## PEER REVIEW HISTORY



## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | Impact of a phone-call with a medical student/general practitioner team on morbidity of chronic patients during the first French COVID-19 lockdown. COVIQuest: A cluster randomised trial |
| **AUTHORS** | Dibao-Dina, Clarisse; Léger, Julie; Ettori-Ajasse, Isabelle; BOIVIN, ESTELLE; Chambe, Juliette; Abou-Mrad-Fricquegnon, Karim; Sun, Sophie; Jego, Maeva; Motte, Baptiste; Chiron, Benoit; Sidorkiewicz, Stéphanie; Khau, Cam-Anh; Bouchez, Tiphanie; Ghali, Maria; Bruel, Sébastien; LEBEAU, Jean-Pierre; Camus, Vincent; El-Hage, Wissam; Angoulvant, Denis; Caille, Agnès; Guillon-Grammatico, Leslie; Laurent, Emeline; Saint-Lary, Olivier; Boussageon, Rémy; Pouchain, Denis; Giraudeau, Bruno |

## VERSION 1 – REVIEW

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| **REVIEWER** | Mariani, Javier<br>GEDIC (Grupo de Estudio, Docencia e Investigaci﷿n Cl﷿nica) |
| **REVIEW RETURNED** | 28-Jan-2022 |

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| **GENERAL COMMENTS** | Thank you for the invitation.<br>Authors report the results of randomized, open-label, cluster, trial, evaluating the effects of GPs initiated phone calls early during lockdown vs delayed phone calls among CVD and MHD patients, on one-month hospitalization rates.<br>The study is very interesting and, as stated by the authors challenging since involved GPs that participated for the first time in clinical research.<br>Major Comments:<br>-In sample size considerations authors stated that expected 200 GPs and 16,000 CVD and 6,000 MHD patients to participate in the trial. The actual figures were 149 GPs, and 3,344 CVD patients and 1,380 MHD patients. Also, the event rates were something lower than expected. Both factors affected the power of the trial to detect the prespecified difference.<br>-The loss in follow up (particularly in the intervention group) was excessive (348/1834 for CVD patients and 282/548 for MHD patients). In those cases, authors imputed the primary outcome as not occurring. Maybe, this decision could be challenge in sensitivity analyses to evaluate alternative scenarios.<br>-Please, follow CONSORT statement for reporting cluster studies and add the corresponding checklist.<br>Minor comments:<br>-In table 1: Only CVD number of participants are displayed.<br>-More baseline participant characteristics would be useful to understand the hospitalization rate and the external validity of the study. |

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| **REVIEWER** | van Doorn, Sander<br>University Medical Center Utrecht, Julius Center for Health Sciences and Primary Care |
| **REVIEW RETURNED** | 14-Feb-2022 |

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| **GENERAL COMMENTS** | Dear editor,<br><br>Thank you for allowing me to review the study protocol entitled "Does a systematic phone-call contact by the general practitioner in patients suffering from a chronic condition during the containment period due to COVID-19 epidemic in France impact one-month hospitalization's rate? A cluster randomized trial." In this protocol, Dibao-Dina and colleagues describe an intervention aiming to evaluate the short-term impact of a phone-contact with patients with a chronic cardiovascular or mental disease initiated by their GP (helped by medical students) during the COVID-19 epidemic containment period on hospitalizations in these populations at 1 month.<br>The proposed study addresses the very relevant problem of under-use of care during containment measures for Covid-19. Please find my comments below.<br><br>Although the protocol is well written and clear, its current form (including many details, standard headings and a large table of contents) may not be well suited for publication in a journal.<br><br>Especially in this study domain, many hospital admission may (have) occur(ed), e.g. for Covid-19. What efforts will the researchers take to precisely record the reason of admission?<br><br>The term ALD was unknown to me and only explained later on. This might need better explanation for readers where the abbreviation is used first (p. 16)<br><br>At some points, the English language may need improvement. |

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| **REVIEWER** | Rias, Yohanes<br>Institut Ilmu Kesehatan Bhakti Wiyata Kediri, School of Nursing |
| **REVIEW RETURNED** | 21-Feb-2022 |

