

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Cohort Profile: A Multi-centre Prospective Validation Cohort of the Chinese Acute-on-Chronic Liver Failure (CATCH-LIFE) Study
<b>AUTHORS</b>	QIAO, LIANG; Wang, Xianbo; Deng, Guohong; Huang, Yan; Chen, Jinjun; Meng, Zhongji; Zheng, Xin; Shi, Yu; Qian, Zhiping; Liu, Feng; Gao, Yanhang; Lu, Xiaobo; Liu, Junping; Gu, Wenyi; Zhang, Yan; WANG, TONGYU; WU, DANDAN; DONG, FUCHEN; Sun, Xin; LI, Hai

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Pro.f M. S. Khuroo Dr. Khuroo Medical Center India
<b>REVIEW RETURNED</b>	03-Aug-2020

<b>GENERAL COMMENTS</b>	The authors have done a study on Acute on Chronic Liver Failure (ACLF) in the past in which 2,600 patients were recruited from 14 centers from 12 provinces from China. The results of this study have already been published. In this paper, authors have developed a validation protocol and enrolled 1370 patients from 13 nationwide centers in the protocol and given baseline data of the patients enrolled. These patients are under follow up and results shall be available in around 12 months. The protocol is well developed with data categories/elements (table 1), data collection methodology/time to recorded events (table 2), and baseline data (table 3). As of today no data on the follow up of patients are available. I believe once data are available, the findings of the study done in earlier will undergo validation and shall be useful. This protocol can be made available at the time of publishing the validation trial as attached documents.
-------------------------	---

<b>REVIEWER</b>	Rajiv Jalan University College London
<b>REVIEW RETURNED</b>	07-Sep-2020

<b>GENERAL COMMENTS</b>	This is an interesting study plan. We look forward to seeing the data from this validation cohort.
-------------------------	--

<b>REVIEWER</b>	Andreas Schnitzbauer Frankfurt University Hospital, Goethe-University
<b>REVIEW RETURNED</b>	29-Oct-2020

<b>GENERAL COMMENTS</b>	. Summary:
-------------------------	------------

	<p>Presentation and specific comments Liang Qiao and coworkers present a cohort of already recruited patients with ACLF. The study includes a future plan to follow up patients until 12 months after the acute setting has occurred.</p> <p>Title The expression "The cohort profile" is irritating. What do you want to express with that?</p> <p>Abstract: No comment</p> <p>Introduction/Article Summary: - Why do you report a study protocol after you have included all patients that you are going to follow up for one year now? I assume that you are already capable of answering all your questions associated with ACLF based on a 28 day follow up. - What is the rationale to extend your study period to 1 year?</p> <p>Methods: No comments, see above</p> <p>Results: - What is the rationale to report baseline data? You should already know early and the most relevant outcomes, like death recovery, LT in those patients as well.</p> <p>Discussion and Conclusion: - Basically, I congratulate the group to establish such a large cohort of patients. However, I simply and please explain it to me, don't understand the approach of the manuscript very well. Recruitment has been accomplished. Baseline data are reported, and now you are following up with the patient. I recommend to change the approach and really report only the protocol and no results. Formulate your hypothesis carefully and how you want to achieve it.</p> <p>Reliability: some reliability Originality: original Importance: highly important Suitability: needs to be amended Figures and tables: no comments</p>
--	---

### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Pro.f M. S. Khuroo

Institution and Country: Dr. Khuroo Medical Center

India

Please state any competing interests or state 'None declared': None.

#### Comments to the Author

The authors have done a study on Acute on Chronic Liver Failure (ACLF) in the past in which 2,600 patients were recruited from 14 centers from 12 provinces from China. The results of this study have

already been published. In this paper, authors have developed a validation protocol and enrolled 1370 patients from 13 nationwide centers in the protocol and given baseline data of the patients enrolled. These patients are under follow up and results shall be available in around 12 months. The protocol is well developed with data categories/elements (table 1), data collection methodology/time to recorded events (table 2), and baseline data (table 3). As of today no data on the follow up of patients are available. I believe once data are available, the findings of the study done in earlier will undergo validation and shall be useful. This protocol can be made available at the time of publishing the validation trial as attached documents.

Answer: Thank you very much for reviewing our manuscript and your positive comments on it.

Reviewer: 2

Reviewer Name: Rajiv Jalan

Institution and Country: University College London

Please state any competing interests or state 'None declared': None

Comments to the Author

This is an interesting study plan. We look forward to seeing the data from this validation cohort.

Answer: Thank you very much for your reviewing our manuscript and your positive comments on it.

Reviewer: 3

Reviewer Name: Andreas Schnitzbauer

Institution and Country: Frankfurt University Hospital, Goethe-University

Please state any competing interests or state 'None declared': none

Comments to the Author

Summary:

Presentation and specific comments

Liang Qiao and coworkers present a cohort of already recruited patients with ACLF. The study includes a future plan to follow up patients until 12 months after the acute setting has occurred.

Title

The expression "The cohort profile" is irritating. What do you want to express with that?

Answer: Thank a lot for this comment. "Cohort profile" is an article type set up in BMJ Open. As the journal requests, the rationale for a cohort's creation, its methods, baseline data and future plans should be described in a cohort profile. In this type of article, using "the cohort profile:" at the beginning of the title is a common format in BMJ Open.

Abstract:

No comment

Introduction/Article Summary:

- Why do you report a study protocol after you have included all patients that you are going to follow up for one year now?

Answer: Thank you very much for asking. This manuscript is not only a study protocol, it contains the baseline data of the participants as well. This type of articles is named "cohort profiles" in BMJ Open. As the journal's requests, cohort profiles should not be reported before the recruitment and baseline data collection are completed.

I assume that you are already capable of answering all your questions associated with ACLF based on a 28 day follow up.

Answer: Thanks a lot for this comment. However, a 28-day follow-up is far from enough to answer all our questions associated with ACLF. According to the data in the CATCH-LIFE investigation cohort (unpublished), the number of death or LT events within 28 days and between 28 and 90 days accounted for 40% and 30% of the total one-year adverse events respectively. Therefore, 28-day follow-up is not enough, which would possibly miss a large proportion of patients with poor outcomes, causing inevitable bias in ACLF characteristics and natural history. We believe that 1-year follow-up will provide us with detailed information on the clinical context prior to and after ACLF development.

- What is the rationale to extend your study period to 1 year?

Answer: Thank you very much for this question. We have answered it in the previous question.

Methods:

No comments, see above

Results:

- What is the rationale to report baseline data? You should already know early and the most relevant outcomes, like death recovery, LT in those patients as well.

Answer: Thanks a lot for the question and comment. Reporting the baseline data in Results is accord with the requirements of BMJ Open on cohort profiles. After the follow-up is completed, the outcomes and relevant analysis will be reported in other articles.

Discussion and Conclusion:

- Basically, I congratulate the group to establish such a large cohort of patients. However, I simply and please explain it to me, don't understand the approach of the manuscript very well. Recruitment has been accomplished. Baseline data are reported, and now you are following up with the patient. I recommend to change the approach and really report only the protocol and no results. Formulate your hypothesis carefully and how you want to achieve it.

Answer: Thank you very much for the comments. About your concerns on the approach of the manuscript, we have answered in the previous questions.