PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Systematic review protocol assessing the potentiality of algorithms and artificial intelligence adoption to disrupt patient care with a safer and faster medication management.
AUTHORS	Oliva, Antonio; Altamura, Gerardo; Nurchis, Mario Cesare; Zedda, Massimo; Sessa, Giorgio; Cazzato, Francesca; Aulino, Giovanni; Sapienza, Martina; Riccardi, Maria Teresa; Della Morte, Gabriele; Caputo, Matteo; Grassi, Simone; Damiani, Gianfranco

VERSION 1 – REVIEW

REVIEWER	Siefkas, Anna Harvard University T H Chan School of Public Health
REVIEW RETURNED	30-Nov-2021

GENERAL COMMENTS	The authors have laid out a generally clear strategy for performing their systematic literature review and meta-analysis. I look forward to reading the completed study in the future. My major concern is that the search strategy is not detailed enough – simply listing examples of the key terms likely to be used does not fully describe the search strategy the authors intend to you. A detailed search strategy, including the exact terms that will be searched and how they will be combined with Boolean operators, should be included for each database the authors intend to search. While it is unlikely the authors will find any existing meta-analyses of this topic, it should be listed as an exclusion criterion in case one is found. Only original primary analyses should be included. What do the authors mean by NRCT? It is not clear whether these refer to observational (e.g., cohort) studies. If the authors intend to include both randomized and observational studies, I suggest that the authors perform separate pooled analyses for these groups of studies. Additionally, the authors may need to separately pool studies by each included outcome (e.g., hospitalization should be examined separately from mortality reductions). If small numbers of studies are found, simply pooling the estimates for percent reduction in medication errors may be more appropriate.

REVIEWER	Saha, Sajal Monash University, Australia, General Practice

REVIEW RETURNED	22-Dec-2021

GENERAL COMMENTS	This is an interesting systematic review protocol aims to investigate the impact of AI algorithms on drug management in primary care. The review protocol has been well designed and well written. However, few areas might be further considered and improved. 1. The limitations and risk of doing meta-analysis could be elaborately described. 2. Detail plan of meta-analysis and sensitivity analysis might be clarified with sufficient explanations 3. What if enough studies are not available for meta-analysis or analysis of the outcomes? 4. Implications of the study could be described under a separate discussion section 5. AI can be defined and introduced with examples 6. Inclusion criteria in relation to AI can be explained 7. How specificity and sensitivity of the search strategy will be determined?

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

1. My major concern is that the search strategy is not detailed enough – simply listing examples of the key terms likely to be used does not fully describe the search strategy the authors intend to you. A detailed search strategy, including the exact terms that will be searched and how they will be combined with Boolean operators, should be included for each database the authors intend to search.

We thank the reviewer for the insightful suggestion. We proceeded to attach the full search strategy, for each scientific database queried, as a supplementary material file. In case the reviewer thinks it should be directly added to the text, we will be happy to comply.

1. While it is unlikely the authors will find any existing meta-analyses of this topic, it should be listed as an exclusion criterion in case one is found. Only original primary analyses should be included.

We thank the reviewer for the valuable advice. We specificized the criteria, as requested, in page 3 (see "study selection criteria" paragraph).

1. What do the authors mean by NRCT? It is not clear whether these refer to observational (e.g., cohort) studies. If the authors intend to include both randomized and observational studies, I suggest that the authors perform separate pooled analyses for these groups of studies.

We thank the reviewer for the indication. We intend to include both randomized and observational studies, thus, as you suggested, we will perform separate pooled analyses for each group of studies. Therefore, we added in the manuscript the following sentence: "Separate pooled analyses will be performed for each group of studies (i.e., RCTs and NRCTs).".

1. Additionally, the authors may need to separately pool studies by each included outcome (e.g., hospitalization should be examined separately from mortality reductions). If small numbers of

studies are found, simply pooling the estimates for percent reduction in medication errors may be more appropriate.

We thank the reviewer for the precious comment. We specified as suggested in the methods section, "Descriptive analysis and meta-analysis" paragraph.

Reviewer 2

1. The limitations and risk of doing meta-analysis could be elaborately described.

We thank the reviewer for this precious advice. We added the following brief paragraph in the methods section (Descriptive analysis and meta-analysis paragraph): "The main limitations related to the meta-analysis are the biases affecting primary studies, publication, reporting and selection bias, and the heterogeneity. Nonetheless, quality assessment and sensitivity analyses will be conducted, by two independent authors, to overcome these caveats".

1. Detail plan of meta-analysis and sensitivity analysis might be clarified with sufficient explanations

We thank the reviewer for this observation. We detailed the plan in the "Descriptive analysis and meta-analysis" paragraph.

1. What if enough studies are not available for meta-analysis or analysis of the outcomes?

We thank the reviewer for this observation. If enough studies are not available for meta-analysis, as described in the methods section (Descriptive analysis and meta-analysis paragraph), a narrative synthesis of the retrieved evidence will be performed including also tables and figures.

1. Implications of the study could be described under a separate discussion section

We thank the reviewer for the valuable suggestion. We added a separate paragraph describing the implications of the study.

1. AI can be defined and introduced with examples

We thank the reviewer for this observation. In the introduction, AI was defined and introduced with examples according to the reviewer indications (page 2).

1. Inclusion criteria in relation to AI can be explained

We thank the reviewer for this observation. We did not put any restriction in terms of AI type. Given that, we specified, in the methods section, the exclusion criteria related to AI-based interventions.

1. How specificity and sensitivity of the search strategy will be determined?

We thank the reviewer for the observation. Following this comment, we added a brief paragraph to the methods section highlighting this process.

REVIEWER	Siefkas, Anna Harvard University T H Chan School of Public Health
REVIEW RETURNED	09-Mar-2022

GENERAL COMMENTS	The authors have thoroughly revised the protocol and have addressed my major concerns. I am looking forward to seeing the final meta-analysis.