PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol for a Randomized Controlled Trial of an Artificial Intelligence Mobile Health Platform for Early Detection of COVID-19 in Quarantine Subjects using a Wearable Biosensor
AUTHORS	Wong, Chun Ka; Ho, Deborah Tip-Yin; Tam, Anthony Raymond; zhou, Mi; LAU, Yuk-Ming; Tang, Milky Oi-Yan; Tong, Raymond Cheuk-Fung; Rajput, Kuldeep Singh; Chen, Gengbo; Chan, Soon-Chee; SIU, Chung-Wah; Hung, Ivan Fan-Ngai

VERSION 1 – REVIEW

REVIEWER	M. Shafiqur Rahman ISRT, University of Dhaka, Bangladesh
REVIEW RETURNED	06-Apr-2020

GENERAL COMMENTS	This is very good study design and useful. The paper is written very well and clearly. I have few observations. i) If the outcome is time to event (detection of COVID-19) and there will be several longitudinally measured clinical and physiological information (variable) over the follow up period. In this case, only Cox model or only GEE will not be enough statistical method to explore (and estimate of) the effect of longitudinally measured variable on the survival outcome (time-to-event outcome). However, Joint Model of both longitudinal covariate and survival outcome could be better choice. ii) Sample size of 100 at the first phase seems arbitrary choice. Better to have it with some statistical justification.

REVIEWER	Kristen A Pickett University of Wisconsin - Madison United States of America
REVIEW RETURNED	29-Apr-2020

GENERAL COMMENTS	The authors have described their study protocol for a wearable biosensor and related AI platform designed to improve detection time of individuals currently quarantined due to suspected COVID-19 exposure. 1. Overall the study is well described, however, the paper does have numerous grammatical and editorial errors that need to be addressed. 2. The SPIRIT check-list appears complete with the authors addressing all relevant areas.

	3. The study hypothesis, presented on pg 6, ln 34, is more of a study goal. The clear and testable hypothesis should be presented. 4. The sensitivity and specificity of the device should be discussed. Is the device and the related AI designed to focus on the sensitivity or specificity of COVID-19 detection. 5. Are there any previously published papers addressing any safety of the Biovitals device? No mention of safety, side effects or risks to wearing these devices was provided. 6. Finally, it would be advisable to remove any reference to specific dates and daily impact values as inclusion of these figures will cause the manuscript to be out of date very quickly, given the scope of the pandemic.

VERSION 1 – AUTHOR RESPONSE

Response to Reviewer 1:

This is very good study design and useful. The paper is written very well and clearly. I have few observations.

> Thank you for the comments of the reviewer.

i) If the outcome is time to event (detection of COVID-19) and there will be several longitudinally measured clinical and physiological information (variable) over the follow up period. In this case, only Cox model or only GEE will not be enough statistical method to explore (and estimate of) the effect of longitudinally measured variable on the survival outcome (time-to-event outcome). However, Joint Model of both longitudinal covariate and survival outcome could be better choice.

> Thank you for the advice. Section on statistical analysis has been updated including description of joint modelling of longitudinal and time-to-event data analysis.

ii) Sample size of 100 at the first phase seems arbitrary choice. Better to have it with some statistical justification.

> As there was no previous study on the research theme, convenience sampling was implemented to determine sample size.

D. Response to Reviewer 2:

The authors have described their study protocol for a wearable biosensor and related AI platform designed to improve detection time of individuals currently quarantined due to suspected COVID-19 exposure.

> Thank you for the comments of the reviewer.

1. Overall the study is well described, however, the paper does have numerous grammatical and editorial errors that need to be addressed.

> We carefully reviewed and edited grammatical and editorial errors as suggested by the reviewer.

2. The SPIRIT check-list appears complete with the authors addressing all relevant areas.

> Thank you for the comments of the reviewer.

3. The study hypothesis, presented on pg 6, ln 34, is more of a study goal. The clear and testable hypothesis should be presented.

> Thank you for the advice and the hypothesis statement has been modified.

4. The sensitivity and specificity of the device should be discussed. Is the device and the related AI designed to focus on the sensitivity or specificity of COVID-19 detection.

> Section on outcomes have been updated to further elaborate the mentioned issue.

5. Are there any previously published papers addressing any safety of the Biovitals device? No mention of safety, side effects or risks to wearing these devices was provided.

> To the best of our knowledge, there has been no published paper addressing safety aspect of the device in concern. Due to the non-invasive nature of the wearable device, it is unlikely to induce severe adverse effect but we will closely monitor any adverse effect by monitoring the recruited subjects.

6. Finally, it would be advisable to remove any reference to specific dates and daily impact values as inclusion of these figures will cause the manuscript to be out of date very quickly, given the scope of the pandemic.

> Thank you for the advice and the figures have been modified accordingly.

VERSION 2 – REVIEW

REVIEWER	M. Shafiqur Rahman ISRT, University of Dhaka
REVIEW RETURNED	19-May-2020

GENERAL COMMENTS	Thank you for addressing my comments. I have no more comments.

REVIEWER	Kristen A Pickett University of Wisconsin - Madison, United States of America
REVIEW RETURNED	08-Jun-2020

GENERAL COMMENTS	The revisions completed by the authors have improved the manuscript and have clarified all points previously raised. I have two minor concerns. 1) As it currently stands, there is no discussion or statement regarding the limitations of the study protocol in the discussion section. 2) A small number of grammatical errors persist. One final read through should be completed. A minor addition point. If the clinicaltrials.gov registration has been completed, the paper should be updated.

VERSION 2 – AUTHOR RESPONSE

Response to Reviewer 1:

Thank you for addressing my comments. I have no more comments.

Response: Thank you for the comments of the reviewer.

D. Response to Reviewer 2:

The revisions completed by the authors have improved the manuscript and have clarified all points previously raised. I have two minor concerns.

1) As it currently stands, there is no discussion or statement regarding the limitations of the study protocol in the discussion section.

Response: Thank you for the comments of the reviewer. The discussion section was updated accordingly.

2) A small number of grammatical errors persist. One final read through should be completed.

Response: The whole article was reviewed and amended to improve the quality of English.

A minor addition point. If the clinicaltrials.gov registration has been completed, the paper should be updated.

Response: The clinical trial was registered on clinicaltrials.gov (NCT04343794). The manuscript was updated accordingly.