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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

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ABSTRACT

Objectives The first COVID-19 lockdown led to a significantly reduced access to healthcare, which may have increased decompensations in frail patients with chronic diseases, especially older patients living with a chronic cardiovascular disease (CVD) or a mental health disorder (MHD). The objective of COVIQuest was to evaluate whether a general practitioner (GP)-initiated phone call to patients with CVD and MHD during the COVID-19 lockdown could reduce the number of hospitalisation(s) over a 1-month period.

Design This is a cluster randomised controlled trial. Clusters were GPs from eight French regions.

Participants Patients ≥70 years old with chronic CVD (COVIQuest_CV subtrial) or ≥18 years old with MHD (COVIQuest_MH subtrial).

Interventions A standardised GP-initiated phone call aiming to evaluate patients' need for urgent healthcare, with a control group benefiting from usual care (ie, the contact with the GP was by the patient's initiative).

Main outcome measures Hospital admission within 1 month after the phone call.

Results In the COVIQuest_CV subtrial, 131 GPs and 1834 patients were included in the intervention group and 136 GPs and 1510 patients were allocated to the control group. Overall, 65 (3.54%) patients were hospitalised in the intervention group vs 69 (4.57%) in the control group (OR 0.82, 95% CI 0.56 to 1.20; risk difference −0.77, 95% CI −2.28 to 0.74). In the COVIQuest_MH subtrial, 136 GPs and 832 patients were included in the intervention group and 131 GPs and 548 patients were allocated to the control group. Overall, 27 (3.25%) patients were hospitalised in the intervention group vs 12 (2.19%) in the control group (OR 1.52, 95% CI 0.82 to 2.81; risk difference 1.38, 95% CI 0.06 to 2.70).

Conclusion A GP-initiated phone call may have been associated with more hospitalisations within 1 month for patients with MHD, but results lack robustness and significance depending on the statistical approach used.

Trial registration number NCT04359875.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ There were a lot of missing data on the primary outcome due to the vagaries of telephone collection; however, missing data will be completed with data collection from the national health insurance when available.
⇒ The absence of blinding due to the very nature of the intervention and the shorter time between the intervention and the primary outcome collection may have led to an underestimation of the intervention effect.
⇒ In total, 149 general practitioners included 10 275 patients during 1 month in the COVIQuest trial.
⇒ By randomising the order of patients receiving the intervention, all patients could receive a medical phone call in accordance with the Ministry of Health recommendations while we evaluated the impact of the intervention.

INTRODUCTION

The COVID-19 pandemic grew exponentially in Europe from January 2020.[1 2] Given the fast-growing case fatality rate in Italy, lockdown measures were decided in several European countries to limit the spread of the virus. These lockdown measures were set in France on 17 March 2020, as the epidemic curve for

the period from 23 February to 9 March 2020 yielded the best fit for exponential growth as compared with Italy, Germany and Spain.[3] Lockdown measures limited people from urban travel, including seeking healthcare, because the government announced on 23 March 2020 that only travel for 'urgent care or care that respond to a summons from a doctor' was allowed.[4] This measure significantly reduced patients' access to care. Indeed, in France, access to care (except for serious emergencies) is primarily through the general practitioner (GP), especially access to specialists.

Following this announcement, the number of consultations with GPs notably decreased in France.[5] Communication on lockdown and protection measures against the spread of the SARS-CoV-2 virus targeted more specifically patients with chronic diseases and those over 75 years of age, who were considered at increased risk of severe COVID-19.[6] Furthermore, an exemption was granted to community pharmacies to deliver an extra month of usual prescriptions for patients with chronic diseases without the need to contact their GP.[7] As a consequence, even patients with regular follow-up for one or more chronic disease(s) stopped consulting/contacting their GP in massive numbers. People requiring regular monitoring to detect certain decompensations of their chronic disease no longer consulted their GP. Teleconsultations were generalised but were at the time scarcely used due to the lack of such practice by the general population, especially by older people.[5] This decrease in consultations in general practice may constitute an underuse of care, leading to delayed diagnosis and treatment of serious diseases in the short and medium term, but also decompensation of chronic diseases.[8] This underuse of care could lead to excess morbidity and mortality in this population, indirectly linked to the COVID-19 epidemic.[5]

Two populations are particularly at risk of decompensation. Patients ≥70 years old with a chronic cardiovascular disease (CVD) are at risk of decompensation, with severe cardiovascular events such as stroke, myocardial infarction, heart failure or death without a regular medical follow-up.[8] This follow-up is usually performed by the GP.[9] The first hypothesis was that underuse of care induced by strict lockdown measures may have led to ignoring symptoms possibly indicating a major cardiovascular event. The 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 patients' 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. 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]

In France, patients with chronic CVD or MHD are regularly followed by the GP, and contact with their GP is traditionally according to the patient's initiative. On 8 April 2020, because of the underuse of care, the French government recommended that GPs directly contact their patients with 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 CVD or MHD on hospital admissions within 1 month after the phone call.

