Systematic review on the physiological and health-related effects of 5G-relevant radiofrequency fields (3-4 GHz and 20-30 GHz).

Citation

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Review question

The introduction of the latest mobile communications standard of the fifth generation (5G) is accompanied by controversial discussions about potential health risks. According to the current state of knowledge, there is no health risk for frequencies in the range of existing mobile communications applications (approx. 800 MHz–3 GHz) below the recommended international limits. However, higher frequencies up to the millimeter-wave range are used for 5G (>3 GHz). For these frequencies, there are significantly fewer studies available on physiological and health-related effects than for the mobile communications frequencies used in the past. In addition, the higher the frequency, the more energy of the electromagnetic field is absorbed on the body surface resulting in potentially different sites of effects.

The systematic review will provide a comprehensive analysis of the following PECOS (Population, Exposure, Comparator, Outcome, Study design) question:

Are there any physiological or health-related effects (O) of exposure to 5G-relevant radiofrequency electromagnetic fields (3–4 GHz and 20–30 GHz) (E) in humans and mammals (P) compared to no or lower exposure level (C) in experimental and observational epidemiological studies (S)?

Searches

The following databases will be searched: PubMed (https://PubMed.ncbi.nlm.nih.gov/), Web of Science (www.webofscience.com), and the EMF-Portal, a dedicated database of the scientific literature on biological and health-related effects of exposure to electromagnetic fields (https://www.emf-portal.org/en). The search will be supplemented by checks of reference lists in included publications and relevant reviews.

We will consider studies written in English and German.

We will consider studies published in any year.

We will run our first search at the start date of the systematic review process and will re-run searches prior to the final analysis.

Types of study to be included

We will consider peer-reviewed journal articles that report primary data from experimental animal studies (EA) and human controlled trials (HCT) (single-blind or double-blind) as well as observational cohort (Co), case-control (CaCo),

and cross-sectional (CrSe) studies.

We will exclude reviews, statements, research reports, opinion papers, comments, editorials, conference abstracts, proceedings, dosimetric studies, and studies on electromagnetic interference involving implants. Studies investigating electromagnetic fields exceeding or falling below the frequency range or only investigating co-exposures will be excluded. Studies which apply radiofrequency electromagnetic fields with the sole intent of heating tissues significantly above physiological relevant levels (> 42°C) and damaging or destroying tissues will also be excluded. Observational studies using geocoded or self-reported distance to base stations as sole exposure metrics are not eligible.

Condition or domain being studied

The conditions of interest in relation to 5G-relevant radiofrequency electromagnetic fields exposure for this systematic review will be all health-related endpoints, behavior, and other physiological endpoints.

Participants/population

We will be non-restrictive with regard to the population and will include healthy and non-healthy participants of the general population and workers as well as mammals of all ages.

Intervention(s), exposure(s)

Studies will be included if they investigate exposures to radiofrequency electromagnetic fields in the frequency range 3–4 GHz and 20–30 GHz. In case the body of eligible studies after study selection does not prove to be sufficient for a sensible analysis, the frequency range will be expanded to 3–30 GHz. Studies will be included that report at least one of the following descriptors of exposure:

A) body/tissue internal exposure metrics measured or calculated for the particular experimental conditions:

• SAR [W/kg]

• SA [J/kg]

• induced electric field strength [V/m]

• internal magnetic field strength [A/m]

B) body/tissue external or internal exposure metrics describing superficial absorption at frequencies above 6 GHz measured or calculated for the experimental conditions:

• incident power flux density [W/m2]

• incident energy density [J/m^2]

• transmitted (absorbed) power flux density [W/m^2]

• transmitted (absorbed) energy density [J/m^2]

C) body/tissue external exposure metrics (at the location of the exposed body):

• incident electric field strength [V/m]

• incident magnetic field strength [A/m]

• incident power flux density [W/m^2]

Moreover, for observational epidemiological studies, we will also accept self-reported or operator-recorded parameters of use of devices, like mobile phones or wearables, e.g., ‘cumulative hours of use’ and ‘cumulative number of calls’. For occupational exposure scenarios, we also accept Job Exposure Matrices (JEMs).

Comparator(s)/control

We will only include studies with non-exposed control condition (i.e., no exposure beyond background exposure level) or an exposure condition at a lower level.

Main outcome(s)

We aim to assess all physiological (e.g., brain activity), behavioral (e.g., motor activity or anxiety), and health-related effects (e.g., ocular damage, cancer) of exposure to 5G-relevant radiofrequency electromagnetic fields. Therefore, the main outcomes are not predefined by protocol but depend on the included studies.

Additional outcome(s)

None

Data extraction (selection and coding)

Records and extraction data will be managed using the Covidence web application for systematic reviews (http://www.covidence.org/).

Screening for eligibility of all potentially relevant articles will be conducted in two stages. First, the titles and abstracts of the identified articles will be screened independently by two authors. We will exclude records that do not fulfill the inclusion criteria (see points 15.-21.). In the second stage, the full text will be retrieved for those publications that meet the inclusion criteria and the articles will independently be reviewed by two authors. The authors will jointly make a final decision about the inclusion or exclusion of the reviewed articles and possible disagreement will be resolved by discussion with a further reviewer. We will document the selection process in a study flow diagram according to the PRISMA reporting guidelines (Page et al., 2021). A separate table will be provided including articles excluded at the stage of full-text screening, with at least one reason for exclusion for each article.

