exposure to whole body exposures on headache in the general population.

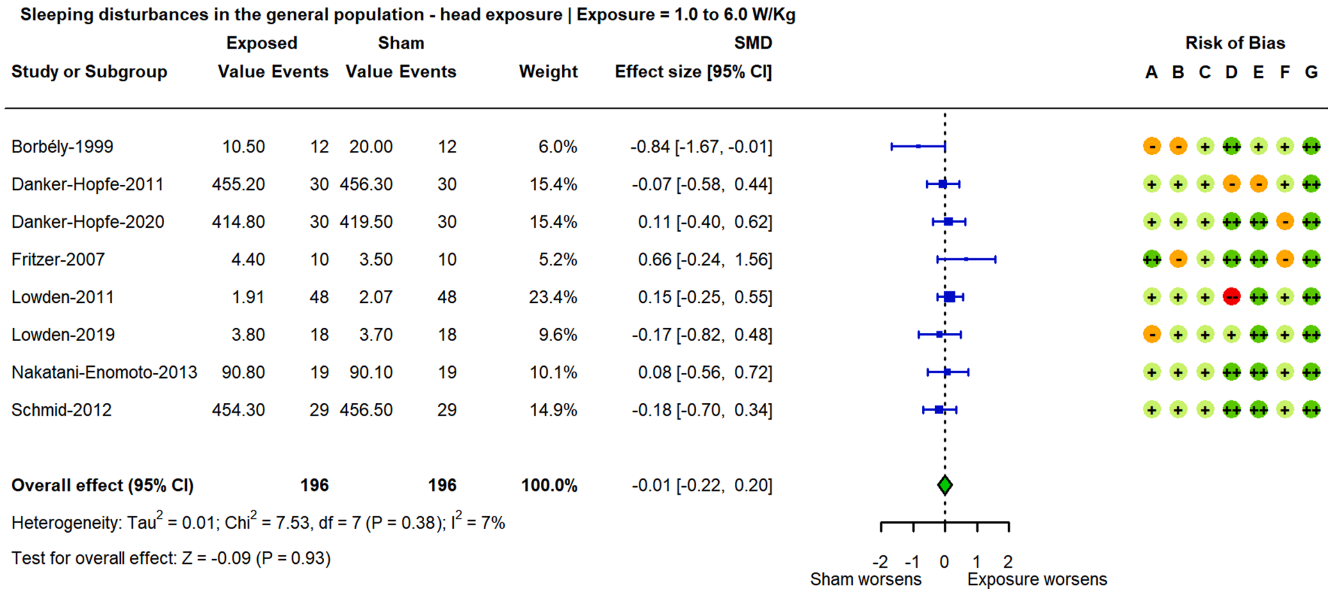

Fig. 5. Forest plot of the effects of EMF exposure to head exposures on sleep disturbances in the general population.

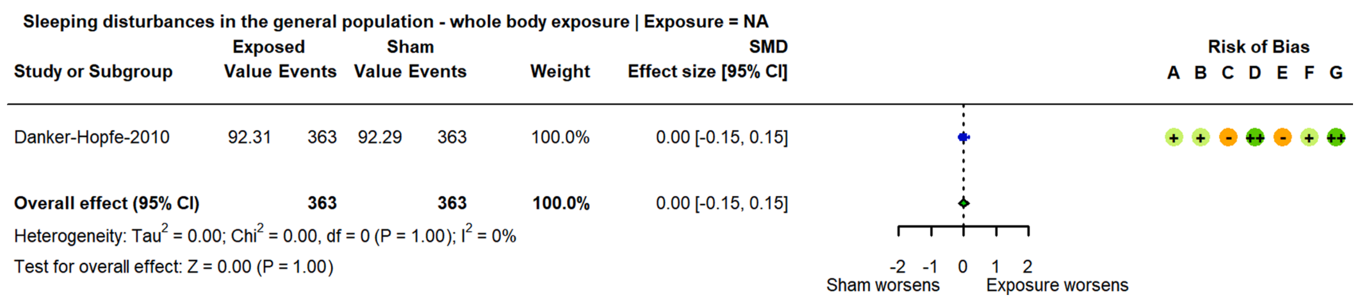

Fig. 6. Forest plot of the effects of EMF exposure to whole body field exposures on sleep disturbances in the general population.

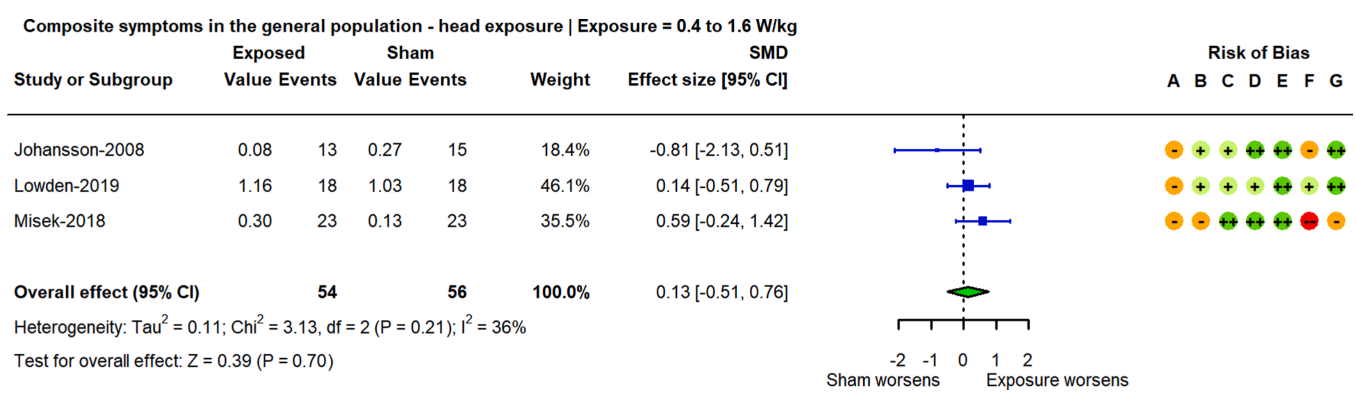

Fig. 7. Forest plot of the effects of EMF exposure to head exposures on composite symptoms in the general population.

3.4.1. PECO 1a: In the general population (P), is exposure to RF-EMF (E), as compared to no or lower exposure levels (C), related to immediate effects on symptoms (O)? – Primary outcomes

(a) Headache in the general population - head exposure | Exposure = 0.5 to 1.6 W/kg

Seven studies (total of 766 events) provided data on the effects of near field exposure in headache (Choi et al., 2014; Cinel et al., 2008; Curcio et al., 2009; Hillert et al., 2008; Lowden et al., 2019; Nieto-Hernandez et al., 2011 and (Stovner et al., 2008)) in the exposure range of 0.5 to 1.6 W/Kg; see Fig. 3. All comparisons showed small or no effects (SMD < 0.2) and all 95% CI contained the value of zero. The overall effect estimate was SMD 0.08 (95% CI −0.07 to 0.22, I^2 = 0%).