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| **GENERAL COMMENTS** | BMJ Open; bmjopen-2021-059464<br><br>I am pleased to read and review manuscript ID BMJ Open; bmjopen-2021-059464<br>entitled "Effectiveness of a general practitioner-initiated phone call to patients with a chronic cardiovascular disease or mental health disorder on hospitalisations during the first French covid-19 lockdown. COVIQuest: A cluster randomised trial". The study is interesting. However, I consider that specific questions need to be addressed to improve its presentation, as below;<br>1. The title is long and can be adjusted to be more interesting for the reader.<br>2. Please provide brief gaps statements in the objective to significantly enhance this study's interest in the abstract-objective.<br>3. Page 5 line 11, Please explain specifics definition of hospitalisations "Number of hospitalization(s) or Time to hospitalization or other" |

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| | 4. In the abstract-participants, the Patients ≥ 70 years old with chronic CVD. Regarding the statements, please elaborate on the gaps statements in the abstract-objective section<br>5. In the abstract-intervention; I suggest to straightforward about usual care<br>6. In the abstract-results, page 3, line 47, could you please double-check the result, especially CI 0.56 to 1.20, and the CI result on page 3, line 57. Does it indicate the significant differences?<br>7. In the abstract-conclusion; please to a more precise explanation about the "lack of robustness."<br>8. Page 6; line 17. NCT04359875 (ClinicalTrials.gov) "A Phone-call With a Student/General Practitioner Team to Impact Morbidity of Chronic Patients During COVID-19 Containment". Regarding the NCT04359875 (ClinicalTrials.gov), "Systematic phone contact of the patient by a medical student, under the indirect supervision of the general practitioner. This phone contact will be standardized with 3 questions to ask the patient and Number of hospitalization(s) [ Time Frame: 6 months ]; Time to hospitalization(s) [ Time Frame: 6 months ] (https://clinicaltrials.gov/ct2/show/NCT04359875)"; it is mot linear with your study (morbidity; contact phone by medical students; time), please confirm which one is correct.<br>9. Page 9 line 5, reference number 8. Please must be double-check because the population do not Patients ≥ 70 years old with a chronic cardiovascular disease (CVD). Its indicated citation bias.<br>10. Please add the references for the sentences in page9, lines 5-24 “Underuse……. hospitalisation and death”<br>11. in general, what is the importance of seeing patients with CKD and MH disease? Is there a relationship or similarity between the two. Could you please add more information about it in the introduction section?<br>12. what percentage of CKD patients will have the chance of having MH disease?<br>13. Page 9, line 29-40. “On April 8, 2020, because of the underuse of care, the French government recommended that GPs directly contact their patients with chronic disease to prevent decompensation. However, the average number of patients with a chronic disease regularly followed by their GP is approximately 150 per GP , which questioned the feasibility of this recommendation. Furthermore, choosing which patients to contact first was ethically challenging”. Regarding the statements, what kind of reason to explain those statements? and please specific to explain only CVD and MHD patients<br>14. In the last paragraph on page 7. Suddenly, the author expresses the connection with "The development of the COVIQuest project in this context solved the ethical dilemma of which patient to call first and increased the number of possible calls while meeting the research". This is very unscientific; I advise first explaining the COVIQuest project, gaps, problems, and solutions.<br>15. Methods; page 8 line 13-16; please double-check and the meaning of two parallel group 1:1,<br>16. Page 8 line 16. “cluster randomised trials with clusters defined as GPs”. Are you sure defined as GPS; is it cluster randomized trial, please explain about it?<br>17. I really apricated for the authors to use a wait-list control design after the intervention process<br>18. Page 12, lines 10-12. Please double-check the reference no 14 “ ICC of 0.03 indicated median value”?. |

