Peer Review File

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Reviewer Comments

(1) Provide an explicit statement of the objective(s) or question(s) the review addresses
1. Response: We appreciate the reviewer's insightful comments and suggestions. Accordingly, we have explained the objective of this review in detail. The revised content is added to the last paragraph of the Introduction section.**(Page 6,Lines 113-118)**

Changes in the text：The objectives of this narrative review are to (1) understand the role of AI in improving the management of patients with ARDS;(2) explore the subgroup classification of patients with ARDS via unsupervised clustering; (3) explore the use of supervised predictive models for the early detection of ARDS; (4) focus on research gaps in ARDS prediction; and (5) point out the current problems that could be solved by applying AI in ARDS.

(2) Consider using PRISMA checklist for reporting systematic review (BMJ. 2021 Mar 29;372:n71. doi: 10.1136/bmj.n71.)
2. Response: We appreciate the reviewers' suggestions very much.We also considered the use of a checklist to report the review and thank you for your rigorous review and careful work. However, let us politely indicate that this is a narrative review. On the official website of this journal, different checklists are used for narrative reviews and systematic reviews. For narrative reviews, the special narrative review checklist is used, whereas, for systematic reviews, the PRISMA checklist is used. According to your suggestion, we will use the narrative review checklist strictly based on journal requirements.

Thanks again for the reviewer's suggestions. In the future, we will report reviews in strict accordance with each checklist when writing them.

Website:https://atm.amegroups.com/pages/view/guidelines-for-authors#content-2-2-1
Narrative review checklist:

Narrative Review Checklist

Section/Topic	Item No	Item	Reported on Page Number/Line Number	Reported on Section/Paragraph
TITLE				
Title	1	Identify the report as a Narrative Review or Literature Review.	Page 1 Lines 2-3	Title
ABSTRACT				
Structured summary	2	Provide a structured summary with the subsections as: Background and Objective, Methods, Key Content and Findings, Conclusions.	Page 3-4 Lines 40-75	Abstract
INTRODUCTION				
Rationale/background	3	Describe the rationale for the review in the context of what is already known.	Page 4-6 Lines 79-111	Introduction Paragraph1-3
Objectives	4	Specify the key question(s) identified for the review topic.	Page 6 Lines 113-119	Introduction Paragraph4
METHODS				
Research selection	5	Specify the process for identifying the literature search (eg, years considered, language, publication status, study design, and databases of coverage).	Page 6-7 Lines 122-141	Methonds
DISCUSSION/SUMMARY				
Narrative	6	Discuss: 1) research reviewed including fundamental or key findings, 2) limitations and/or quality of research reviewed, and 3) need for future research.	Page 8-27 Lines 145-505	Discussion
Summary	7	Provide an overall interpretation of the narrative review in the context of clinical practice for health professionals, policy development and implementation, or future research.	Page 27-28 Lines 507-519	Conclusion

Please leave this space alone as it will be supplemented by the editorial office when needed.

(3) Suggest to indicate precise date range for search (from MMDDYY to MMDDYY) instead of year only in Table 1 (Timeframe)

3.Response: We sincerely thanks for the reviewer's comments.We have added a precise date range for search in Table 1 and its description in the Methods section.**(Table 1 and Page 6,Lines 123)**

Changes in the text：December 1, 2011, to August 5, 2022

(4) Consider provide more precise query terms such as ((ARDS) AND (machine learning)) AND ((diagnosis) OR (prognosis)). In the current manuscript, by providing just a list of keywords is insufficient to capture the exact search terms.

4.Response: Thanks for the reviewer's excellent suggestion.We have added more precise query terms in this manuscript in the Methods section.**(Page 6,Lines 125-127)**

Changes in the text: The following terms were used as index terms: ((ARDS) AND (machine learning) OR (artificial intelligence)) AND ((diagnosis) OR (prognosis) OR (complications) OR (phenotype)) to identify eligible studies.

