

Spotlight on EMF Research

Spotlight on “WHO assessment of health effects of exposure to radiofrequency electromagnetic fields: systematic reviews”, a special series in Environment International

Category [radiofrequency, review]

Spotlight - Apr/2024 no.2 (Eng)

Competence Centre for Electromagnetic Fields (KEMF)

1 WHO process towards a new EHC monograph on radiofrequency electromagnetic fields

The World Health Organization (WHO) has been evaluating the potential health effects of exposure to electromagnetic fields (EMF) for decades. The Environmental Health Criteria (EHC) monographs are WHO's formal health risk assessments for chemical, biological and physical agents. They are prepared by independent scientists and are the result of a thorough critical review of the entire body of evidence on a specific chemical or physical agent, such as EMF [1]. To date, the WHO has published three EHC monographs on EMF, including static [2], extremely low frequency (ELF) fields [3] and radiofrequency (RF) EMF [4]. The EHC monograph on RF-EMF was first published in 1993. In light of a mass of new publications in this field this monograph is currently undergoing a comprehensive update, which will result in a new EHC monograph on RF-EMF.

Exposure to RF-EMF (frequencies 100 kHz to 300 GHz) is ubiquitous. The use of RF-EMF has grown steadily since the 1950s and includes various applications, especially telecommunications. In telecommunications, RF-EMF is used for radio and TV broadcasting as well as for mobile telephony and other wireless communications [5]. Since the late 1990s and early 2000s, when mobile telephony became prevalent among the general public, there have been concerns about potential health effects of this technology. Especially, because exposure is highest during mobile phone calls when the device is held close to the ear, concerns focused on potential effects to the brain as a sensitive organ.

Furthermore, with the advent of new technological developments, including 5G mobile networks, and increasing wireless connectivity of devices via the internet, known as Internet of Things, these concerns



remain relevant [6]. This is why conducting an evidence-based health risk assessment regarding RF-EMF is essential to verify whether the current exposure limits are adequate, and to prevent potential health risks. As part of this activity, the WHO conducted a comprehensive global survey in 2018, targeting 300 leading experts in the field of RF-EMF health effect research to identify the most pressing health effects potentially associated with RF-EMF exposure [6]. The 164 responding experts came from 28 different countries. Based on the survey findings, the highest rated outcomes of interest were identified, and the WHO commissioned a series of systematic reviews of observational and experimental studies [6]. In 2019, the WHO launched an open public call for expressions of interest to select the best qualified teams for each systematic review. A committee of the WHO ranked the teams based on predefined criteria. A team must consist of a minimum of two members and WHO strongly encouraged geographical diversity among the team members. In addition, a number of topic-related skill and qualifications were required. For example, for the systematic review on cancer in human observational studies these following qualifications and skills were required by WHO [7]: "expertise in cancer epidemiology, in epidemiological methods, and documented experience conducting epidemiological studies; expertise in RF exposure assessment for epidemiological studies; demonstrated experience in conducting systematic reviews in environmental health; experience in scientific writing and communications on environmental health and/or epidemiology; strong communication skills in English, both written and oral."

The following systematic reviews (SR) were commissioned:

- SR1 – Effect of exposure to RF-EMF on cancer (human observational studies) [5]
- SR2 – Effect of exposure to RF-EMF on cancer (animal studies) [8]
- SR3 – Effect of exposure to RF-EMF on adverse reproductive outcomes (human observational studies) [9]
- SR4 – Effect of exposure to RF-EMF on adverse reproductive outcomes (animal and in vitro studies) [10]
- SR5 – Effect of exposure to RF-EMF on cognitive impairment (human observational studies) [11]
- SR6 – Effect of exposure to RF-EMF on cognitive impairment (human experimental studies) [12]
- SR7 – Effect of exposure to RF-EMF on symptoms (human observational studies) [13]
- SR8 – Effect of exposure to RF-EMF on symptoms (human experimental studies) [14]
- SR9 – Effect of exposure to RF-EMF on biomarkers of oxidative stress [15]
- SR10 – Effect of exposure to heat from any source on pain, burns, cataract and heat-related illnesses

The synthesis of these systematic reviews in combination with a scoping report will be published as a new WHO EHC monograph on RF-EMF. The synthesis process will be carried out by a WHO Task Group. The Task Groups are the highest-level committees within WHO for health risk assessment. Task Group members are individual scientists from different organizations. However, they will serve solely in their individual expert capacity and do not represent their organization, institution or government. The composition of the Task Group is driven by the range of expertise needed to tackle the subject and furthermore by a balance in gender, geographical distribution and the range of opinions on the subject [1]. In addition, the WHO and the Task Group will identify research gaps [16]. Each individual systematic review and the corresponding protocol are being published in a special issue of the international peer-reviewed journal *Environment International* under the title "WHO assessment of health effects of exposure to radiofrequency electromagnetic fields: systematic reviews" (<https://www.sciencedirect.com/journal/environment-international/special-issue/109J1SL7CXT>).

