

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Ethical and social implications of using predictive modeling for Alzheimer's disease prevention: a systematic review protocol
AUTHORS	Angehrn, Zuzanna; Nordon, Clémentine; Turner, Andrew; Gove, Dianne; Karcher, Hélène; Keenan, Alexander; Neumann, Monika; Sostar, Jelena; de Reydet de Vulpillieres, Frederic

VERSION 1 – REVIEW

REVIEWER	Zaven Khachaturian Alzheimer's & Dementia
REVIEW RETURNED	03-Oct-2018

GENERAL COMMENTS	<p>The authors are encouraged to include a brief history the concept or construct of 'Prevention' in relation to AD-dementia in the context of how or the evolution the notion of 'interventions' changed during the course of the last 40-years struggle to find a cure.</p> <p>The idea of 'interventions', which connotes a broad range or types of 'treatments' was not part of the lexicon in the world of therapy development 20-30 years ago. I think this type of discourse will add value to this manuscript because as the authors have pointed out there is a major shift in the field to intervene earlier and earlier; it would be important for the reader to understand how and why this shift occurred. The ultimate ethical challenge/question for society - what or where is the ethics of not intervening in asymptomatic stages of the disease - because of ethical concerns, that is how do you deal with the problem of [or when] 'ethical concerns' themselves become the source of 'harm' ?</p>
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REVIEWER	Martin Knapp LSE, UK
REVIEW RETURNED	12-Oct-2018

GENERAL COMMENTS	<p>This review covers an under-researched topic, and - once completed - the review will make a valuable contribution to the literature. The protocol is well-written and the review is well-designed. My only suggestion would be to provide a fuller description of what are meant by 'ethical and social implications' earlier in the paper. There is some detail on p.9 that could usefully be added into the Introduction perhaps.</p>
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REVIEWER	Michael Arribas-Ayllon Cardiff University, United Kingdom
REVIEW RETURNED	12-Oct-2018

GENERAL COMMENTS	<p>I have no particular reservations concerning the protocol, however, the authors may want to clarify the issue of generalizability of their data analysis in terms of how it differs from statistical-probabilistic generalizability (see Smith 2017 https://www.tandfonline.com/eprint/TdSrZrgz7WMZzPz5i7YM/full).</p> <p>Also, the protocol highlights that thematic analysis will entail 'interpretation' of complex ethical arguments, but it doesn't really explain what this entails. How do the authors account for group interpretation of key or indicative texts? Given the multidisciplinary nature of the team, how will you achieve consensus regarding interpretation.</p>
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VERSION 1 – AUTHOR RESPONSE

- Comments from Reviewer 1: We re-wrote the introduction section so that it briefly describes the evolution of possible interventions in the context of our increasing understanding of Alzheimer's Disease.
- Comments from Reviewer 2: We provided an explicit definition of "ethical concern" and "social implication".
- Comments from Reviewer 3: We provided additional explanation of how group interpretation will be achieved/facilitated in our research. We also included a passage clarifying our position on validity and generalizability of this study. However, we chose not to comment on the differences between the concepts of generalizability in qualitative vs. quantitative studies as we felt that this topic is more suited for methodological and philosophical paper, where it can be analysed in due detail.
- Comments from the Editor: We updated the order of Co-authors, corrected page numbers in the PRISMA checklist, checked the order of citing supplementary files in the main document, added the data sharing statement and submitted all supplementary files as PDF. Please kindly advise us in case there are any further editing requirements that need to be met.

VERSION 2 – REVIEW

REVIEWER	Zaven Khachaturian Alzheimer's & Dementia
REVIEW RETURNED	19-Dec-2018

GENERAL COMMENTS	No comments
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REVIEWER	Martin Knapp LSE, UK
REVIEW RETURNED	23-Dec-2018

GENERAL COMMENTS	None
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VERSION 2 – AUTHOR RESPONSE

Upon your feedback, the following changes have been made to make sure that this protocol adheres to BMJ Open editorial policies:

- "Ethics and Dissemination" section was added to the main body of the manuscript.

- The abstract and main body of the manuscript were updated with specific dates, to reflect the current status of the review (study selection has been finalized on October 8th 2018, and currently data extraction and qualitative analysis are ongoing).

- The Research Checklist has been updated, so that that the page and line numbers to which we point there match the current version of the manuscript.

Based on our judgement, the manuscript now includes all the required sections and pieces of information, however we will be happy to make further adjustments if required.