Subject: FW: Your Submission DRAA-D-23-00015

Date: Thursday, April 6, 2023 at 9:46:22 AM Eastern Daylight Time

From: Rasheeda Hall, M.D.

To: Abimereki Muzaale

CC: McAdams DeMarco, Mara

Attachments: Supplemental Material 1.17.23.docx, PIM Classes and Mortality Edit DAA 1.17.23.docx,

Figure 2.tif, Figure 1.tif

Abi,

There are some statistical requests from the reviewers. Particularly Reviewer #1 "Methodology" pasted again below:

b) Methodology:

- -Add a table comparing patients included and excluded from the study.
- -How many patients were loss to follow-up? How did you deal with attrition biases?
- -in the selection of covariates, which is the weight of the variable "number of medications" or polypharmacy?
- -Add a measure of prognostic accuracy (C index, C statistics) for the survival models. Additionally, to evaluate the non-variability of prognostic accuracy between the two cohorts, compare the prognostic accuracies of the development and valdiation cohorts
- c) Results
- -Report the mortality rates in the two cohort in person years.
- d) Supplementary Table 1: is fairly informative. Please modify it by adding the specific Beers Criteria for each class/drug, and also report the prevalence of each drug (inappropriate) prescription. Which was the prevalence of inappropriate antibiotic prescription?

The deadline is May 3.

Please start to work on these requests, and we can check in next Thursday on your progress.

I have attached the documents submitted to the journal.

Thanks so much!

Rasheeda

----Original Message-----

From: em.draa.0.827b57.2cd6cb08@editorialmanager.com

<em.draa.0.827b57.2cd6cb08@editorialmanager.com> On Behalf Of Drugs & Aging (DRAA)

Sent: Wednesday, April 5, 2023 6:26 PM

To: Rasheeda Hall, M.D. <rasheeda.hall@duke.edu>

Subject: Your Submission DRAA-D-23-00015

Dear Dr Hall,

I have now received comments from the reviewers of your manuscript, 'Association of Potentially Inappropriate Medication Classes with Mortality Risk Among Older Adults Initiating Hemodialysis' that is being considered for publication in Drugs & Aging.

Based on our editorial assessment and the reviewer comments received, I can advise that your manuscript

can be accepted for publication after you have carried out the suggested minor revisions.

When preparing your revised manuscript, you are asked to carefully consider the reviewer and editorial comments, which can be found below.

Please submit your revised manuscript together with a point-by-point summary of how you have dealt with each of the comments. Please provide a clean version of the revised manuscript and a version that highlights (with 'tracked changes' or coloured/highlighted/underlined text) all changes made during the revision process.

In order to submit your revised manuscript, please access the following website:

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Your username is: Your username is: RasheedaHall If you have forgotten your password, you can click the 'Send Login Details' link on the Editorial Manager Login page.

I look forward to receiving your revised manuscript by 03 May 2023. However, please let me know if this deadline does not fit with your current schedule, to allow a more suitable deadline to be arranged. In addition, please do not hesitate to contact me should you need to discuss any of the points raised by the peer review process.

Finally, you may like to consider adding a digital feature to your revised manuscript. The journal can accept a range of features, including animated abstracts, video abstracts, slide decks, audio slides, instructional videos, infographics and animations. Plain-language summaries (PLS) can also be published with articles. For more information on digital features and PLS, please see the 'Guidelines for Digital Features and Plain Language Summaries' that are available on the journal homepage under submission guidelines. PLEASE NOTE - digital features submitted after acceptance will be subject to a charge to cover editorial processing. If submitted post publication, the journal may also be required to publish a correction notice alongside the feature. We therefore encourage authors to submit features before acceptance.

With kind regards,

Alison Fitches, PhD
Section Editor
Drugs & Aging
Adis Journals, Editorial Office

Comments for the Author:

Editorial comment:

1. Please delete the key words (leave the key points)

Reviewer #1: In this manuscript, the authors explored the prognostic impact of potentially inappropriate medications among older patients undergoing hemodialysis; this segment of the geriatric population is particularly vulnerable and shares a high mortality risk, thus identification of risk factors is deemed necessary to identify individuals at increased risk of adverse outcomes.

In this study, the authors developed and validated a prognostic model including a list of 30 PIMs and evaluated the risk of mortality in this population.

The topic is up to date, and the manuscript is interesting, with all the analyses well conducted. I have only some minor concerns:

a) Introduction:

- -are there any PIMs that can be reverted by hemodialysis?. Briefly, discuss this topic.
- -Line 66-68: "several studies demonstrated prevalence and harm.. " is too generic; I suggest the authors to report some data regarding prevalence of PIMs in patients with CKD and more specifically in those with advanced CKD.

b) Methodology:

- -Add a table comparing patients included and excluded from the study.
- -How many patients were loss to follow-up? How did you deal with attrition biases?
- -in the selection of covariates, which is the weight of the variable "number of medications" or polypharmacy?
- -Add a measure of prognostic accuracy (C index, C statistics) for the survival models. Additionally, to evaluate the non-variability of prognostic accuracy between the two cohorts, compare the prognostic accuracies of the development and valdiation cohorts
- c) Results
- -Report the mortality rates in the two cohort in person years.
- d) Supplementary Table 1: is fairly informative. Please modify it by adding the specific Beers Criteria for each class/drug, and also report the prevalence of each drug (inappropriate) prescription. Which was the prevalence of inappropriate antibiotic prescription?

Reviewer #3: The manuscript reports a cohort study that analyzed prescription data from patients on hemodialysis, especially those about medications on Beers list, that explicitly should not be prescribed to elderly. The authors identified some high risk PIMs associated with mortality using Cox regression. Methodology is appropriate and statistics conducted correctly. The authors honestly admitted limitations of their study, and made appropriate conclusions. Since majority of patients were prescribed with PIMs, it is not surprising that many classes of PIMs turned out to be not associated with mortality, but this is probably type 2 statistical error. se The manuscript should be accepted for publication. My only suggestion is to rephrase methodology section and avoid repeating in the first person: "We did that..."

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