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| | 19. Authors did not explain the ICC results in the result section, please explain it as well as discuss about it in the discussion section.<br>20. Table 1. Could you please why the authors to investigated and or reported the baseline characteristic of general practitioners (GPs) by group. It will relate to question no 16.<br>21. Please the confirm the criteria inclusion and exclusion for general practitioners (GPs), because the author repot the baseline characteristic of GPs in table 1.<br>22. Please the confirm the criteria inclusion and exclusion for participants with CVD and MHD.<br>23. Page 10, last paragraph. “During the same phone call, for GPs allocated to group A, the intervention was also delivered to MHD patients; and for GPS allocated to group B, the intervention was also delivered to CVD patients”. Regarding the statements, groups A and B differed in intervention provider or inventing as well as differences characteristic of GPs by group in table 1. It is possible to intervention bias.<br>24. Page 17, lines 43-47. “Group A (cardiovascular disease [CVD] patients called first); group B (mental health disorder [MHD] patients called first)”. is there any difference if GPs calls mental people first than CVD?; How does it relate to your research objectives? This makes it very confusing, and the research procedures need more specific and detail.<br>25. Page 18, line 3-15. “In 80.4% of cases, the medical trainee initiated the intervention phone call as a representative of the GP”. Could you please explain who the medical trainee is, and are you sure about your title?<br>26. For the adjustment analysis, do you include the duration of CVD or mental health among your participants?. If, not please to explain in your limitation study.<br>27. Discussion section. Results were not discussed sufficiently and not linier with the objective study. For instance, it should compare previous studies, both linear and contradictory compared with the results of this research. Moreover, please add more opinions on why this could be different from the research done. In fact, based on Tables 2 and 3, there is no significant difference, so the discussion will be richer in the discussion section.<br>28. Finally, In conclusion; how the information presented in this study can help to improve policies, and what the recommendations. |

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| **REVIEWER** | Zhang, Dr Jufen<br>Anglia Ruskin University |
| **REVIEW RETURNED** | 16-Mar-2022 |

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| **GENERAL COMMENTS** | The paper is well written and organised. I have a number of comments as detailed below.<br><br>Methods<br>Page 8, lines 55-57. “Eligible GPs were volunteer GPs practising as training supervisors from 8 different administrative regions in France (see Appendix 1)”. It appears that Appendix 1 shows more than 8 different administrative regions.<br><br>Page 11, lines 9-14. In this study, the information of outcomes was collected based on patient self-reported, which could be biased. This may need to be addressed in the discussion selection.<br><br>Page 12. The logistic regression model within a generalized estimating equation framework was used for the primary outcome |

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| | analysis. As indicated, for the primary outcome, missing data were considered as no hospitalisation, whatever the study groups. It is not clear how the missing values were handled in the logistic regression analysis? Did the authors consider using mixed model?<br><br>Please indicate the statistical software used in the analysis.<br><br>Results<br>Page 16, line 43. Suggest adding the percentages of the numbers reported: 348 and 39. In addition, please specify the imputation method used for imputing the missing values.<br><br>Page 20. Suggest inserting label “Table 3” in the section of primary and secondary 1-month outcomes.<br><br>Table 1, line 31. Please show the number of patients in the intervention and control groups for MHD patients.<br><br>Table 2. What’s the definition of “Crude difference”? Is it the difference in hospitalization rate?<br><br>In addition, please make it clear in the result section about the intention-to-treat analysis and sensitivity analysis. |

**VERSION 1 – AUTHOR RESPONSE**

Reviewer: 1
Dr. Javier Mariani, GEDIC (Grupo de Estudio, Docencia e Investigaci﷿n Cl﷿nica)

Comments to the Author:
Thank you for the invitation.
Authors report the results of randomized, open-label, cluster, trial, evaluating the effects of GPs initiated phone calls early during lockdown vs delayed phone calls among CVD and MHD patients, on one-month hospitalization rates.
The study is very interesting and, as stated by the authors challenging since involved GPs that participated for the first time in clinical research.
Major Comments:
-In sample size considerations authors stated that expected 200 GPs and 16,000 CVD and 6,000 MHD patients to participate in the trial. The actual figures were 149 GPs, and 3,344 CVD patients and 1,380 MHD patients. Also, the event rates were something lower than expected. Both factors affected the power of the trial to detect the prespecified difference.
We are aware that the number of patients included is far from the expected number of patients specified in the sample size section. However, as explained in the Statistical analyses section, the planned sample size was specified pragmatically rather than by pre-specifying a quantitative hypothesis. Therefore, we considered the average number of CV and MH patients per GP and the number of GPs interested in participating. Moreover, as pointed out by the reviewer, the event rate was lower than expected, which may also have affected the nominal power. This is a limitation of our study, which has been acknowledged in the Discussion section: “This lack of difference could be explained by a lack of power of the study because the sample size had not been reached, particularly because of GP withdrawals.”