METHODS

Study design

The COVIQuest trial consisted of two simultaneous subtrials (although only one randomisation took place; see Randomisation and masking section): COVIQuest_CV for patients with CVD and COVIQuest_MH for patients with MHD. Both subtrials were open-label, two-parallel group, 1:1 cluster randomised trials with clusters defined as GPs.

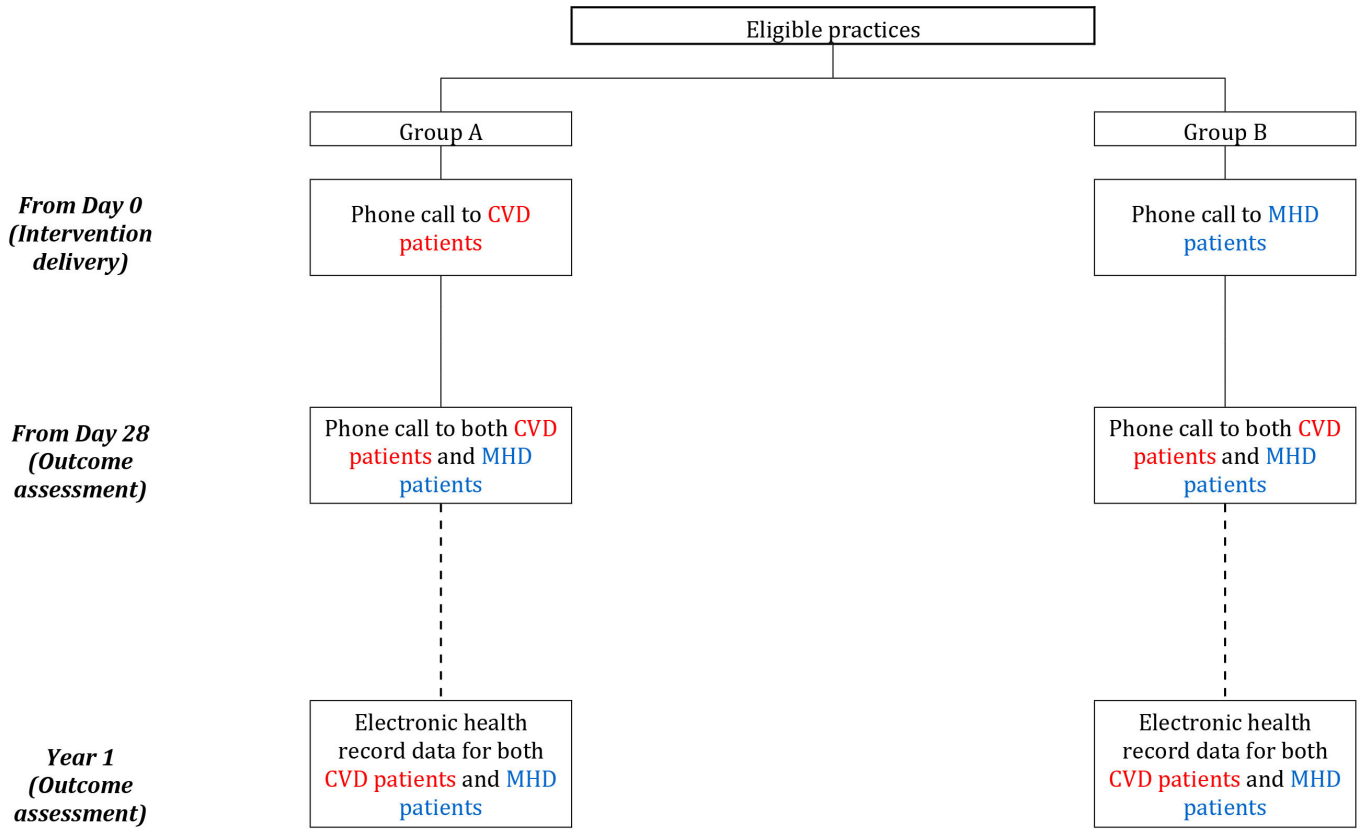
Because each patient included in the trial had to benefit from the intervention, as recommended by the French government on 8 April 2020,[11] the COVIQuest study used a wait-list control design with GPs randomised to call their patients with CVD first (group A) or their patients with MHD first (group B). With such a procedure, each GP participated in the two subtrials: those allocated to the intervention group for the subtrial focusing on patients with CVD actually formed the control group for the subtrial focusing on patients with MHD and vice versa (figure 1).

The timeline of each subtrial[12] is shown in figure 2.

Participants: GPs and patients

Eligible GPs were volunteer GPs practising as training supervisors from eight different administrative regions in France, including 11 academic sites (see online supplemental appendix 1), who had medical trainees and a dedicated time to call patients. 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.