The certainty of evidence was considered moderate because there were no concerns in any of the criteria but one (ROB). In summary, in the general population, the head exposure to EMF likely does not increase the presence of headache as compared with those not exposed (moderate certainty evidence).

(b) Headache in the general population - whole body exposure | Exposure = 1.0 to 19.4 V/m

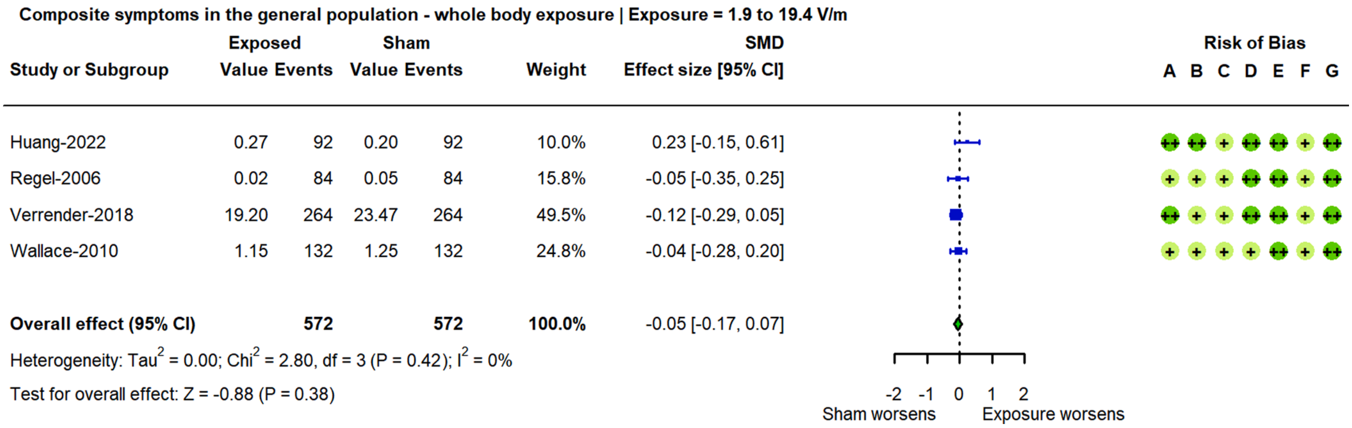

Fig. 8. Forest plot of the effects of EMF exposure to whole body field exposures on composite symptoms in the general population.

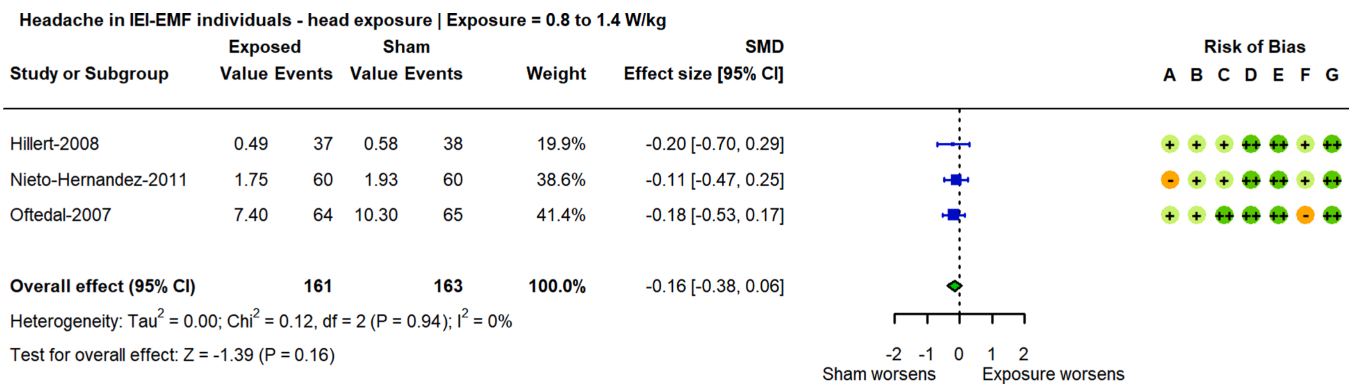

Fig. 9. Forest plot of the effects of EMF exposure to head exposures on headache in IEI-EMF individuals.

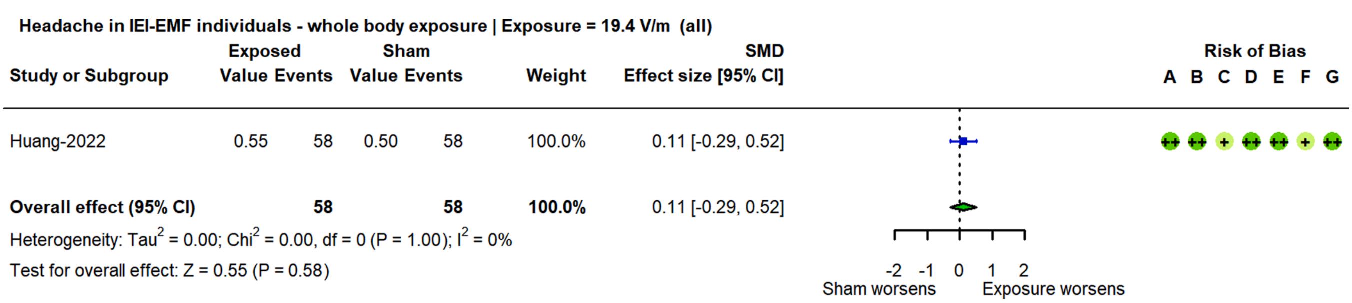

Fig. 10. Forest plot of the effects of EMF exposure to whole body field exposures on headache in IEI-EMF individuals.

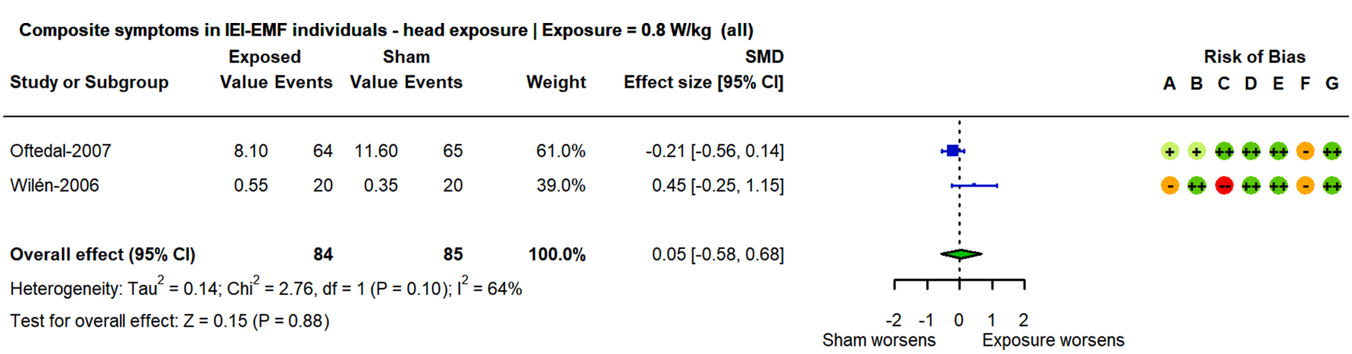

Fig. 11. Forest plot of the effects of EMF exposure to head exposures on composite symptoms in IEI-EMF individuals.