-The loss in follow up (particularly in the intervention group) was excessive (348/1834 for CVD patients and 282/548 for MHD patients). In those cases, authors imputed the primary outcome as not

occurring. Maybe, this decision could be challenge in sensitivity analyses to evaluate alternative scenarios.
We fully agree that the decision taken is based on a very strong hypothesis, because we considered that patients lost to follow-up had not been hospitalized. Ideally, such missing data should be handled by using a multiple imputation approach, as explained in Caille et al (Stat Methods Med Res. 2016 Dec;25(6):2650-2669.). However, we collected few baseline data because we did not want this study to be a burden for the GPs and therefore collected only the minimal data. As a consequence, such a sophisticated approach cannot be used. Other more basic imputation strategies could be used, such as considering that all missing observations actually correspond to a hospitalisation, or the maximal bias approach (i.e., considering that a missing value in the experimental group corresponds to a hospitalisation, and in the control group, missing data corresponds to the non-occurrence of a hospitalisation). However, such approaches are even worse than the one we used, notably because doing so, the hospitalisation rates would no longer have any relevant meaning. This is a major limitation of our trial, which has been acknowledged in the Discussion section and we completed as follows: “Finally, patients from the intervention group who could not be reached at month 1 had missing data, which were considered absence of hospitalisation in the intervention group (the quasi absence of baseline data impeded considering a multiple imputation approach) but could not be considered so in the control group.”

-Please, follow CONSORT statement for reporting cluster studies and add the corresponding checklist.
We made the change and provided the right checklist.

Minor comments:
-In table 1: Only CVD number of participants are displayed.
We added this information.

-More baseline participant characteristics would be useful to understand the hospitalization rate and the external validity of the study.
As previously explained, we did not collect more baseline data because the study was considered a way to associate both care and research and we involved a large number of GPs, many of them not familiar with clinical research. The main consequence is that we collected very few data and therefore are not able to better characterise our groups of patients.

Reviewer: 2
Dr. Sander van Doorn, University Medical Center Utrecht

Comments to the Author:
Dear editor,

Thank you for allowing me to review the study protocol entitled “Does a systematic phone-call contact by the general practitioner in patients suffering from a chronic condition during the containment period due to COVID-19 epidemic in France impact one-month hospitalization’s rate? A cluster randomized trial.” In this potocol, Dibao-Dina and colleagues describe an intervention aiming to evaluate the short-term impact of a phone-contact with patients with a chronic cardiovascular or mental disease initiated by their GP (helped by medical students) during the COVID-19 epidemic containment period on hospitalizations in these populations at 1 month.
The proposed study addresses the very relevant problem of under-use of care during containment measures for Covid-19. Please find my comments below.

Although the protocol is well written and clear, its current form (including many details, standard headings and a large table of contents) may not be well suited for publication in a journal.
We would like to specify that the submitted report does not present a clinical study protocol but rather the results of a large trial in which 3344 cardiovascular patients and 1380 patients with mental health disorders have been included.

Especially in this study domain, many hospital admission may (have) occur(ed), e.g. for Covid-19. What efforts will the researchers take to precisely record the reason of admission?
We acknowledge that in the present report, we do not have the reasons for admission. Such information will be obtained from the national health insurance database, and as explained in the report, this will correspond to a secondary analysis, which will be reported later on.

The term ALD was unknown to me and only explained later on. This might need better explanation for readers where the abbreviation is used first (p. 16)
As explained, ALD refers to long-term illness (affection longue durée [ALD]). We added the explanation for the ALD term as follows:
“To identify patients with a chronic disease, we chose the affection longue durée (ALD) system. The ALD system allows for financial coverage by the national health insurance for pathologies that require prolonged and costly treatment. Each patient's GP declares the ALD and thus has access to their list of ALD patients”.

At some points, the English language may need improvement.
We submitted the protocol to an English native writer.

