Dear Reviewer Team

Continuing Medical Education of

The Indonesian Society of Internal Medicine XXXV, Surabaya 2020.

Thank you for your letter. We appreciate the thoughtful comments from you and the reviewers. As the reviewers suggested, we have rephrased several sentences. We removed some unnecessary lengthy discussion about APC-based vaccine. We also replace the previous figure with higher quality picture as suggested. We also added a special discussion about the public acceptance under the section of Opportunity and Challenges.

The revised manuscript was fully evaluated in consideration of the reviewer's individual comments, and we believe that their suggested changes helped us to substantially improve our manuscript. We hope that these revisions and our accompanying responses will be sufficient to make our manuscript suitable for publication in the upcoming edition of The New Armenian Medical Journal as has been informed to all the speakers in the Continuing Medical Education XXXV, The Indonesian Society of Internal Medicine, Surabaya.

We are looking forward to hear a positive response from the reviewers soon.

Best regards,

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Reviewer #1:
The manuscript "Vaccination for Coronavirus Disease 2019: Opportunity, Hope and Challenges" is an interesting topic that is a concern actually. However, the picture is at lower quality and must be submitted to a vectorial software.

Author response: Thank you for your concern and suggestion. We have submitted a new figure with higher quality in a TIFF format.

The subsection about the Antigen Presenting Cell Based Vaccine is too long. This kind of vaccine is not approved yet for infectious disease and none of the currently proposed vaccine proceeds into phase II clinical trial. So, the author should shorten the description about this vaccine to a minimum length.

Author response: Thank you for your comment. I agree with your suggestion. In this version of revised manuscript, I have eliminated the unnecessary lengthy paragraph and only mentioning about the concept of this kind of vaccine.

The author should also discuss about public acceptance or hesitancy to receive the COVID-19 vaccine, because this is also an important challenge to vaccination enrolment by the government.

Author response: Thank you for your comment and suggestion. I have added a special paragraph to discuss about public acceptance under the Opportunity and Challenges section (page 8, line 164-169).

Reviewer #2: This is an interesting manuscript and can be accepted provided the following questions are answered:

1. The authors have to elaborate, as much as possible, on the concept of the adverse sequelae as a result of 'antibody dependent enhancement' (ADE), following vaccination. This is an important issue that has to be discussed elaborately.

Author response: Thank you for your comment. I have made some revision to the particular paragraph about ADE (page 6, line 128-136). Although the ADE phenomenon has been reported for several other types of viruses, particularly the Dengue virus, fortunately, there has not been a single case of ADE reported in all clinical trials of the COVID-19 vaccine that are currently being carried out. People who have been infected with COVID-19 can also still receive the COVID-19 vaccine without the risk of worsening the disease due to ADE. Perhaps this is because the SARS-CoV-3 virus does not target immune cells as its target, as happened in Dengue virus infection and subsequent vaccination. In contrast to DENV, SARS-CoV, MERS-CoV and SARS-CoV-2 predominantly infect respiratory epithelium, not macrophages.

2. The authors are asked to give some data, from the literature, on the possible percentage of people who had this condition.

Author response: Thank you for your comment. But I should apologize because currently there is not been a single report about ADE due to COVID-19 vaccine published in the literature. Neither COVID-19 disease nor the new COVID-19 vaccines have shown evidence of causing ADE. So, currently we cannot give you the data as you requested.

3. Is it possible to test for the ADE routinely. Are the vaccine producing companies making this risk clearly for people receiving the vaccine?

Author response: Thank you for your question. This is also an interesting question. Although it is generally not clearly or specifically stated in published reports of phase 1/2 and 3 clinical trials of COVID-19 vaccines in the literatures, I believe that every vaccine manufacturer will always take vaccine safety factors into account, including the possibility of an ADE. I can only assume that this matter had been mentioned in the information for consent before the participants give their consent to join a vaccine clinical trial. In my opinion, mitigating ADE has been a priority in COVID-19 vaccine development. Some strategies during this process include monitoring and evaluating animal and human trials for ADE, looking over real-world COVID-19 infection data, and specifically targeting a SARS-CoV-2 protein that was the least likely to cause ADE in early vaccine design. Fortunately, so far there have been no verified reports of ADE occurring as a result of COVID-19 vaccines.

Minor comments:

* Line 11, remove "very"

Author response: Thank you for your comment. I have revised the sentence as you suggested.

* Line 15, Excellent point about diversity and genotypes, and comorbidities.

Author response: Thank you for your kind comment to that particular section.