Fw: Reminder: Expert Opinion On Drug Metabolism and Toxicology #TrackingId:13920584

Omid Mehrpour <omid.mehrpour@yahoo.com.au>

Wed 1/18/2023 10:00 AM

To: Biswas, Ashis <ASHIS.BISWAS@UCDENVER.EDU>;Abdullah Al Masud <abdullahalmasud.buet@gmail.com>

[External Email - Use Caution]

I could extend the deadline till 01-Feb-2023. Sincerely Omid

"Do not let what you cannot do interfere with what you can do." -John Wooden

---- Forwarded message -----

From: "iemt-peerreview@journals.tandf.co.uk" <iemt-peerreview@journals.tandf.co.uk>

To: "omid.mehrpour@yahoo.com.au" <omid.mehrpour@yahoo.com.au>

Sent: Wednesday, 18 January 2023 at 01:54:08 am GMT-7

Subject: Re: Re: Reminder: Expert Opinion On Drug Metabolism and Toxicology #TrackingId:13920584

Dear Dr. Mehrpour,

Due date is 01-Feb-2023

Best regards,

Rekha - Journal Editorial Office

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Expert Opinion On Drug Metabolism & Toxicology

From:omid.mehrpour@yahoo.com.au

Sent:14-01-2023 06:02 **To:**rekha.g@straive.com

Cc:

Subject: Re: Reminder: Expert Opinion On Drug Metabolism and Toxicology

Would you kindly extend our deadline for 10 days please?

Sent from Yahoo Mail for iPhone

On Friday, January 13, 2023, 10:54 PM, Expert Opinion On Drug Metabolism and Toxicology <onbehalfof@manuscriptcentral.com> wrote:

14-Jan-2023

Dear Dr Omid Mehrpour:

This e-mail is simply a reminder that your revision is due on 18-Jan-2023. If it is not possible for you to submit your revision within this time frame, we will consider your paper as a new submission.

Please see a copy of the decision letter below which contains details of how to submit your revision and any comments from the editor/reviewers:

04-Jan-2023

Dear Dr. Mehrpour,

Thank you for your patience while your manuscript was under review. Your manuscript, entitled "Deep Learning Neural Network Derivation and Testing to Distinguish Acute Poisonings", which you submitted to Expert Opinion On Drug Metabolism and Toxicology, has now been reviewed. The referee comments are included at the bottom of this letter.

The referees would like to see some revisions made to your manuscript before it can be considered any further. Therefore, I invite you to respond to the referees' comments and editorial comments below and submit a revised manuscript by 18-Jan-2023.

PLEASE NOTE: When you revise your manuscript please highlight the changes you make in the manuscript by using the track changes mode in MS Word or by using bold or coloured text.

To start the revision, please click on the link below:

*** PLEASE NOTE: This is a two-step process. After clicking on the link, you will be directed to a webpage to confirm. ***

https://mc.manuscriptcentral.com/eomt?URL_MASK=e2df6af9485149719535669032e4c4c1

This will direct you to the first page of your revised manuscript. Please enter your responses to the comments made by the referees and editorial office in the space provided. You can use this space to document any changes you made to the original manuscript. Please be as specific as possible in your response to the referees.

This link will remain active until the due date stated above. If you begin a revision and intend to finish it at a later time, please note that your draft will appear in the "Revised Manuscripts in Draft" queue in your Author Centre.

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Alternatively, you can also submit by logging into https://mc.manuscriptcentral.com/eomt: Click on 'Author Centre' > 'Manuscripts with Decisions' > 'Create a Revision'.

Because we are trying to facilitate timely publication of manuscripts submitted to Expert Opinion On Drug Metabolism and Toxicology, your revised manuscript should be uploaded by the due date specified above. If it is not possible for you to submit your revision by this date, please do let me know as soon as possible.

Once again, thank you for submitting your manuscript to Expert Opinion On Drug Metabolism and Toxicology and I look forward to receiving your revision.

Sincerely,

Sharon Salt

Expert Opinion On Drug Metabolism and Toxicology

Comments from the Editorial Office to the Author (important - please ensure that a response is provided for each comment listed below in order to avoid delays with processing your revised manuscript submission):

- Please complete and upload the attached author disclosure form. In addition, please include a Declaration of Interest section, at the end of the manuscript. This section should include any sources of funding, along with any financial/other relationships for each author (such as consultancies, employment, expert testimony, honoraria, speakers bureaus, retainers, stock options or ownership).
- Please could you confirm if the following funding statement is correct, and insert any relevant grant numbers, if applicable:
- This paper was not funded.
- Please could you confirm if the following declaration of interests statement is correct:
- The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.
- Section numbering: please ensure each section heading/subheading in the main body of text is numbered (Your introduction should be numbered 1 and any subheadings therein 1.1, 1.2, 1.3 and so on etc). The Abstract does not need to be numbered. Please include appropriate subheadings, and ensure these are numbered sequentially.
- References: I would be very grateful if you could check that your references match our house style:
- o References should be numerically listed in the reference section in the order that they occur in the text.
- o Please ensure no references are duplicated in the reference list.
- o References should appear as a number i.e., [1,2] in the text in square brackets. (Please move any superscript reference citations, to inside the sentence-end punctuation). All reference citations in the text should appear at the end of the sentence, prior to punctuation. (e.g., "....[2]."
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- o Please include your websites / patents in the main reference list if citing a website, please ensure your access date is also included. If you have included a weblink in the main text, please change this to

a numbered citation and include it within the reference list.