Reviewer: 3
Dr. Yohanes Rias, Institut Ilmu Kesehatan Bhakti Wiyata Kediri

Comments to the Author:
BMJ Open; bmjopen-2021-059464

I am pleased to read and review manuscript ID BMJ Open; bmjopen-2021-059464 entitled "Effectiveness of a general practitioner-initiated phone call to patients with a chronic cardiovascular disease or mental health disorder on hospitalisations during the first French covid-19 lockdown. COVIQuest: A cluster randomised trial". The study is interesting. However, I consider that specific questions need to be addressed to improve its presentation, as below;
1. The title is long and can be adjusted to be more interesting for the reader.
If it suits with the editor’s guidelines, we can propose: Impact of a phone-call with a medical student/general practitioner team on morbidity of chronic patients during the first French COVID-19 lockdown. A cluster randomized trial.

2. Please provide brief gaps statements in the objective to significantly enhance this study's interest in the abstract-objective.
We followed the Authors guidelines of the BMJ Open for the Abstract structure. However, we can complete the objective section of the abstract as follows:
Objectives: The first COVID-19 lockdown led to significantly reduced access to healthcare, which may have increased decompensations for frail patients with chronic diseases, especially older patients living with a chronic cardiovascular disease (CVD) or a mental health disorder (MHD). The COVIQuest objective was to evaluate whether a general practitioner (GP)-initiated phone call to CVD patients and MHD patients during the COVID-19 lockdown could reduce the number of hospitalisation(s) over a 1-month period.

3. Page 5 line 11, Please explain specifics definition of hospitalisations “Number of hospitalization(s) or Time to hospitalization or other”
We specified the “number of hospitalsation(s)”.

4. In the abstract-participants, the Patients ≥ 70 years old with chronic CVD. Regarding the statements, please elaborate on the gaps statements in the abstract-objective section
We completed it (see point n°2)

5. In the abstract-intervention; I suggest to straightforward about usual care
We completed as follows:
“The control group benefited from usual care; that is, contact with the GP was by the patient’s initiative”

6. In the abstract-results, page 3, line 47, could you please double-check the result, especially CI 0.56 to 1.20, and the CI result on page 3, line 57. Does it indicate the significant differences?
As specified in Table 2, the non-adjusted odds ratio, which quantifies the intervention effect on the COVIQuest_CV subtrial, is 0.82, 95%CI 0.56 to 1.20. For the COVIQuest_MH subtrial, this odds ratio is estimated at 1.52, 95%CI 0.82 to 1.81. So we confirm that there is no error in the reporting. Otherwise, 1 being included in the two 95% confidence interval, one directly deduces that the result is not statistically significant. We do not consider it necessary to add this detail.

7. In the abstract-conclusion; please to a more precise explanation about the "lack of robustness."
We propose “A GP-initiated phone call may have been associated with more hospitalisations within 1 month for MHD patients, but results lack robustness and significance depending on the statistical approach used”

8. Page 6; line 17. NCT04359875 (ClinicalTrials.gov) "A Phone-call With a Student/General Practitioner Team to Impact Morbidity of Chronic Patients During COVID-19 Containment". Regarding the NCT04359875 (ClinicalTrials.gov), "Systematic phone contact of the patient by a medical student, under the indirect supervision of the general practitioner. This phone contact will be standardized with 3 questions to ask the patient and Number of hospitalization(s) [ Time Frame: 6 months ]; Time to hospitalization(s) [ Time Frame: 6 months ] (https://clinicaltrials.gov/ct2/show/NCT04359875)"; it is mot linear with your study (morbidity; contact phone by medical students; time), pleasconfirm which one is correct.
We checked the trial registry and updated the manuscript.

9. Page 9 line 5, reference number 8. Please must be double-check because the population do not Patients ≥ 70 years old with a chronic cardiovascular disease (CVD). Its indicated citation bias.
It is true that this reference is about patients ≥ 75 years old with diabetes. The literature on the impact of the underuse of care on decompensations in patients at cardiovascular risk is poor, so we chose to cite this reference, which was not ideal. Because many patients have a chronic cardiovascular disease and we had a very short time for our intervention, we focused on older patients because the risk of cardiovascular decompensations increase with age. The age 70 years old was preferred to the age 75 years old for identification and acceptance reasons. We changed the reference as you advised, opting for a reference showing that the risk of decompensation of chronic cardiovascular disease increases with age: An J, Zhang Y, Muntner P, Moran AE, Hsu JW, Reynolds K. Recurrent Atherosclerotic Cardiovascular Event Rates Differ Among Patients Meeting the Very High Risk Definition According to Age, Sex, Race/Ethnicity, and Socioeconomic Status. J Am Heart Assoc. 2020 Dec;9(23):e017310. doi: 10.1161/JAHA.120.017310.