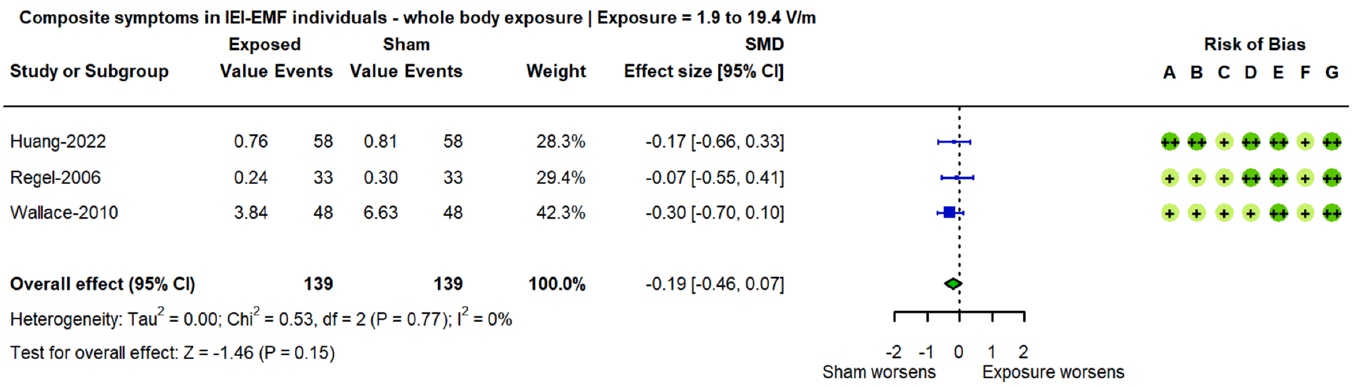

Fig. 12. Forest plot of the effects of EMF exposure to whole body field exposures on composite symptoms in IEI-EMF individuals.

Table 2
Summary of findings table across all primary outcomes.

	Certainty assessment: N of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Summary of findings: Number of events: Exposure	Comparison	SMD (95% CI)	Certainty
General population											
1	**Outcome**	Headache - head exposure | Exposure = 0.5 to 1.6 W/kg									
	7	Trial	Some concerns	No concerns	No concerns	No concerns	No concerns	384	382	0.08 (−0.07 to 0.22)	**Moderate**
2	**Outcome**	Headache - whole body exposure | Exposure = 1.0 and 19.4 V/m									
	2	Trial	No concerns	No concerns	No concerns	No concerns	No concerns	132	132	0.09 (−0.35 to 0.54)	**High**
3	**Outcome**	Sleeping disturbances - head exposure | Exposure = 1.0 to 6.0 W/Kg									
	8	Trial	Some concerns	No concerns	No concerns	No concerns	No concerns	196	196	−0.01 (−0.22 to 0.20)	**Moderate**
4	**Outcome**	Sleeping disturbances - whole body exposure | Exposure = NA									
	1	Trial	Some concerns	Some concerns	No concerns	No concerns	No concerns	363	363	0.00 (−0.15 to 0.15)	**Low**
5	**Outcome**	Composite symptoms - head exposure | Exposure = 0.4 to 1.6 W/kg									
	3	Trial	Some concerns	Some concerns	Some concerns	No concerns	No concerns	54	56	0.13 (−0.51 to 0.76)	**Very low**
6	**Outcome**	Composite symptoms - whole body exposure | Exposure = 1.9 to 19.4 V/m									
	4	Trial	No concerns	No concerns	No concerns	No concerns	No concerns	572	572	−0.05 (−0.17 to 0.07)	**High**
IEI-EMF individuals											
7	**Outcome**	Headache - head exposure | Exposure = 0.8 to 1.4 W/kg									
	3	Trial	Some concerns	No concerns	No concerns	No concerns	No concerns	161	163	−0.16 (−0.38 to 0.06)	**Moderate**
8	**Outcome**	Headache - whole body exposure | Exposure = 19.4 V/m (all)									
	1	Trial	No concerns	Some concerns	No concerns	No concerns	No concerns	58	58	0.11 (−0.29 to 0.52)	**Moderate**
9	**Outcome**	Composite symptoms - head exposure | Exposure = 0.8 W/kg (all)									
	2	Trial	Some concerns	Serious concerns	No concerns	No concerns	No concerns	84	85	0.05 (−0.58 to 0.68)	**Very low**
10	**Outcome**	Composite symptoms - whole body exposure | Exposure = 1.9 to 19.4 V/m									
	3	Trial	No concerns	No concerns	No concerns	No concerns	No concerns	139	139	−0.19 (−0.46 to 0.07)	**High**

Note: a negative sign of standardized mean difference (SMD) implicates a reduction of symptoms, a positive sign a worsening.

We could identify two studies (with 264 events) reporting the effects of whole body exposure on headache (Huang et al., 2022 and Riddervold et al., 2008), with exposure levels of 1.0 and 19.4 V/m. The pooled SMD was 0.09 with 95% CI −0.35 to 0.54 ($I^2 = 24\%$), a small or no effect. See Fig. 4.

The certainty of evidence was high because there were no concerns in any of the criteria. Despite that Riddervold et al., 2008 was carried out on adolescents, we did not penalise the indirectness criterion. In the general population, whole body exposure to EMF does not increase the presence of headache (high certainty evidence).

(c) Sleeping disturbances in the general population - head exposure | Exposure = 1.0 to 2 W/Kg

This comparison in the general population was the one with the largest number of studies (8 studies with 392 events): Borbély et al., 1999; Danker-Hopfe et al., 2017; Danker-Hopfe et al., 2020; Fritzer et al., 2007; Lowden et al., 2011; Lowden et al., 2019; Nakatani-Enomoto et al., 2013, and Schmid et al., 2012 (see the description of studies section for examples of sleeping disturbances). In four studies the exposure to EMF worsened the symptoms (in one of them with confidence intervals not crossing the zero effect line) and in the other four it was the contrary. The overall SMD was 0.03 (95% CI −0.23 to 0.29, $I^2 = 7\%$), a small or null effect, as shown in Fig. 5.

The certainty of evidence was moderate due to the concerns in the ROB. In summary, in the general population, the effect of head exposure to EMF on sleeping disturbances likely makes no difference (moderate certainty evidence).

(d) Sleeping disturbances in the general population - whole body exposure | Exposure = NA

Only one study (726 events) reported subjective sleeping disturbances in a situation of whole body exposure to EMF: Danker-Hopfe et al., 2010, with an overall SMD of 0.00 (95% CI −0.15 to 0.15, with no heterogeneity since this is only one study); see Fig. 6.

The certainty of evidence was low because this was a Tier-2 ROB study and this particular population-outcome had only one study. In summary, in the general population, the effect of whole body exposure to EMF may not increase the presence of sleeping disturbances (low certainty evidence).

