Reviewer’s report

Title: Key challenges for delivering clinical impact with artificial intelligence

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Reviewer: John P. Fox

**Reviewer's report:**

This paper is one of a clutch of recent overviews of AI in medicine (to which this reviewer has contributed) but it is particularly important because it is provided by a highly influential organisational that has led key developments in AI/machine learning (Google Deepmind). While it is a technically well informed and sophisticated discussion the authors are also mostly medically trained and include senior members of the company (its CMO and one of its founders).

Despite the authors' having a commercial interest in the subject of the review the authors are very clear about the level of hype about ML alongside the current lack of evidence of adoption and clinical value (with the likely exception of medical imaging) and a variety of other significant challenges. This review is a valuable contribution that will help BMC Medicine readers and the wider healthcare community, medtech developers, AI researchers etc to have an informed conversation about what is required to deliver the potential benefits of AI for better patient care and improved clinical services.

This reviewer's most general concern is the absence of even a brief acknowledgement of the long history of research on using traditional symbolic AI techniques in medicine, which have also tried to address some of the challenges that are rightly identified (e.g. the importance of explanation) and can be applied to others. In the following I will refer to the traditional approach as AI/KE (Knowledge Engineering). However this reviewer has worked on AI/KE for many years, so one might say I have a vested interest in promoting them so it seems appropriate to identify myself; my name is John Fox and my interests and expertise can be reviewed at linkedIn profile is https://www.linkedin.com/in/john-fox-914a19b/.

**Specific comments**

The paper starts with a very useful compilation of published trials and evaluation studies on AI/ML and an honest recognition of the limited adoption of these methods to date. It is commonly said that medical imaging seems closest to large scale adoption but this is only a small part of medical technology and an even smaller part of everyday clinical practice. AI/KE has not been extensively applied to imaging or signal processing generally, but it has significant progress in other aspects of routine care (e.g. many kinds of clinical decision-making, treatment planning, workflow management) so perhaps we should be looking for hybrid approaches?

I strongly support the authors' positions on rigorously designed and executed trials, the issue of prospective/retrospective comparisons etc - educating the technology community whose members are
frequently new to medical research norms is key to clinical credibility. The start-up mantra "move fast and break things" is not appropriate in healthcare, where the primary goal is to maximise quality, safety and improved patient experience.

Transparency, accountability, bias and ethics of AI are already topics of significant public concern. The suggestion that we need a better understanding of interaction between human and algorithm is correct. I would add that KE methods already address these issues to some extent and research on explainable AI by behavioural and cognitive scientists and others is increasingly focused on topics like meaningful representation of medical knowledge and expertise, explanation strategies and dialogues etc. This again speaks to the need for hybrid methods perhaps.

Over-generalisation across different patient populations, case mixes, territories etc is a well known concern (the pioneer of Bayesian diagnosis methods Tim de Dombal made this point in the seventies) and is exacerbated by a lack of transparency. In my view AI/KE offers a way of empowering clinicians to participate critically in design, development and deployment of point of care services like decision support, workflow and patient management services.

I believe that the point about the ability to compare different algorithms in a way that is clinically intelligible is key to large scale engagement with clinicians, many of whom are currently bemused about whether AI is their friend or foe. I have recently completed a paper on this topic and would be happy to share and discuss it with the authors.

Author declarations

The authors say they are employed by Google LLC but that funding is "not applicable" - is that saying there is no conflict of interest? If that is the intention I think it needs explanation.

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Yes, I have shares in a commercial company in the medical AI field. I have declared this and my name to the authors of the paper.

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