Two authors will independently extract details regarding the design, methods, and analysis of results of each study. Extracted data will include bibliographic data, fundings, Conflicts of Interest (CoI), study design, examined species and number of study subjects, source of exposure, study focus (endpoint) and method, results, and additional remarks. In addition, for the observational studies, the study population investigated, the type and level of exposure, and the estimation method (e.g., measurement, questionnaire) will be recorded. In experimental studies, the number and size of groups, and exposure parameters (e.g., frequency, field strength, exposure duration, and estimation method) will additionally be recorded.

Risk of bias (quality) assessment

The risk of bias and the quality of included studies will be assessed using a modified version of the recommended approach by the Office of Health Assessment and Translation (OHAT) of the National Toxicology Program (NTP 2019, 2015). This approach has been validated and proven suitable in our previous systematic reviews (Bodewein et al., 2022, 2019; Driessen et al., 2020; Petri et al., 2017; Schmiedchen et al., 2018).

We will consider eleven different criteria to evaluate different types of bias (selection, confounding, performance, attrition/exclusion, detection, and selective reporting). The OHAT criteria will be independently assessed by at least two authors for all included studies. Disagreements in the assessment will be discussed between the authors and resolved by consensus.

Finally, the OHAT approach will be utilized to place individual studies into quality categories. This approach outlines a 3-tier system to rate study quality (1st tier: high confidence in the reported results, 2nd tier: moderate confidence in the reported results, or 3rd tier: low confidence in the reported results). The placement of a study into a quality tier will be based on the risk-of-bias ratings.

Strategy for data synthesis

We will assess the confidence in the body of evidence according to the approach described in the OHAT guidelines, which is based on the GRADE approach. Only studies assigned to be 1st and 2nd tier in the OHAT study quality approach will be included in the evidence synthesis. According to OHAT, available studies on a particular outcome will be initially grouped by key study design features and each grouping of studies will be given an initial confidence rating by those features. This initial rating will be downgraded for factors that decrease confidence in the results (e.g., risk of bias and unexplained inconsistency) and it will be upgraded for factors that increase confidence in the results (e.g., large magnitude of effect, dose response, and consistency across study designs/populations). The evidence appraisal will be conducted at endpoint level. Four descriptors will be used to indicate the level of confidence in the body of evidence: “high”, “moderate”, “low”, and “very low” confidence.

• High Confidence: The true effect is highly likely to be reflected in the apparent relationship.

• Moderate Confidence: The true effect may be reflected in the apparent relationship.

• Low Confidence: The true effect may be different from the apparent relationship.

• Very Low Confidence: The true effect is highly likely to be different from the apparent relationship.

Finally, according to OHAT, the confidence in the body of evidence will be translated into 5 descriptors of the evidence for health effects using the confidence ratings and direction of the effect (“health effect” or “no health effect”): “high”, “moderate”, “low”, “evidence of no health effect”, and “inadequate evidence”. “High,” “moderate,” and “low” level of evidence directly translate from the ratings of confidence in the evidence (see above) in case the exposure is associated with a health effect. If only a “very low” or “no confidence” in the body of evidence is identified, then the level of evidence will be characterized as “inadequate evidence of health effect”. According to OHAT, the descriptor “evidence of no health effect” is used to indicate confidence that the exposure is not associated with a health effect. Because of the inherent difficulty in proving a negative effect, the conclusion “evidence of no health effect” is only reached when there is high confidence in the body of evidence.

Analysis of subgroups or subsets

Heterogeneity within the included studies will determine the type of analysis that is appropriate. We will perform a meta-analysis for subgroups of studies homogeneous in terms of endpoint and exposure characteristics. We consider at least 10 studies sufficient to conduct meaningful analyses. If there is a sufficient number of homogeneous subgroups investigating more than one level or duration of exposure, a dose–response meta-analysis will be conducted. Findings from investigations of study subsets not amenable to quantitative synthesis will be summarized in a narrative synthesis of the available evidence, as suggested by NTP (2019).

Contact details for further information

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Type and method of review

Systematic review

Anticipated or actual start date

21 November 2022

Anticipated completion date

31 January 2024

Funding sources/sponsors

This work is supported by the Ministry of Economic Affairs, Industry, Climate Action and Energy of the State of North Rhine-Westphalia, Germany in the framework of the 5G.NRW-Förderwettbewerb. The funder had no role in the protocol development.

Conflicts of interest

All authors declare that they have no known conflicts of interest.

None known

Language

English

Country

Austria, Germany

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Animals; Electromagnetic Fields; Epidemiologic Studies; Humans; Mammals; Outcome Assessment, Health Care; Radio Waves

Date of registration in PROSPERO

20 November 2022

Date of first submission

09 November 2022

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

20 November 2022

20 November 2022