10. Please add the references for the sentences in page9, lines 5-24 “Underuse……. hospitalisation and death”
We do not have references because these sentences were our hypotheses, as it was the first time the lockdown occurred. To be fully clear, we reformulated these sentences as followed:
“A first hypothesis was that underuse of care induced by strict lockdown measures may have led to ignoring symptoms possibly indicating a major cardiovascular event. A second hypothesis was that patients living with a chronic mental health disorder (MHD) may be particularly at risk of decompensation secondary to the lockdown measure, which could increase their anxiety and risk of suicide. The exemption granted to the pharmacist to deliver the patient’s usual treatment for an extra month without consulting the GP may have favoured the abuse of drugs, especially psychotropic, hypnotics and substitute drugs. The situation could lead to drug dependence and then withdrawal syndromes at the end of the lockdown, increased risk of hospitalisations and death”.

11. in general, what is the importance of seeing patients with CKD and MH disease? Is there a relationship or similarity between the two. Could you please add more information about it in the introduction section?
We added some information about it in the introduction as follows:
We chose patients with a chronic CVD or MHD because we were afraid that they may be part of the populations in which the reduction of primary care contact during the lockdown could be the largest, as was shown later in the literature[10]; there was no proof to ascertain whether these reductions reflected changes in disease frequency or missed opportunities for care[10].

12. what percentage of CKD patients will have the chance of having MH disease?
As specified in the Participants: GPs and patients section, patients with both a cardiovascular disease and a mental health disease were not eligible.

13. Page 9, line 29-40. “On April 8, 2020, because of the underuse of care, the French government recommended that GPs directly contact their patients with chronic disease to prevent decompensation. However, the average number of patients with a chronic disease regularly followed by their GP is approximately 150 per GP , which questioned the feasibility of this recommendation. Furthermore, choosing which patients to contact first was ethically challenging”. Regarding the statements, what kind of reason to explain those statements? and please specific to explain only CVD and MHD patients
To be clearer, we reformulated the end of the introduction as follows:
“In France, patients with a chronic CVD or MHD are regularly followed by a GP, and contact with their GP is traditionally according to the patient’s initiative. On April 8, 2020, because of the underuse of care, the French government recommended that GPs directly contact their patients with a chronic disease to prevent decompensation[11].
The development of the COVIQuest project in this context was the opportunity to apply the recommendations of the French government to patients while meeting the research objective: to assess the impact of a GP-initiated phone call to patients with a CVD or MHD on hospital admissions within 1 month after the phone call.”

14. In the last paragraph on page 7. Suddenly, the author expresses the connection with "The development of the COVIQuest project in this context solved the ethical dilemma of which patient to call first and increased the number of possible calls while meeting the research". This is very unscientific; I advise first explaining the COVIQuest project, gaps, problems, and solutions.
We reformulated as indicated above.

15. Methods; page 8 line 13-16; please double-check and the meaning of two parallel group 1:1,

We confirm that both the COVIQuest-CV and COVIQuest_MH are two parallel-group 1:1 cluster randomised trials. Indeed, in each trial there are two independent (i.e., parallel) groups; randomization is clustered (GPs rather than patients are randomized) and balanced, which is expressed by the classical 1:1 formulation.

16. Page 8 line 16. “cluster randomised trials with clusters defined as GPs”. Are you sure defined as GPS; is it cluster randomized trial, please explain about it?
We confirm that by randomising GPs, this study is a cluster randomised trial, which is a design specificity well known to the last author of the present manuscript.

17. I really apricated for the authors to use a wait-list control design after the intervention process
We have to acknowledge that we do not understand this comment.

18. Page 12, lines 10-12. Please double-check the reference no 14 “ ICC of 0.03 indicated median value”?.
We confirm that the 0.03 value is derived from Campbell’s paper and that it corresponds to a median value of a series of ICCs.