(e) Composite symptoms in the general population - head exposure | Exposure = 0.4 to 1.6 W/kg

Composite symptoms were reported by authors in variety of ways; e.g. recording specific symptoms from participants and summarising them into a score. If headache or sleeping disturbances were separately reported in the studies, we would have included these outcomes in the sections above.

There were three studies (100 events) reporting on these composite symptoms: Johansson et al., 2008; Lowden et al., 2019 and Misek et al., 2018 (Fig. 7), with exposure levels ranging from 0.4 to 1.6 W/Kg. Two studies had a point estimate suggesting that exposure may worsen the symptoms, although all of them had confidence intervals crossing the zero line. The overall SMD was 0.13 (95% CI −0.51 to 0.76, with some heterogeneity, $I^2 = 36\%$), a small effect.

The certainty of evidence was 'very low' because there were concerns on indirectness (i.e. only young adults) and all studies were classified as Tier-2 ROB. In summary, the head exposure to EMF in the general population may result in little or no effect on composite symptoms (very low certainty evidence).

(f) Composite symptoms in the general population - whole body exposure | Exposure = 1.0 to 19.4 V/m

The effects of whole body exposure in composite symptoms was reported in four studies (1,144 events): Huang et al., 2018; Regel et al., 2006; Verrender et al., 2018a and Wallace et al., 2012, with exposure levels of 1.0 and 19.4 V/m. The overall SMD was very small, 0.07 (95% CI −0.19 to 0.05, $I^2 = 2\%$), see Fig. 8.

The certainty of evidence was high, as all studies were classified in Tier-1 of the ROB and there were no concerns in the other criteria. In summary, in the general population, whole body exposure to EMF does not increase the occurrence of composite symptoms (high certainty evidence).

3.4.2. *PECO 1b: In participants with IEI-EMF (P), is exposure to RF-EMF (E), as compared to no or lower exposure levels (C), related to immediate effects on symptoms (O)? – Primary outcomes*

We report in this section the effects of EMF in participants with IEI-EMF, as reported in the included studies.

(g) Headache in IEI-EMF individuals - head exposure | Exposure = 0.8 to 1.4 W/kg

Three studies (with 324 events) reported the effects of EMF head exposure in headache of IEI-EMF participants: Hillert et al., 2008; Nieto-Hernandez et al., 2011 and Oftedal et al., 2007a (Fig. 9), with exposure levels ranging from 0.8 to 1.4 W/Kg. All studies showed small effects with confidence intervals crossing the zero line. The overall SMD was small and non-significant: 0.16 (95%CI −0.38 to 0.06, $I^2 = 0\%$).

There were some concerns in the ROB, with two Tier-2 studies. The certainty of evidence was moderate because of some concerns in the ROB. In summary, in IEI-EMF populations, the head exposure to EMF likely has no effects on headache (moderate certainty evidence).

(h) Headache in IEI-EMF individuals - whole body exposure | Exposure = 19.4 V/m

Only one study (116 events), Huang 2022, reported this outcome in IEI-EMF individuals, with an exposure level of 19.4 V/m. The SMD was 0.11 (95%CI −0.29 to 0.52). See Fig. 10.

The certainty of evidence was moderate because this was a single study, which downgraded inconsistency. The ROB was classified as Tier-1. In summary, the exposure to EMF likely has no effect on headache reported by IEI-EMF individuals (moderate certainty evidence).

(i) Composite symptoms in IEI-EMF individuals - head exposure | Exposure = 0.8 W/kg (all)

Two studies (with 169 events) reported the effects of head exposure in composite symptoms among IEI-EMF participants: Oftedal et al., 2007a and Wilén et al., 2006, all studies with exposure of 0.8 W/Kg. The pooled SMD was small, 0.05 (95%CI −0.58 to 0.68). See Fig. 11.

The certainty of evidence was very low due to the high degree of inconsistency (two studies with I^2 of 64%) and the ROB of included studies, both Tier-2 studies. In summary, in IEI-EMF populations, exposure to EMF may have little or no effect on composite symptoms but we are very uncertain about this evidence (very low certainty evidence).

(j) Composite symptoms in IEI-EMF individuals - whole body exposure | Exposure = 1.0 to 19.4 V/m

Three studies (with 278 events) (Huang et al., 2022; Regel et al., 2006 and Wallace et al., 2012, with exposures ranging from 1.0 and 19.4 V/m) reported the effects of EMF exposure on composite symptoms in IEI-EMF participants. All studies showed point estimates suggesting that exposure improves the symptoms, although all confidence intervals crossed the zero line. The overall SMD was −0.19 (95% CI −0.46 to 0.07, $I^2 = 0\%$), see Fig. 12.

The certainty of evidence was high due to the fact that the ROB in the three studies were classified in Tier-1 and there were no other concerns. In summary, in IEI-EMF populations, the whole body exposure to EMF does not increase the occurrence of composite symptoms (high certainty evidence).

3.4.3. *PECO 1c: In any type of participant (P), is exposure to RF-EMF (E), as compared to no or lower exposure levels (C), related to immediate effects on symptoms (O)? – Secondary outcomes*

We have extracted and analysed the effects of EMF on other symptoms, which are reported in Tables 11 and 12 of supplementary material 6. We have recodified the outcomes to classify them by similarities. We did not attempt to carry out meta-analyses due to the underlying heterogeneity of the outcomes as reported in the studies. In total, we produced 84 additional individual effect estimates across 14 studies. 59 (70%) data points referred to head exposure and 25 (30%) to whole body exposure; in 59 (70%) comparisons participants where from the general population and in 30 (28%) IEI-EMF only (n ote that the coincidence in the numbers -59-of head and whole body exposure and the types of participants is casual). We report 25 different outcomes, in the domains of psychological distress, skin manifestations, heart and digestive complains and vision problems, to mention some examples.

23 of the 84 effects sizes were larger than 0.2 and all 95% confidence intervals crossed the zero value.

3.4.4. *PECO 2: In volunteers with IEI-EMF and without IEI-EMF (P), are different exposure levels to RF-EMF (E, C) related to the intensity of self-reported symptoms (O)?*

In order to investigate a potential association between the intensity of exposure and the outcomes, we carried out a meta-regression analysis, using the values of exposure as moderator variable, across all primary outcomes.

We could include 17 of the 18 comparison with participants belonging to the general population and with near-field exposure.

There was no indication of an exposure–response association. According to the meta-regression SMD decreased by 0.01 units for each unit increase of exposure (p = 0.88), suggesting no exposure–response association.

Six of the seven comparisons with exposure values, for participants from the general population and whole body exposure, the coefficient was 0.03 per each unit increase in exposure (p = 0.96).

Looking at comparisons having IEI-EMF participants, the coefficient for near-field exposure (five comparisons) was −0.05 per 1 W/kg (p = 0.90); and for far-field (four comparisons) the coefficient was 0.02 per 1 V/m (p = 0.26), both of them suggesting that changes in exposure had negligible, statistically non-significant, effects on symptoms.

In summary, we could not find any exposure–response relationship in the sense that SMD increased with increasing exposure.

