Peer Review Report

Review Report on Mobile phone use, genetic susceptibility and new-onset chronic kidney diseases

Original Article, Int J Public Health

Reviewer: Frank de Vocht
Submitted on: 15 Oct 2022
Article DOI: 10.3389/ijph.2023.1605358

EVALUATION

Q 1 **Please summarize the main findings of the study.**

The study describes the analyses of associations between mobile phone use and new-onset chronic kidney disease in the in a population of 408,743 participants in the UK Biobank. The authors conclude that Mobile phone use was significantly associated with a higher risk of new-onset CKD in the general population.

Q 2 **Please highlight the limitations and strengths.**

The main strength of the research is that it is conducted in the well characterised population of the UK Biobank, and as a result has a very large population size.

The main limitations are that mobile phone use (the exposure) is not well characterised, in particular across the lifecourse of the participants, and that the manuscript would benefit from more sophisticated statistical analyses (refer to report to authors).

Q 3 **Please provide your detailed review report to the authors. The editors prefer to receive your review structured in major and minor comments. Please consider in your review the methods (statistical methods valid and correctly applied (e.g. sample size, choice of test), is the study replicable based on the method description?), results, data interpretation and references. If there are any objective errors, or if the conclusions are not supported, you should detail your concerns.**

The authors present an interesting analysis of the association between mobile phone use and chronic kidney disease, and also look at gene-environment interactions potentially modifying this association, in the very large and well characterised UK Biobank. The manuscript is well written and provide extensive analyses and discussion of the results.
However, in this reviewer's opinion the authors should first conduct additional, more sophisticated analyses of the results before it would be prudent to discuss specifics. The background to this concern is that a priori the hypothesis is quite unlikely. That does of course not mean that it is impossible, but it does mean that the strong inferences made by the authors should be based on strong results. I provide some suggestions to improve this.

MAJOR
1) The results describes in the manuscript show relatively small effect sizes as well as distinct differences between the populations with different mobile phone use patterns. Residual confounding or possibly some collider bias therefore seem equally plausible, if not more plausible explanations than the one the author report. The potential for stronger causal inferences would benefit from (a) providing a discussion of the hypothesized causal model and whether there might be colliders in the current statistical analyses, and (b) conduct a 2-step approach in which the outcome model is either based on propensity score weighting or, potentially better given the sample size, on a propensity-matched dataset. Given the extent of the UK biobank dataset, I would imagine that an extensive and elaborate propensity score model can be developed which might also include non-linear correlations.

2) the exposure is based on several snapshots of self-reported mobile phone use. This is known to be a weak metric, but improvements are also out of the control of the authors. However, it is strange that significant associations are observed for the weakest measure (current(?) user yes/no) and for weekly usage (in the most recent 3 months), but not for duration of exposure; the latter being much more plausible given the disease development. There is also no association with hands-free calling. This will need to be discussed, as it makes the inferences made implausible.

3) Following on from (2); the available metrics allow for the construction of a 'cumulative exposure metric'. This would seem the most logical metric. Why did the authors not do this, and could this be added.

4) In this study associations are observed with use time of mobile phone. However, when the phone is used it would be taken away from the kidney and thus reduce the exposure, right? This makes it distinctively different from studies of brain cancer. This also weakens the causal potential of the reported associations?

MINOR
1) why is model 3 not conducted for mobile phone user yes/no in Table 2?

2) 4) the authors make reference to a single rat study. Presumably this is a high exposure experiment with rats receiving full-body exposure to RF. This might have induced possible heating effects. Can this be checked and discussed as a possible mechanism.

PLEASE COMMENT

Q 4 **Is the title appropriate, concise, attractive?**

yes

Q 5 **Are the keywords appropriate?**

yes

Q 6 **Is the English language of sufficient quality?**

yes

Q 7 **Is the quality of the figures and tables satisfactory?**

Yes.

Q 8 **Does the reference list cover the relevant literature adequately and in an unbiased manner?)**

yes

QUALITY ASSESSMENT

Q 9 **Originality**

Q 10	Rigor	■■□□□
Q 11	Significance to the field	■■■□□
Q 12	Interest to a general audience	■■□□□
Q 13	Quality of the writing	■■■■□
Q 14	Overall scientific quality of the study	■■■□□

REVISION LEVEL

Q 15 Please make a recommendation based on your comments:

Major revisions.