19. Authors did not explain the ICC results in the result section, please explain it as well as discussbout it in the discussion section.
We do not consider it necessary to provide more information on the ICC than reporting its values, as is done in the Tables 2 & 3. Such values are mainly useful for future studies.

20. Table 1. Could you please why the authors to investigated and or reported the baseline characteristic of general practitioners (GPs) by group. It will relate to question no 16.
As advised by the CONSORT extension for cluster randomised trials, baseline characteristics of clusters (i.e., GPs in the present trial) and participants (i.e., patients) need to be reported. This is what has been done in Table 1.

21. Please the confirm the criteria inclusion and exclusion for general practitioners (GPs), because the author repot the baseline characteristic of GPs in table 1.
Again, in a cluster randomised trials, there are selection criteria both for clusters and participants. This is why we reported GP selection criteria.

22. Please the confirm the criteria inclusion and exclusion for participants with CVD and MHD.
We confirm the selection criteria for CVD and MHD patients. Such information is also available in the protocol and on the ClinicalTrials.gov website.

23. Page 10, last paragraph. “During the same phone call, for GPs allocated to group A, the intervention was also delivered to MHD patients; and for GPS allocated to group B, the intervention was also delivered to CVD patients”. Regarding the statements, groups A and B differed in intervention provider or inventing as well as differences characteristic of GPs by group in table 1. It is possible to intervention bias.
Group A is the experimental group for the COVIQuest-CV subtrial and the control one for the COVIQuest_MH subtrial; group B is the experimental group for the COVIQuest-MH subtrial and the control one for the COVIQuest_CV subtrial. Providers were notably different between the two groups because providers (i.e., GPs and their students) are the randomization units and the two subtrials are two parallel-group trials.

24. Page 17, lines 43-47. “Group A (cardiovascular disease [CVD] patients called first); group B (mental health disorder [MHD] patients called first)”. is there any difference if GPs calls mental people

first than CVD?; How does it relate to your research objectives? This makes it very confusing, and the research procedures need more specific and detail.
As previously explained, Group A is the experimental group for the COVIQuest-CV subtrial and the control one for the COVIQuest_MH subtrial; group B is the experimental group for the COVIQuest-MH subtrial and the control one for the COVIQuest_CV subtrial.

25. Page 18, line 3-15. “In 80.4% of cases, the medical trainee initiated the intervention phone call as a representative of the GP”. Could you please explain who the medical trainee is, and are you sure about your title?
The medical trainee was a medical student who was on placement with the GP for several weeks at the start of the study. We can propose the following title if it fits with the editor’s guidelines:
Impact of a phone-call with a medical student/general practitioner team on morbidity of chronic patients during the first French COVID-19 lockdown. A cluster randomized trial.

26. For the adjustment analysis, do you include the duration of CVD or mental health among your participants?. If, not please to explain in your limitation study.
We agree with this comment. However, we did not collect this information (cf previous comment on the need to include only very few patients). We completed the limitations of our study as followed:
“Beyond these limitations, including the limited data collected at inclusion for feasibility reasons in the emergency context,…”

27. Discussion section. Results were not discussed sufficiently and not linier with the objective study. For instance, it should compare previous studies, both linear and contradictory compared with the results of this research. Moreover, please add more opinions on why this could be different from the research done. In fact, based on Tables 2 and 3, there is no significant difference, so the discussion will be richer in the discussion section.
We did not find previous studies on a similar subject to compare with our results. We completed our discussion as detailed in point 28.

28. Finally, In conclusion; how the information presented in this study can help to improve policies, and what the recommendations.
We completed the discussion as follows:
“The lack of differences in hospitalization at 1 month for CVD patients does not allow us to draw any useful conclusions for practice. For the MHD patients, if the increase in the use of hospitalisation is confirmed by the 6-month data, the question will be raised as to the relevance of these hospitalisations and their impact on the morbimortality of these patients. Are these preventive hospitalisations that have allowed for avoiding more serious decompensations (which may even lead to suicide) and/or later on? If so, this could lead to a better identification of peoplet risk of decompensation to be contacted as a priority. It may also allow for a rethinking of access to care for these fragile patients, by checking on them. The completeness of the mortality and morbidity data (consumption of medication, hospitalisations, use of care) at 6 months after the intervention, which will be provided by the national health insurance, will enable us to answer this question and will be published as soon as we receive these results.”