3.4.5. Sensitivity analyses

We re-estimated the confidence intervals of the effects of exposure (SMD) of cross-over trials assuming a within individual correlation (r) of 0.5, as described in the methods. We report this additional meta-analyses in the supplemental figures SAFig03 to SAFig12, corresponding to the Figs. 3–12, describing the main meta-analyses.

All 95% CI narrowed to some extent when considering an r of 0.5, both for the individual studies SMD estimates and for the pooled effect estimates. However, most of 95% CI remained large enough to include the zero value.

The exceptions were two comparisons, both with IEI-EMF participants: near-field effects on headache (SMD: −0.16, 95%CI −0.31 to −0.00) and whole body exposure effects on composite symptoms (SMD; −0.19, 95%CI −0.36 to −0.02). In both cases, exposure would 'improve' the outcomes.

3.4.6. EMF perception

We have plotted sensitivity and specificity for guessing the presence or absence of exposure by type of participants. In the general population, sensitivity was 0.30 (95% CI 0.16 to 0.49) and specificity 0.72 (95% CI 0.53 to 0.86) (Fig. 13a). In the IEI-EMF population (Fig. 13b), sensitivity was 0.67 (95% CI 0.61 to 0.72) and specificity 0.37 (95% CI 0.32 to 0.43). Sensitivity and specificity differed significantly between IEI-EMF and general population samples indicating that IEI-EMF individuals were more likely to indicate the presence of exposure if there was a true exposure but less likely to indicate absence of exposure if there was no exposure. Consequently summarized ROC curve was similar for both samples and close to the 1:1 line indicating that the accuracy of the field detection corresponds to pure chance hit rate (area under the curve: 0.5) (Fig. 14).

The overall O/E perception ratio was 1.01 (0.98 to 1.05) with little heterogeneity ($I^2 = 0$) (Fig. 15), suggesting that the observed accuracy was close to the expected one if exposure was guessed only by chance. In the general population, O/E ratio was 1.00 (95% CI 0.96 to 1.05) and in the IEI-EMF sample O/E ratio was 1.05 (95% CI 0.97 to 1.12). There was no difference in the accuracy of perception between the two groups (p = 0.32). Analysis restricted to studies applying local exposure to the head yielded a pooled O/E ratio of 1.01 (95% CI: 0.95 to 1.08) with virtually no difference between general population and IEI-EMF sample (p = 0.87).

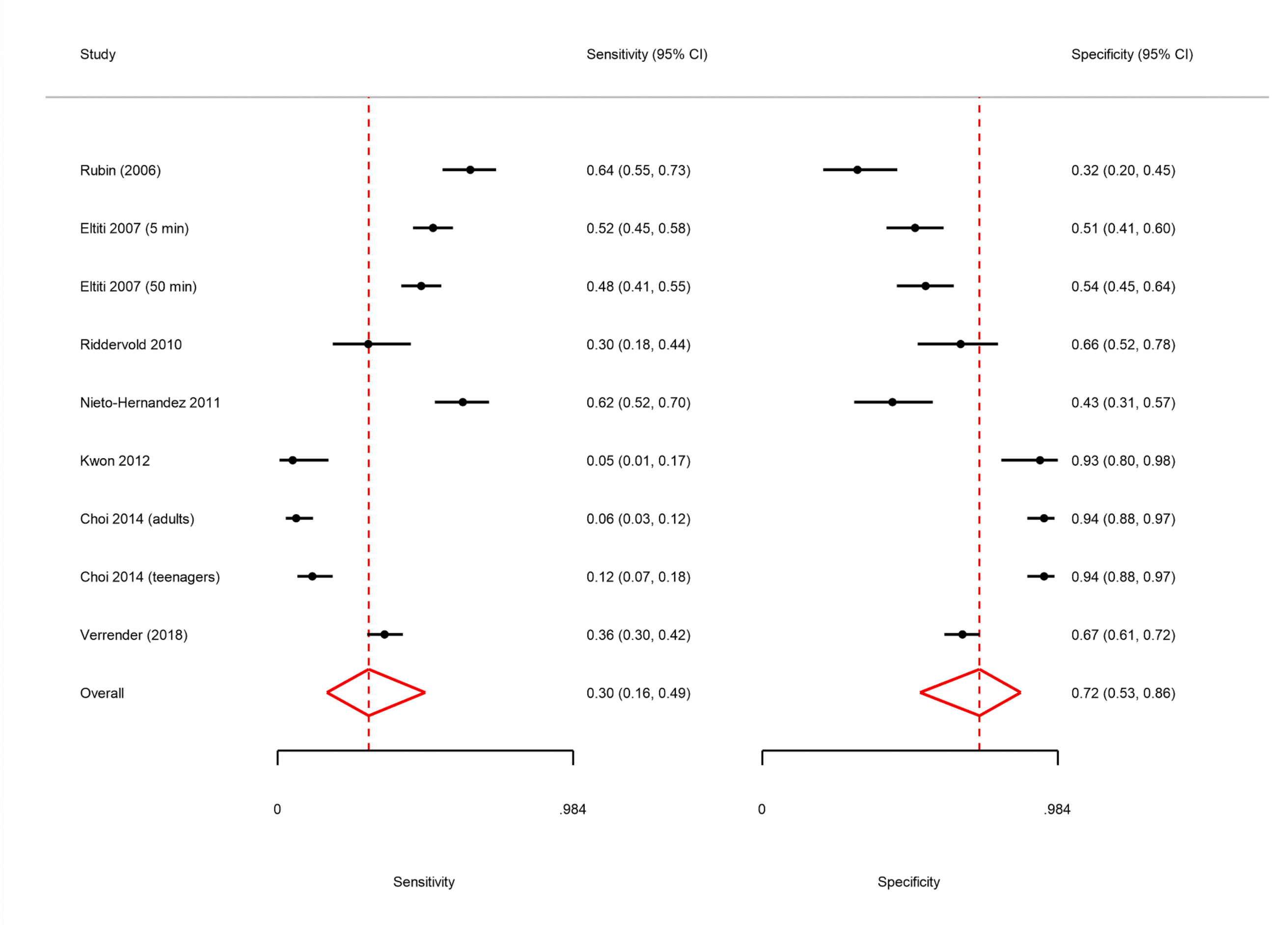

Fig. 13a. Pooled sensitivity and specificity stratified by general population.