(5) Exclusion criteria: "Some COVID-19 related ARDS articles are excluded". Why

are COVID-19 related ARDS articles excluded from the analysis? There are quite a few ARDS prediction models developed for pandemic; the rationale for this exclusion is not clearly explained in the manuscript.

5.Response: Thanks for the reviewer's comments.Indeed, we excluded some COVID-19 related ARDS articles. Please allow us to explain politely.

1) The purpose of this narrative review is to summarize the use of AI in the typical ARDS subtype and prediction models. While searching the literature, some studies [1-3] showing significant differences between COVID-19 related ARDS and typical ARDS were considered, for example, differences in the injury site, clinical features, the timing of onset, respiratory system compliance, and management protocols. At present, COVID-19 related ARDS is usually proposed separately for the study; therefore, we excluded COVID-19 related ARDS.

-1.Li X, Ma X. Acute respiratory failure in COVID-19: is it "typical" ARDS? Crit Care. 2020;24(1):198. doi: 10.1186/s13054-020-02911-9.

-2.Bos LDJ. COVID-19-related Acute Respiratory Distress Syndrome: Not So Atypical. Am J Respir Crit Care Med. 2020 ;202(4):622-624. doi: 10.1164/rccm.202004-1423LE.

-3.Gibson PG, Qin L, Puah SH. COVID-19 acute respiratory distress syndrome (ARDS): clinical features and differences from typical pre-COVID-19 ARDS. Med J Aust. 2020;213(2):54-56.e1. doi: 10.5694/mja2.50674.

2) As you indicated, "there are quite a few ARDS prediction models developed during the COVID-19 pandemic," we are more willing to conduct a separate study on COVID-19 related ARDS. Our team is also currently writing a review on the application of AI in COVID-19 related ARDS.

We have added the reasons for exclusion in the Methods section.**(Page 6-7,Lines 132-135)**

Changes in the text:Considering that some studies [8-10] suggest that COVID-19 related and typical ARDS are significantly different in multiple ways, such as the injury site, clinical features, time of onset, respiratory system compliance, and management protocols. Therefore, COVID-19 related ARDS articles were excluded.

(6) Further to (4), why only some COVID-19 articles excluded? What is the exact criteria for deciding which article to be included? This will prevent other researchers from verifying the findings as criteria are not laid out clearly.

6.Response: Thanks for the reviewer's comments.We apologize for our unclear description. We acknowledge that our inclusion and exclusion criteria were not fully written. We are very grateful to the reviewer for raising this issue and allowing us to correct it. We agree with Li X, Bos LDJ, Gibson PG et al., and distinguish COVID-19 related ARDS from typical ARDS to review. Therefore, some COVID-19 articles were

excluded.We added the above-modified content in the Methods section.**(Page 7,Lines 135-140)**

Changes in the text:The exact article inclusion criteria were whether full-texts could be obtained; AI and ARDS data were used in subtype or prediction models; publication types were formal; and English language was used. The exact article exclusion criteria were those that were COVID-19 related ARDS; were duplicate records; included no adults; and were reviews.

(7) "These searches yielded nine articles related to ARDS subtypes and five articles related to diagnosis and survival prediction." It is a little surprising that only very limited papers that study the ARDS subtypes, and diagnosis/prognosis.
Suggest to include a clear search strategy and flowchart including the resulting number of papers. Examples: We used four online research databases: PubMed, IEEE Xplore, ArXiv, and Web of Science. Initial screening used the keywords AAA, augmented with terms BBB resulting in xx articles. We excluded xx duplicate articles and articles due to reason CCC, resulting in xx articles. Finally, the articles based on DDD, resulting in xx articles. Records with insufficient data were removed, leading to xx resources
7.Response: We sincerely appreciate that you gave us such a detailed example. When we completed the inclusion of studies, we were as surprised as you that the use of AI in subgroup clustering and prediction models in medicine is very popular at present, but the number of AI in ARDS is not that large. Perhaps in the future, more AI research can focus on the heterogeneous syndrome: ARDS.