Reviewer: 4
Dr Jufen Zhang

Comments to the Author:
The paper is well written and organised. I have a number of comments as detailed below.

Methods
Page 8, lines 55-57. “Eligible GPs were volunteer GPs practising as training supervisors from 8 different administrative regions in France (see Appendix 1)”. It appears that Appendix 1 shows more than 8 different administrative regions.
We organised GP recruitment by academic sites. There may be several university/academic sites per administrative region. Appendix 1 shows the 11 academic sites. We specified it in the text as follows: Eligible GPs were volunteer GPs practising as training supervisors from 8 different administrative regions in France, including 11 academic sites (see Appendix 1), who had medical trainees and a dedicated time to call patients.

Page 11, lines 9-14. In this study, the information of outcomes was collected based on patient self-reported, which could be biased. This may need to be addressed in the discussion selection.
We agree and added this limitation of self-reported outcomes in the discussion as follows:
“Furthermore, information on outcomes was patient self-reported, thus leading to a possible declaration bias. We could not totally avoid this risk. However, this performance bias, if present, may have resulted in an underestimation of the intervention effect, and for declaration bias, information will be confirmed by data from the national health insurance”.

Page 12. The logistic regression model within a generalized estimating equation framework was used for the primary outcome analysis. As indicated, for the primary outcome, missing data were considered as no hospitalisation, whatever the study groups. It is not clear how the missing values were handled in the logistic regression analysis? Did the authors consider using mixed model?
Missing data were considered as no hospitalisation in the logistic model.

Please indicate the statistical software used in the analysis.
The software use was SAS. We specified it: “All analyses were conducted using SAS 9.4.”

Results
Page 16, line 43. Suggest adding the percentages of the numbers reported: 348 and 39. In addition, please specify the imputation method used for imputing the missing values.
We completed as follows:
“In the COVIQuest_CV subtrial, missing information for the primary outcome was imputed as no hospitalisation for 348 (19.0%) participants in the intervention group and 39 (2.6%) in the control group.”
In the COVIQuest_MH subtrial, missing information for the primary outcome was imputed as no hospitalisation for 282 (33.9%) participants in the intervention group and 48 (8.8%) in the control group.

Page 20. Suggest inserting label “Table 3” in the section of primary and secondary 1-month outcomes.
We did it.

Table 1, line 31. Please show the number of patients in the intervention and control groups for MHD patients.
We added this information.

Table 2. What’s the definition of “Crude difference”? Is it the difference in hospitalization rate?
Crude difference is indeed the difference in hospitalisation rate. To be clearer, and in accordance with the CONSORT Statement, we changed it to “risk difference”.

In addition, please make it clear in the result section about the intention-to-treat analysis and sensitivity analysis.
Results reported in the text are those obtained on the full datasets, whereas adjusted analyses and analyses restricted to completers are reported only in Tables 2 & 3. We specified it as follows:
“In the COVIQuest_CV subtrial, missing information for the primary outcome was imputed as no hospitalisation for 348 (19.0%) participants in the intervention group and 39 (2.6%) in the control group. Thus, considering the full dataset, overall, 65 (3.54%) patients (…)”

In the COVIQuest_MH subtrial, missing information for the primary outcome was imputed as no hospitalisation for 282 (33.9%) participants in the intervention group and 48 (8.8%) in the control group. Thus, considering the full dataset, the primary outcome occurred in 27 (3.25%) and 12 (2.19%) patients (…)”.

**VERSION 2 – REVIEW**

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| **REVIEWER** | van Doorn, Sander<br>University Medical Center Utrecht, Julius Center for Health Sciences and Primary Care |
| **REVIEW RETURNED** | 30-May-2022 |

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| **GENERAL COMMENTS** | I have no further comments. |

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| **REVIEWER** | Zhang, Dr Jufen<br>Anglia Ruskin University |
| **REVIEW RETURNED** | 25-May-2022 |

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|---|---|
| **GENERAL COMMENTS** | The authors have addressed the previous comments. The revised version has been much improved. |