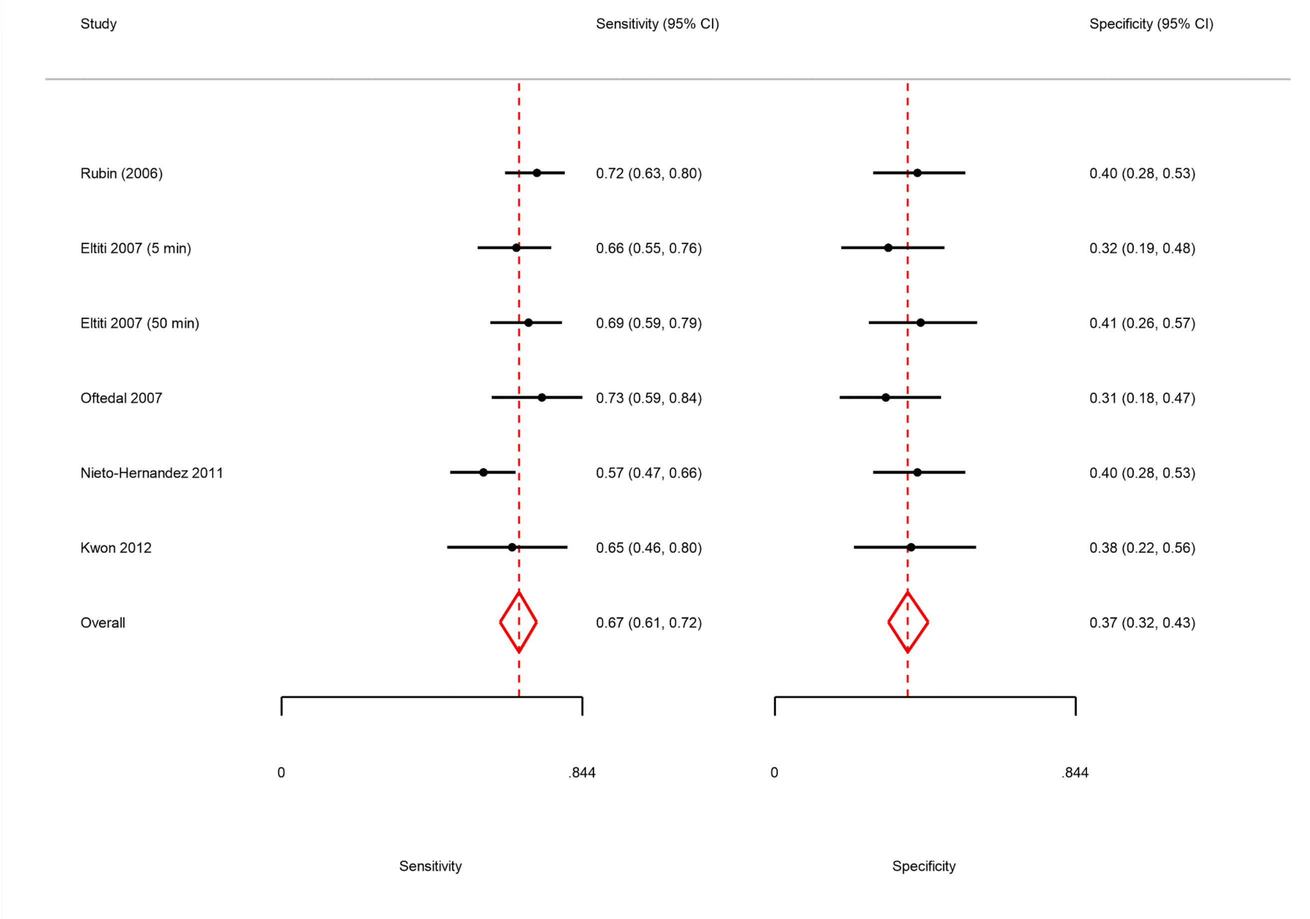

Fig. 13b. Pooled sensitivity and specificity stratified for IEI-EMF individuals.

In a meta-regression analysis, no association between O/E ratio and magnitude of exposure to the head (p = 0.75) or whether participants were IEI-EMF or not (p = 0.98) was observed, suggesting that the lack of differences in the accuracy of observed guesses in relation to the expected ones by chance was not influenced by the level of exposure or the type of participant.

Analysis restricted to studies exposing the whole body yielded an O/E ratio of 1.01 (0.97 to 1.06) with non-significant group differences (p = 0.27) and no indications of an exposure–response trend (p = 0.52) and no difference between the IEE-EMF and the general population sample (p=0.24).

4. Discussion

4.1. Summary of the evidence and interpretation of the results

We have synthesised the evidence reported in 41 experimental studies on the effects of exposure to EMF on subjective symptoms. All the effects estimated on primary outcomes, both in the general population and in the IEI-EMF only groups, were small and non-significant, some of them favouring exposure and others against; these included headache, sleeping disturbances and composite symptoms. The evidence was of moderate or high certainty (depending on the exposure type) for headache in the general population and moderate in IEI-EMF individuals. For sleeping disturbances, the certainty of evidence was moderate for head exposure and low for whole body exposure. The certainty of evidence for composite symptoms was high for whole body exposure (both in the general population and on IEI-EMF individuals) and very low for head exposure comparisons (also in both types of individuals) (see Table 2). The most important driver of level of certainty was related to the ROB, because of the studies classified in Tier-2.

We also did not find any indication that study volunteers could perceive the exposure status better than what is expected by chance. There was, however, an interesting pattern that IEI-EMF individuals rated more often than the general population the presence of a field (higher sensitivity) whereas they had a lower performance in rating correctly the absence of true field status (lower specificity). This can be attributed to IEI-EMF individuals typically self- reporting as being exposed. Overall, there was no difference in the rating accurateness between the two groups.

4.2. Limitations in the evidence

Experimental studies provide the most robust evidence to ascertain the association between exposures and their effects, if the effects are immediate and transient. However, experimental conditions are substantially different from real-life situations: the duration, frequency, distance and position of the exposure vary in real-life situations, as well as the co-exposure to other sources of EMF. This may limit the external validity of the findings. On the one hand, it is conceivable that subtle acute exposure effects are masked in a relative stressful situation of a human experiment, whereas it would be perceived in familiar situations at home. However, the few field studies included in this review did not provide any evidence for this (Danker-Hopfe et al., 2010; van Moorselaar et al., 2017a). Nevertheless, the applied exposure durations may be too short and symptoms may only occur after long-term exposures. From

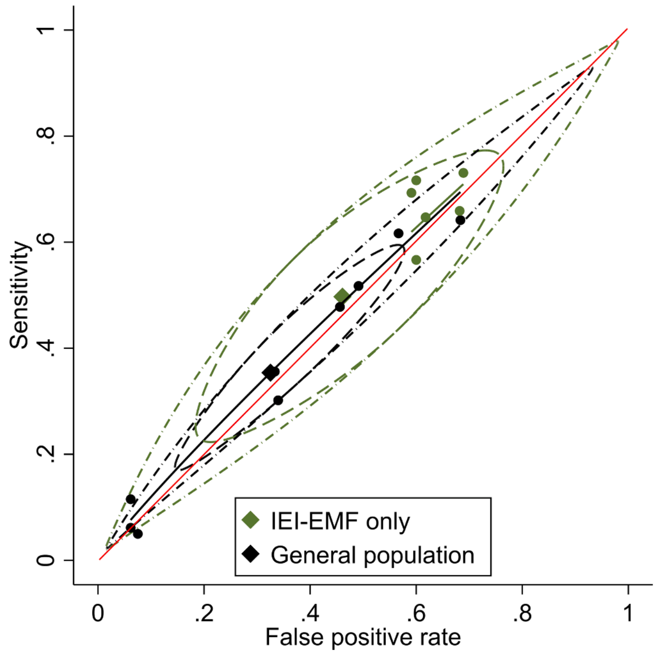

Fig. 14. Summarized ROC curve for general population (black) and IEI-EMF sample (green) including prediction region. Footnote to Fig. 14: the red 1:1 line depicts the random classifier (Area Under Curve value of 0.5). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

an ethical and practical perspective, such effects can only be addressed in epidemiological research. To date, epidemiological studies provide little evidence for long-term effects on symptoms from RF-EMF below regulatory limit, although the certainty of evidence is very low (Röösli et al., 2024).

