

Peer Review File

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Reviewer A

The purpose of this literature analysis is admirable, but I feel that the methods are inadequate. I have thoroughly reviewed the manuscript and would like to give some suggestions that may improve the analysis.

The major problem is only using the search term “artificial intelligence”. This may miss many publications. I would refer the author to several publications where he could study the methods and how they analyzed the data.

The 2021 Stanford AI Index Annual Report (Daniel Zhang, Saurabh Mishra, Erik Brynjolfsson, John Etchemendy, Deep Ganguli, Barbara Grosz, Terah Lyons, James Manyika, Juan Carlos Niebles, Michael Sellitto, Yoav Shoham, Jack Clark, and Raymond Perrault, “The AI Index 2021 Annual Report,” AI Index Steering Committee, Human-Centered AI Institute, Stanford University, Stanford, CA, March 2021. https://aiindex.stanford.edu/wp-content/uploads/2021/03/2021-AI-Index-Report_Master.pdf) reviews the Ai publications in chapter 1 . They use the Scopus database by Elsevier and arXiv. The Appendix shows the methodology and they used approximately 800 AI search terms in their search.

Also looking at another good study . Sreedharan S et al The top 100 most cited articles in medical artificial intelligence. J Med Artif Intell 2020. 3.3. They used these search terms [“artificial intelligence” OR “machine learning” OR “deep learning” OR “natural language processing” OR “support vector machine” OR “naïve bayes” OR “bayesian learning” OR “artificial neural network” OR “random forest” OR “machine intelligence” OR “k-nearest neighbor” OR “decision tree learning” OR “data mining” OR “fuzzy” OR “computational intelligence” OR “computer reasoning”] AND [“medicine” OR “medical” OR “surgery” OR “surgical” OR “healthcare”].

I think using a more search terms will give us a more accurate review.

- Thank you for this good suggestion, and for the two example publications. The Embase database offers the ‘explode’ option (/exp), which maps the search term to the Emtree preferred indexing term and then searches for the related narrower or child terms. This option was already used in the ‘Disease areas and application areas using AI’ section. I now used the search term “machine learning/exp OR 'artificial intelligence/exp”, which gives many more results related to AI. The Emtree entries can be found here: <https://www.embase.com/#emtreeSearch/search/51317::machine%20learning> and

<https://www.embase.com/#emtreeSearch/search/10089::artificial%20intelligence>. I updated all nine figures including the supporting text.

In the first paragraph (Introduction) : mentions that “the field of AI was born at “ . The Dartmouth conference was when the term AI was first used.

→ This has been corrected.

In the section on AI related terms, the purpose of fig 2 (WordCloud of all titles) is unclear and does not add anything.

→ This section has been removed, as both reviewers found it to be not informative.

The paragraph on AI algorithms does not give any meaningful information.

→ This paragraph gives an overview of the ten most popular AI algorithms, and shows their occurrence in the biomedical literature over time. This gives insights into where AI is being used and in what direction AI is developing, For example, CNNs are by far the most popular algorithm. They are mainly used for image analysis and classification, but new applications for CNNs are being invented: video processing, natural language processing, speech recognition, etc. And GANs are gaining popularity since 2018, which might point in the direction of growing importance of synthetic data since the enforcement of the GDPR.

The discussion and conclusion is good but it is not backed up by reliable data.

Because of these flaws I do not feel that the manuscript accurately describes the current state of the literature of Artificial Intelligence in Biomedicine. Major work and revisions are needed. I suggest that the author review some of the references I have mentioned and others and come up with better methods. I have attached a file with some methods which may be helpful.

→ I revised the methodology using the ‘explosion’ option in Embase. The search terms now include many more related terms, such as ‘neural network’, ‘hidden markov model’, ‘random forest’, etc. This resembles the methodology of the two examples provided by the reviewer. All figures and accompanying text were updated. Therefore, the discussion & conclusion section is now based on reliable data.

Reviewer B

The manuscript presents some interesting information about the trends of application of AI in healthcare. This will certainly add to the body of knowledge around translational AI. However, the manuscript is written in the form of a business report or white paper rather than as a research articles. Also, there is a mixture of content about generic AI and applied AI in healthcare, which makes it

confusing for the reader. To make it suitable for publication in this journal, suggest the following:

- 1) Presentation of a clear section as to the methodology of the literature review i.e. number of databases accessed, table of search terms, results, filtered results, methods of screening, inclusion and exclusion criteria, sampling and analysis
 - ➔ Thank you for your suggestion. The methodology is quite straightforward. I now included table 1 which shows an overview of the databases and queries used to create each figure.

- 2) Separation of generic AI and applied AI in healthcare related results
 - ➔ The distinction between generic AI and applied AI is not completely clear to me. The manuscript describes the usage of AI in biomedical literature, so in my eyes this is all about the application of AI in biomedicine. With “generic AI”, do you mean more general sections like “AI over the years” and “AI algorithms”? And with “applied AI”, do you mean more specific sections like “Disease areas and application areas using AI” and “Drugs studied with AI”? I have included this distinction at the end of the introduction. If this is not what you meant, please clarify so I can take further action.

- 3) Author's perspective of what is diagnosis and what is prognosis stated clearly. This is in relation to Figure 4
 - ➔ I have included definitions of both terms using the MeSH database.

- 4) Please take out Figure 2, it is not informative nor suitable for a journal publication
 - ➔ The section (including figure 2) has been removed, as both reviewers found it to be not informative.