- o Annotations for your references: 4-8 references should be chosen from your bibliography and highlighted as being '*' of interest, or "**" of considerable interest, with a brief sentence explaining why in each case.
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- o For more information on our referencing style, please look under the heading 'Journal' on page 3 in the following link: https://www.tandf.co.uk//journals/authors/style/reference/tf NLM.pdf
- Tables 1-3 and Figures 1-4: please ensure that:
- i. Tables and figures are cited in the text
- ii. Tables are in an editable format i.e., .doc, .xls, .ppt
- iii. Study references are separated into a separate column in tables. References in tables should be numbered as if they have appeared in the main body of text where the table was first cited.
- iv. Footnotes contain all abbreviations, symbol information and permission blurbs.
- v. Please provide legends for all of your figures and tables, in a separate section at the end of the document.
- vi. Figures are in the form that they should appear in the final publication. Please note that no editing of figures will occur during the copyediting/typesetting stage, so it is important that they are correct at this stage.
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ORIGINAL RESEARCH-SPECIFIC COMMENTS:

- Please check to ensure p-values have been included wherever significance is claimed. Please add leading zero before all p-values (as per journal style). Include as much data as possible. A p-value or confidence interval must always be cited when data are presented, compared, when a claim is made, or the word significant or significantly is used, including in the abstract.
- Please include the following headings in your abstract: Background, Research design & methods, Results, Conclusion.
- If your manuscript describes a clinical trial, the trial must be registered in a public repository, with the registry name and trial registration number included in the abstract and the Methods section of the paper. Retroactive registration is acceptable as long as the date of registration is included in the above mentioned sections of the manuscript.
- ETHICS APPROVAL & INFORMED CONSENT: If your manuscript describes a clinical trial, please confirm that the research was conducted with approval from a formal ethics review committee (or followed the principles of the Declaration of Helsinki) and with written consent from the patients. This information should be included in the Methods section of the manuscript.

Comments from the Referees to the Author:

Referee 1

The manuscript attempted to develop DNN models which may predict the most probable agent a poisoned patient has been exposed to among eight possible drugs based on clinical features. It's an interesting and valuable topic. But it is felt that the study in its current cannot be accepted and still needs major rework.

1. I cannot find the codes and data. For DNN study, this issue must be resolved before the paper is accepted. Please provide this.

- 2. The application domain of models need to be defined. The poisonings other than these 8 drugs are impossible to predict using the proposed models.
- 3. The definition or composition of a test or validation set needs to be clarified.
- 4. As can be seen from Table 1, there is a serious imbalance between different categories of data. I don't think this metric "overall accuracy" is meaningful in such study.

Referee 2

In the work reporting, acute poisonings of a predetermined list of medications and authors have intended to build a deep learning system that predicts the most likely agent a poisoned patient was exposed to. They have used data from the National Poison Data System (NPDS) and two Deep Neural Networks (PyTorch and Keras) to perform multiclass classification tasks. They have identified that the best performance was achieved in the diagnosis of single-agent poisoning by sulfonylureas, acetaminophen, benzodiazepines, and aspirin.

However, some concerns need to be addressed before considering this manuscript for publication. I have listed these issues below:

- 1) The author should add a graphical abstract so that the paper could be more comprehensible to the readers.
- 2) The authors must highlight the complexity of polysubstance exposure discussed in the paper.
- 3) Details of the Keras framework are missing from the methodology section.
- 4) The author could provide a tabular representation of certain examples of clinical overlaps for single-agent poisonings discussed in the methodology section.
- 5) Conclusion section could be more elaborative.

In my perspective, the findings of this study are worthy of publishing. However, before publishing, the work requires some modification.

Referee 3

The authors explicitly state the 'pilot' (and thus somewhat preliminary) character of the study and this is important and the authors must be complimented for this specification.

1) My basic concern is that 131 features are very difficult to ascertain in 'real world' conditions of patients coming to the an emergency room. That is to say that, in my opinion, the work can greatly benefit by a drastic reduction of scored symptoms in order to find a reduced set of 'most relevant descriptors' that in turn can be fed into the ML process to see if the system keeps (or at least does not degrade too much) its performance.

This selection can be made in many ways but I suggest the Legendre algorithm (INDVAL, see: https://www.sciencedirect.com/science/article/pii/S1476927119302440).

Thus I push the author to check this possibility that in turn can be profitably used for ameliorating the 'explainability' of the ML procedure (see

https://www.sciencedirect.com/science/article/pii/S2666389920300258).

If you have any questions or experience any difficulties submitting your revised manuscript, please contact the journal's editorial office at IEMT-peerreview@journals.tandf.co.uk.

Sincerely,

Rekha Gopinathan
Expert Opinion On Drug Metabolism and Toxicology
IEMT-peerreview@journals.tandf.co.uk