The outcomes of interest in this systematic review were symptoms, which are typically self-reported. This may have been influenced by the perceptions of participants and their characterisation as IEI-EMF individuals or not. However, in a double blind situation, which was predominant in the included studies, this would have equally influenced all groups, regardless of the real exposure level. Furthermore, the separate analyses of participants classified as general population and IEI-EMF only did not show any systematic difference.

The applied exposure conditions mimicked well realistic exposures situations in everyday life. All studies applied exposure values below regulatory limits for the public. For head exposure, either a real phone or an antenna mimicking a phone was used. Exposure levels were express as SAR_{10g}, which were typically close the regulatory limits of 2 W/kg, representing a rather worst case situation. Whole body exposure was mostly produced by a mobile phone base station and applied exposure levels were mostly 1 V/m and higher, which is quite rare in everyday life (Ramirez-Vazquez et al., 2023; Schmutz et al., 2022). We have conducted meta-regression and did not find any indications that intensity of exposure is relevant. However, for head exposure, different antenna settings may produce variable exposure distribution in the head. As a consequence, there is some uncertainty about the distribution of exposure levels in the different brain regions that may be relevant for the occurrence of symptoms (Boutry et al., 2008) and this could contribute to the absence of observed exposure–response association. For far-field exposure, exposure distribution is more homogenous and thus inherent variability smaller. Nevertheless, no indication was found that symptoms may occur more likely with increasing exposure.

It could be argued, although there are not indications for this, that carry-over effects from RF-EMF exposure when travelling to the study site could have affected the outcome of the study. Similarly, the way of being exposed (e.g. switching on and off, changing the relative position of near field exposures) may produce different effects, but again there is no indication for such a mechanism.

Selection of IEI-EMF individuals in all reviewed studies is based on self-attribution given the lack of objective biomarkers for specific vulnerability to EMF. It has been argued that the group of self-attributed IEI-EMF individuals is a heterogeneous group and only a small subgroup might be indeed particularly vulnerable to EMF (Leszczynski, 2022). Thus, it cannot be ruled out that a real EMF effect in this group is masked by insensitive subjects. It has thus been proposed to do individualized tests, where the same person is multiple times exposed to either sham or real EMF conditions to obtain sufficient data for conducting meaningful statistics. A few such studies have been conducted but none of them found any evidence that there are indeed particularly vulnerable individuals in the group of IEI-EMF using symptom reporting and/or field perception as an outcome (van Moorselaar et al., 2017a; Radon and Maschke, 1998; Verrender et al., 2018a; Verrender et al., 2018b). Moreover, some studies have applied open provocation as a positive control condition (Eltiti et al., 2007a; Verrender et al., 2018a; Wallace et al., 2012). In these situations, more symptoms were reported demonstrating the validity of the experimental set-up and indicating that symptoms are associated with perceived exposure but not real exposure.

One of the drivers compromising the certainty of evidence is the indirectness, due to the selection of participants (e.g. young adults in some studies, only males in others). It could be argued that there is a susceptibility factor in the way individuals react or not to EMF, which could be linked to the age or other factors, as seen in a relative increase in the susceptibility of elderly to air pollution (Simoni et al., 2015).

4.3. Limitations in the review process

We carried out some standardisation of items reported in the papers, due to the large variability in how authors report their experiments. These included conversions of the units of exposure, the statistics used to estimate the effects and the outcome measures including conversion to SMD. The same symptom category was measured with different scales in different studies and several studies reporting on outcomes of the same category using different scales. This was particularly the case in studies reporting sleeping disturbances or other studies with measures in multiple points in time. In these cases, we had to select a single outcome for each study to avoid the situation in which a particular study would be counted more than once in the same comparison. These are mostly outcomes that overlap with those included in our main analyses and/or considered as secondary by the authors. Nevertheless, we have also estimated the effects of exposure on those outcomes and we have not detected any instance suggesting significant effects of exposure. We have made a number of assumptions and decisions along the process, which we have documented in Table S.7 in supplemental material 7.

We also faced missing data in the individual groups that precluded us from recalculating the effects of exposure. In some cases, no data at all was available and results were qualitatively reported in the narrative of the article; in others, a critical data item would be missing (e.g. number of subjects included in the analyses), such as in Loughran et al., 2005; Rubin et al., 2006 orSchmid et al., 2012. We wrote to authors to address some of these issues.

Since the narrative of findings in the absence of quantitative data suggested that there were no differences or not statistically significant differences, we can hypothesise that the lack of this data has not biased our findings towards the no effect zone.

Although the search strategy was quite sensitive, looking at the large number of hits obtained with the searches, we may have missed studies that focused only on perceptions because the search strategy focused on symptoms.

It turned out that studies on perception used many different ways to report their results and only a minority of studies reported sensitivity and specificity. For this reason, we have calculated a simpler measure

