

## Reviewer 1

First, the author conducted a systematic review of studies that reported predictive factors for mortality in CKD patients (including non-dialysis dependent CKD patients ) with associated area under the receiver operating characteristic (ROC) curve [AUC] analysis. The findings would help guide the future design of an accurate mortality risk calculator for CKD patients. Second, the systematic review follows the PRISMA statement with two independent researchers. Third, the author proposed limitations of the study and the future directions of the topic described in this manuscript.

A: Thank you reviewer 1 for your comments. We hope that the findings from our study would help guide mortality prediction among CKD patients.

## Reviewer 2

Abstract Methods: need to specify in methods how predictive factors were categorized into outstanding, excellent, and acceptable.

A: We have added the definition of each AUC categories in the abstract; *"AUC of 0.70-0.79 is considered acceptable, 0.80-0.89 is considered excellent, and more than 0.90 is considered outstanding."*

Manuscript Methods: Search strategy: why were the terms "end-stage kidney disease" OR "ESRD" added with an AND and not an OR in the search terms. This means that the population of interest was patients with ESRD and not CKD in general. However, the objective gives an impression that the population of interest is CKD patients. Inclusion criteria: would suggest using the term "CKD patients without renal or kidney transplant" instead of "non-transplant CKD".

A: Thank you reviewer 2 for noticing the error. We apologize for the typo and confusion that might mislead you. The correct statement should be *"("Chronic kidney disease" OR "CKD" OR "end-stage kidney disease" OR "ESKD" OR "end-stage renal disease" OR "ESRD")"* Supplemental Document 1 contains the search protocol for each database. However, we made a typo when briefing the search terms under Methods during manuscript writing. The sentence has been corrected accordingly.

Results Figure 1: For transparency, please provide reasons for all articles excluded by the following broad categories- ineligible population, different outcome of interest, ineligible study design, ineligible outcome metric (i.e., AUC not reported).

A: Thank you for your comment. We have elaborated that categories for which studies were excluded in detail under the footnote of Figure 1, *"Figure 1. Flowchart of the literature search and study selection. "Undesired study design" includes non-human studies (n = 2); "Insufficient data" includes conference abstracts that reported only AUC without 95% CI (n =5); "Subjects are contaminated" refers to a study that has mixed CKD and non-CKD subjects (n = 1)."*

Study population: Need to report total no. of patients before describing the no. of patients without dialysis and with ESRD.

A: Thank you for your comment. We have edited the sentence as follows: *"Of 14579 patients from 18 studies, 832 patients had non-dialysis CKD while 13747 patients had dialysis-dependent CKD."*

Table 2. how were the situations in which the same predictor was found to have different

AUC values from two different studies were handled? Need to include this information in Table 2 footnote or Methods section.

A: Thank you for the question. Some studies may report the same predictor for mortality but with a different AUC. This is because the demographics and clinical characteristics are different. Moreover, because our study is a systematic review only, we did not pool the variables to perform meta-analysis. In fact, we reported the same variable separately because it comes from different studies. To prevent confusion to the readers, we have added this comment in the footnote of Table 2, *“Although some variables may be reported from several studies but with different AUC, each variable is presented separately in the table.”*

Discussion Limitations: it is not possible to "avoid" but "identify" the selection bias by conducting the risk of bias assessment.

A: Thank you. We changed the word *avoid* to *minimize*, *“Second, all included studies were observational in nature, making them susceptible to selection bias. However, we minimized this bias by conducting the risk of bias assessment.”*

Supplemental Table 1: Please cite all articles in the leftmost column of the table.

A: Thank you. All references added.

**Science editor:** 1 Scientific quality: The manuscript describes a systematic reviews of the prediction of mortality among patients with chronic kidney disease. The topic is within the scope of the WJN. (1) Classification: Grade B and Grade B; (2) Summary of the Peer-Review Report: The authors conducted a systematic review of studies that reported predictive factors for mortality in CKD patients with associated area under the receiver operating characteristic curve analysis. The findings would help guide the future design of an accurate mortality risk calculator for CKD patients. However, the questions raised by the reviewers should be answered;

A: The responses to reviewers are provided above.

and (3) Format: There are 2 tables and 2 figures. (4) References: A total of 99 references are cited, including 13 references published in the last 3 years; (5) Self-cited references: There is 1 self-cited reference. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated;

A: Our self-referencing rate is less than 10% ( $1/99 = 1\%$ ). All references cited here are essential in the discussion.

and (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com). The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade C and Grade A. 3 Academic norms and rules: The authors provided

the Biostatistics Review Certificate, and the PRISMA 2009 Checklist. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJN. 5 Issues raised: (1) The language classification is Grade C. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>;

A: Dear Editors Lian-Sheng Ma and Ya-Juan Ma, we apologize appreciate you and the journal for being thorough and help improve our manuscript. We have carefully reviewed and corrected by both with our native English users in our team such as Dr. Michael Mao is American-born Native English user. We also additionally use Microsoft word checking grammar/spelling, as well as subscribed program, Grammarly. Once again, we apologized for the misspells/errors. We have reviewed and corrected accordingly.

(2) The title is too long, and it should be no more than 18 words;

A: We appreciate the editor. The updated title is of 12 words; ***“Prediction of Mortality among Patients with Chronic Kidney Disease: A Systematic Review”***.

(3) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

A: The original figures have been attached along with manuscript submission.

and (4) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text. 6 Recommendation: Conditional acceptance.

A: Article Highlights are present at the end of the main text:

## **ARTICLE HIGHLIGHTS**

### ***Research background***

CKD is a common medical condition with increasing prevalence. Understanding risk factors for mortality in CKD patients could mitigate death.

### ***Research motivation***

Evidence have shown that several clinical characteristics are associated with mortality in CKD patients using regression analyses. However, the accuracy of these mortality prediction factors has not been clearly demonstrated.

### ***Research objectives***

To demonstrate the predicting factors for mortality among CKD patients by utilizing the AUC analysis.

### ***Research methods***

Ovid MEDLINE, EMBASE, and the Cochrane Library were searched for eligible articles through January 2021. Only studies that reported their mortality predictive factors with AUC and 95% CI were included. These factors were classified as acceptable, excellent, or outstanding based on their AUC.

### ***Research results***

Of 1,759 citations, a total of 18 studies (n = 14,579) were included in the systematic review. About 832 patients had non-dialysis CKD and 13,747 patients had dialysis-dependent CKD

(2,160 hemodialysis, 370 peritoneal dialysis, and 11,217 undifferentiated mode of dialysis). Of 24 predicting factors, none were considered out-standing for mortality prediction. A total of seven predicting factors (NT-proBNP, BNP, suPAR, augmentation index, left atrial reservoir strain, CRP, and systolic PAP) were identified as excellent. Seventeen predicting factors were in acceptable range which we classified into the following subgroups: predictors for non-dialysis population, echocardiographic factors, comorbidities, and miscellaneous.

### ***Research conclusions***

This study determined several mortality risk factors for CKD patients that were deemed acceptable or excellent. Echocardiography is an important tool for mortality prognostication in CKD patients.

### ***Research perspectives***

The results of this study provide a preliminary perspective on the importance of identifying better prognostic factors for mortality in CKD patients. There is a lack of risk factors with AUC greater than 0.90. Current identified risk factors may be combined to create a mortality risk calculator for CKD patients, which could be subsequently validated in future research.

**(3) Company editor-in-chief:** I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Nephrology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

A: Thank you.