2 Systematic reviews: What are they and how are they conducted?

To inform the general public and support policy makers and health-care professionals in making sound decisions, all relevant and available scientific evidence should be used. However, current evidence can consist of dozens or even hundreds of studies presenting complex, multifaceted and even conflicting evidence, posing challenges to deriving accurate conclusions. Systematic reviews aim to provide a comprehensive overview based on *a priori* defined methods regarding the inclusion and exclusion of all relevant published articles of primary studies, and evaluate the quality of the body of evidence. In addition, based on a systematic review, a meta-analysis can be conducted. A meta-analysis is a quantitative summary using statistical methods to calculate a pooled effect estimate based on available published data [17]. As such, well conducted systematic reviews are considered a good evidence synthesis tool and crucial for evidence-based decision-making [18]. In comparison, a “review” is a qualitative summary of the results of selected individual studies and is often referred to as a narrative review. These narrative reviews can provide a broader overview of a specific topic. However, the included articles in a narrative review are often selected subjectively and unsystematically [17]. The large number of systematic reviews published over the past two decades indicates the strong demand for this form of evidence synthesis [19]. However, concerns have been raised regarding the rapidly increasing number of systematic reviews and meta-analyses. These concerns include the potential susceptibility to bias in these studies, and the massive production of conflicted, redundant, low-quality and potentially misleading evidence synthesis articles [20]. Therefore, clear guidelines to conduct high quality systematic reviews based on validated and standardized methods were developed.

There is a number of different guidelines for systematic reviews depending on the area they are done for, such as those used for toxicology and environmental health research (COSTER) [21], or for randomised controlled trials (RCTs). All WHO commissioned systematic reviews follow the COSTER guidelines. The eight key steps for conducting a systematic review are [21]:

1. Planning the Review and Preparing the Protocol
2. Searching for Evidence
3. Screening Evidence for Inclusion
4. Extracting Relevant Data from Included Study Reports
5. Appraising the Internal Validity of Included Studies
6. Synthesising the Evidence/Deriving Summary Results
7. Interpreting Results
8. Drawing Conclusions

Regarding step 1, it is important to mention that all WHO systematic reviews on the potential effect of RF-EMF have comprehensive study protocols published in the special issue of *Environment International* and registered in PROSPERO (an international prospective register for systematic review protocols, <https://www.crd.york.ac.uk/prospéro/>). These protocols assure that the methods on how the systematic reviews will be carried out are defined *a priori*. This includes e.g. the definition of the databases that will be systematically searched using tailored search terms. The search terms are based on a PECOS statement, a cornerstone for systematic reviews. PECOS stands for Population, Exposure, Comparator, Outcome, Study type (PECOS). PECOS helps to shape the research question, the search algorithm and the pre-defined in- and exclusion criteria to select relevant publications [22]. Another cornerstone for systematic reviews is the Risk of Bias (RoB) assessment, which is part of step 5 “Appraising the Internal Validity of Included Studies” of the COSTER guidelines. WHO systematic reviews follow the method for RoB assessment developed by the National Toxicology Program – Office of Health Assessment and Translation (OHAT approach) [23]. The OHAT approach was followed by WHO systematic reviews due to its versatility and adaptability. In this way,

it was possible to ensure that the RoB assessment instrument can be customised to the individual systematic review topic while at the same time using a standardised instrument. OHAT has a cohesive framework that is compatible with various evidence streams and therefore allows for harmonization of the RoB assessment throughout the ten different WHO systematic reviews. Still, it allows for developing tailored versions for each different systematic review to account for e.g. different study types such as observational studies or experimental studies. Regarding COSTER step 7 “Interpreting Results”, the GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework is used throughout WHO systematic reviews. Here, GRADE [24, 25] is used to systematically assess the confidence in a body of evidence, e.g. the analysis of the overall trustworthiness of the evidence from human observational studies on RF-EMF and cancer. Finally, the findings of all WHO systematic reviews will be reported in line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline [26], which gives clear-cut recommendations to transparently report why the review was done, what was done and what the key findings are.

3 Statement by the BfS

Systematic reviews aim to comprehensively collect, appraise, synthesize and analyze all available evidence on a specific topic such as exposure to RF-EMF and health effects (e.g. cancer). Applying validated approaches to conduct systematic reviews has the potential to increase objectivity and transparency and therefore improve the overall assessment and communication about potential hazards. Due to the objectivity and transparency, systematic reviews are more comprehensible to third parties. However, beside correctly selecting and applying valid methods and guidelines, systematic reviews could still include some subjective judgment to a certain degree for example regarding the RoB.

WHO systematic reviews on health effects of exposure to RF-EMF will be presented in “Spotlight on EMF Research”. They are all based on study protocols published in advance and use validated approaches such as COSTER, OHAT, GRADE, and PRISMA, and therefore aspire to be of high quality. Furthermore, the systematic reviews are of significant interest because they will to a great extent inform the new EHC monograph on RF-EMF.

The Spotlights on WHO systematic reviews that involve employees of the BfS as authors will not contain the section “Comments by the BfS”. This includes SR1 – Cancer (human observational studies), SR6 - Cognitive impairment (human experimental studies), SR9 – Biomarkers of oxidative stress.

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für Strahlenschutz

Impressum

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[urn:nbn:de:0221-2024042443254](https://nbn-resolving.org/urn:nbn:de:0221-2024042443254)

Spotlight - Apr/2024 no.2 (Eng)