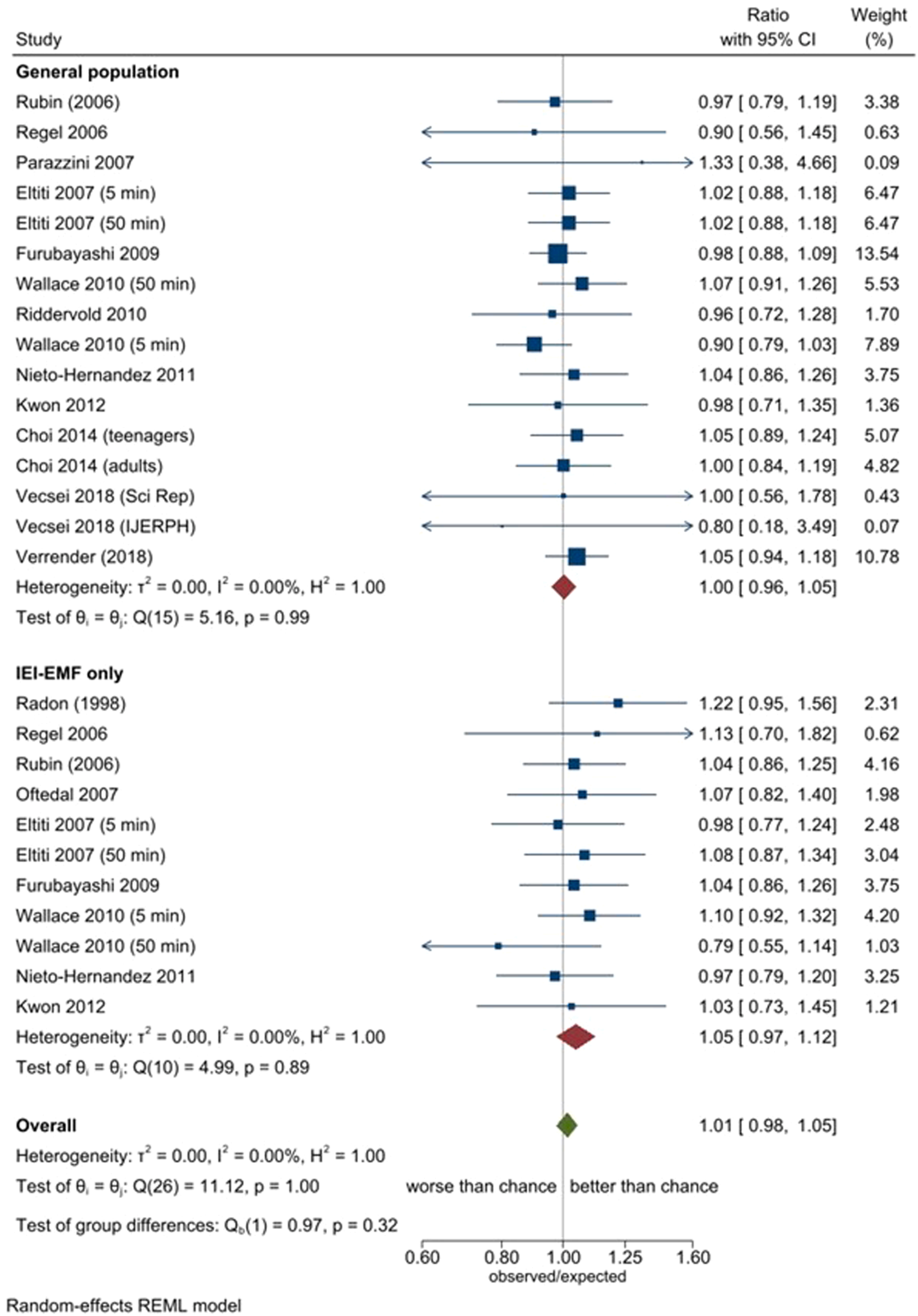

Fig. 15. Pooled ratio between observed and expected correct rating of the exposure condition stratified by population group, ordered by publication year.

comparing observed correct hits in relation to expected correct hits. Of note, we have identified many more studies that looked into perception of fields, some of them as a quality control whether the blinding worked. Such studies usually reported generic statements like "Subjects were not able to distinguish between exposure conditions based on their subjective perception" (Dorn et al., 2014). Other studies with similar statements were: Verrender et al., 2018a; Burgess et al., 2016; van Moorselaar et al., 2017a; Nakatani-Enomoto et al., 2013. Similar statements were also recognized in studies on physiological effects, which were not eligible for this review (e.g. Loughran et al., 2005; Wolf et al., 2006). It is well conceivable that even more studies have collected perception data but not reported as considered not interesting. On the other hand one may speculate that any study that had found a surprising well perception rate, would probably have reported it. This increases the confidence in our certainty of evidence that RF-EMF exposure levels below regulatory limits cannot be perceived.

4.4. Implications for practice

We could not find any evidence that would support an association between exposure to RF-EMF below regulatory recommendations and a large variety of short term reported symptoms; neither evidence that could suggest the capacity of individuals to detect the exposure to RF-EMF. This is the case for the general population, for IEI-EMF individuals, in the main meta-analyses as well as in the exposure–response and sensitivity analyses.

While these findings cannot rule out other long term potential harms of RF-EMF, they suggest that the presence or absence of common symptoms may not become good clinical predictors of the occurrence or evolution of IEI-EMF. It may also indicate that notion of acute effects from RF-EMF below regulatory limits in the everyday environment are better explained with the nocebo or the attribution hypothesis (Dieudonné, 2020).

4.5. Implications for research

The body of evidence in this review seems to consistently suggest the lack of association between EMF exposure and symptoms, in a variety of conditions and populations. The most critical aspect challenging the certainty of the evidence was the limited detail in the methodology of included studies, particularly in the issues related to the exposure randomisation and allocation concealment. While we hardly downgraded the evidence on the grounds of 'indirectness', most of the studies were focusing on adults, young adults and even adolescents, which may have limited the external validity of findings.

In order to confirm the findings of this systematic review, future research should, thus, consider adhering to best reporting practices and considering a wider scope of participants, including, for example, the elderly.

Future research should also be carried out standardising the design of experiments in terms of exposure ranges, timing and sequence of events, so as to make studies more comparable. It may be worth to increase exposure levels above regulatory limits for the general population to explore potential critical threshold for non-specific symptoms. Self-evident such studies need to follow a prudent approach to ensure that any symptoms are transient and do not result in a long term health impairment.

4.6. Deviations from the protocol

- In the protocol we described the perception component of this SR (i. e. to describe the accuracy in the perception of EMF), which has been included in this report. However, it was not formulated as such in the PECO questions.
- In the protocol we suggested that for dichotomous outcomes we would report rate ratios based on the number of persons that report one or more symptom in the intervention and control arms. However, we have converted odds ratios into SMD for effect sizes, as described in the methods.
- In the protocol we suggested to assess the accuracy of the perception of exposure estimating the chance of corrected perception odds ratio. We did not use diagnostic OR but used ROC curves instead because they are more informative.
- In the protocol we suggested that we would combine the effects of local and whole-body exposure from studies that were considered clinically and statistically sufficiently similar. We have presented the findings separately, though, regardless the heterogeneity.
- We did not assess the effects of blinding as suggested in the protocol, since this was one of the exclusion criteria. A few studies reported as well open provocation, the data was not analysed but just narratively reviewed.

4.7. Other information

Registration and protocol

PROSPERO: CRD42021264440 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021264440.

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CRediT authorship contribution statement

Xavier Bosch-Capblanch: Writing – review & editing, Writing – original draft, Software, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Ekpereonne Esu:** Writing – review & editing, Software, Project administration, Methodology, Data curation, Conceptualization. **Chioma Moses Oringanje:** Writing – review & editing, Software, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization. **Stefan Dongus:** Writing – review & editing, Writing – original draft, Methodology, Funding acquisition, Conceptualization. **Hamed Jalilian:** Writing – review & editing, Methodology, Conceptualization. **John Eyers:** Writing – review & editing, Software, Funding acquisition, Data curation. **Christian Auer:** Writing – review & editing, Supervision, Software, Resources, Data curation. **Martin Meremikwu:** Writing – original draft, Methodology, Funding acquisition, Conceptualization. **Martin Röösli:** Writing – original draft, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: All institutions of all authors reports financial support was provided by World Health Organization. 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 (ICNIRP), the Swiss Government (member of the working group "mobile phone and radiation" and chair of the expert group BERENIS), the German Radiation Protection Commission (member of the committee Non-ionizing Radiation (A6) and member of the working group 5G (A630)) and the Independent Expert Group of the Swedish Radiation Safety Authority. From 2011 to 2018, M.R. was an unpaid member of the foundation board of the Swiss Research Foundation for Electricity and Mobile Communication, a non-profit research foundation at ETH Zurich. Neither industry nor nongovernmental organizations are represented on the scientific board of the foundation. For the other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The template for data collection, data extracted from included studies, data used for all analyses and other materials used in the review are available on request.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2024.108612.

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