We have followed your suggestion to draw a flowchart and clearly describe the search strategy. We added the modified content to the Discussion section **(Page 8, Lines 146-154)**; the flowchart is on **Page 9.**

Changes in the text:We used four online research databases: PubMed, Web of Science, Embase, and Medline databases. Initial screening used the keywords respiratory distress syndrome, machine learning, and artificial intelligence augmented with terms diagnosis, prognosis, and complications resulting in 1,074 articles. We excluded 116 duplicate articles and 91 articles for which full text was not available, leaving 867 articles. Finally, after applying the inclusion and exclusion criteria, ten articles associated with ARDS subtypes and five articles related to diagnosis and survival prediction were selected (Figure 1). No studies used AI to predict ARDS-related complications were found.

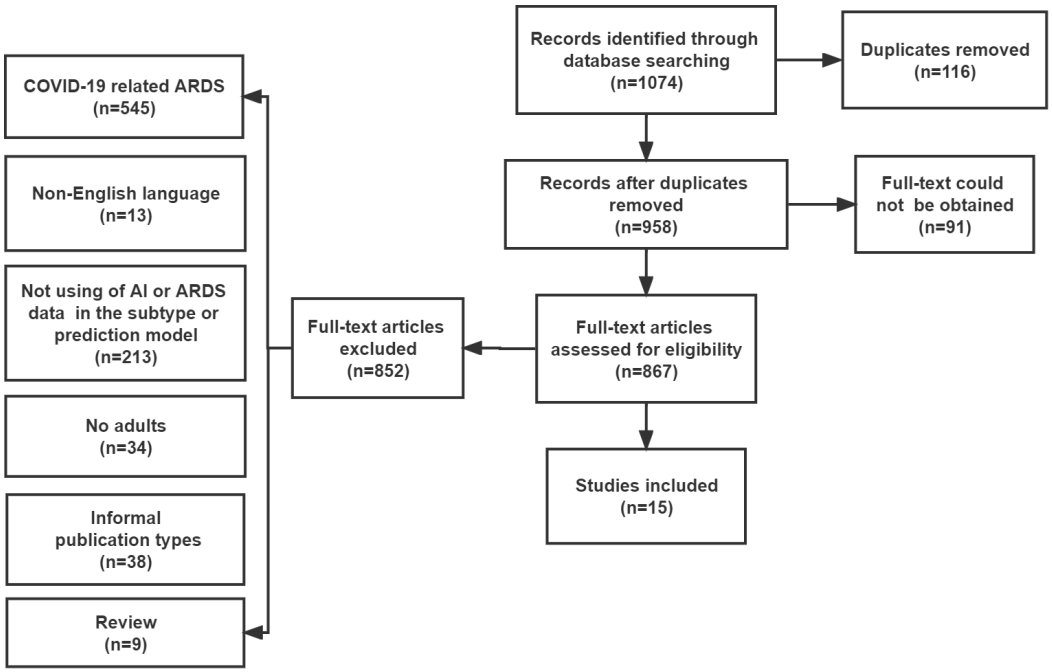

Figure 1 Flowchart for the narrative review

(8) Consider to use PROBAST (Prediction model Risk Of Bias ASsessment Tool) framework to assess the risk of bias (ROB) and applicability of diagnostic and prognostic prediction model studies for systematic review. (Reference Ann Intern Med. 2019 Jan 1;170(1):51-58. doi: 10.7326/M18-1376.

8.Response: We appreciate for raising such an important issue.As suggested, we have carefully read the reference you provided and carefully reviewed PROBAST to assess the risk of bias and applicability of the prediction model.

We have added one Table**(Table 4)** in our revised manuscript and added the modified content in the Discussion section**(Page 24, Lines 436-450;Page 26-27, Lines 489-494).** Thanks for your careful review again!

Changes in the text:

3.2.3 Risk of bias (ROB) and applicability

We used the PROBAST criteria to assess the ROB in the prediction model (Table 4). To assess the intensity of ROB, all models in the predictor domain were rated as low bias. One study in the participant domain was rated as highly biased, and one study was unable to identify bias in outcomes. The risk of bias in the analysis domain is generally high, and the high ROB usually originates from project 4.3-were all enrolled

participants included in the analysis? Moreover, 4.5-was the selection of predictors based on univariable analysis avoided? In the model applicability, all models had good overall applicability, and the consistency of study participants, predictors, and outcomes with the review questions was high.

Table 4 The risk of bias (ROB) and applicability of prediction model studies

Study	ROB				Applicability			Overall	
	Participants	Predictors	Outcomes	Analysis	Participants	Predictors	Outcome	ROB	Applicability
Ding et al.	+	+	+	-	+	+	+	-	+
Zeiberg et al.	+	+	+	-	+	+	+	-	+
Brown et al.	+	+	?	-	+	+	+	-	+
Huang et al.	-	+	+	-	+	+	+	-	+
Zhang	+	+	+	-	+	+	+	-	+

+ indicates low ROB/low concern regarding applicability:- indicates high ROB/high concern regarding applicability;? indicates unclear ROB/unclear concern regarding applicability.

It is important to select high-quality models to provide useful tools for clinical risk screening. Although some models are rated as high risk of bias, this does not negate their predictive value. Therefore, the medical staff should comprehensively consider the predictive performance of the model, availability of predictors, convenience of outcome measurement, and applicable object of the model to select an appropriate model.

(9) Not sure if I agree with the conclusion that "Currently, there is no prognostic prediction model for ARDS complications." How about the following articles?
- van der Zee P, Rietdijk W, Somhorst P, Endeman H, Gommers D A systematic review of biomarkers multivariately associated with acute respiratory distress syndrome development and mortality? Crit Care. 2020; 24: 243
- Fifty years of research in ARDS. Genomic contributions and opportunities.
Am J Respir Crit Care Med. 2017; 196: 1113-1121
- Lancet Respir Med. 2022 Apr;10(4):367-377. doi: 10.1016/S2213-2600(21)00461-6.
9. Response: We sincerely thanks for the reviewer's comments.We apologize for such an inappropriate description. Maybe it would be more appropriate to change the sentence to "Currently, there is no model has used AI to predict ARDS complications were found."
We have carefully read the references you have provided and please allow us to politely explain each study.

-van der Zee P et al.: We have read the reference you provided with great interest and found that this article is a systematic review. This review presents a list of biomarkers for ARDS mortality and development tested in multivariate analyses. It does not meet the scope of our discussion on the AI application in ARDS and rarely involves the prediction of ARDS complications. Thank you again for your reference.
- Fifty years of ARDS research: This article reviews some applications of the genomics research field in ARDS, revealing that the ongoing genetic research offers unique contributions to elucidating ARDS pathogenesis and the paradigm of precision ARDS medicine. It also does not conform to the prediction model of AI in ARDS complications.
-Lancet Respir Med. 2022 Apr: For this article, we agree that it was excluded in the last screening for our reasons. It appeared in our last round of literature list; however, the original text of this article could not be obtained at that time due to various reasons. Now, we added this article to the review**(Page 14-15, Lines 294-306;Table 2)**, thanks again for your kind reminder.

Changes in the text:
Maddali et al. [23] validated the ARDS subphenotypes in two ARDS observation cohorts using clinical classifier models with readily available clinical variables in 2022. The primary model included only vital signs and laboratory variables, whereas ventilatory variables and demography were added to the secondary model. They also assessed the performance of the primary model in the Early Assessment of Renal and Lung Injury (EARLI) using data automatically extracted from an electronic health record. They found that a classifier model using clinical variables alone could also be used in the ARDS observation cohort to prepare for the assignment of ARDS subphenotypes at the bedside. Furthermore, the Lung Safe study identified a lower mortality rate with high PEEP than with low PEEP in the hyperinflammatory subphenotype (54% vs. 62%) and a lower mortality rate with low PEEP than with high PEEP in the hypoinflammatory subphenotype (32% vs. 34%).