Patients with CVD were ≥70 years old with a chronic CVD as referenced in the long-term illness list (ALD; ie, with ALD number 1, 3, 5, 12 and 13; details in online supplemental appendix 2) and regularly followed by their GP (ie, in the list of patients followed by a GP as referenced



CVD patients: patients with a cardiovascular disease - MHD patients: patients with a mental health disorder

Figure 1 COVIQuest design.

in the French health insurance database). Patients with MHD were ≥18 years old with an MHD referenced as number 23 in the ALD. Patients with both a cardiovascular ALD and a mental health ALD or for whom their GP considered their participation in the trial as inappropriate for any reason were not contacted. All participants or their family members or legally authorised representatives were provided with information about the trial, and oral informed consent was obtained at the beginning of the phone call before recruitment.

Randomisation and masking

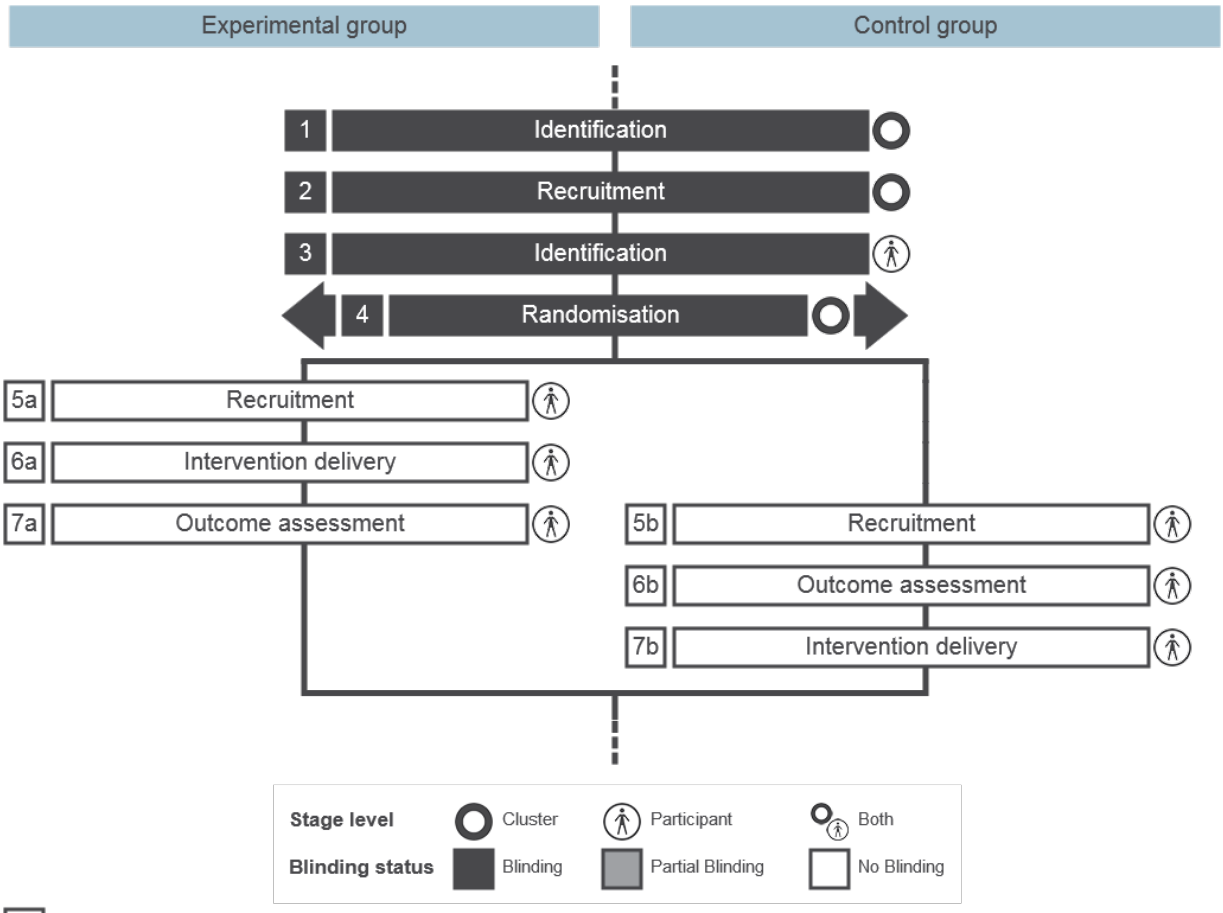
Randomisation units were GPs. If several eligible GPs were working at the same practice, they were all allocated to the same group. GPs were randomised all at once. The randomisation sequence was centrally generated by a statistician not involved in the GP or patient recruitment, who used permuted blocks of variable size. A stratified randomisation on regions was used to allocate GPs in a 1:1 ratio to group A (patients with CVD called first) or group B (patients with MHD called first). After screening their eligible patients (both patients with CVD and patients with MHD) for recruitment (see Procedures section), GPs received the randomisation sequence from the central trial coordinating team, which ensured concealment of allocation.

There was no possible blinding in the present trial due to the nature of the intervention.

Interventions

Interventions were the same in the two simultaneous subtrials. Patients recruited in the intervention arm benefited from a GP-initiated phone call from their GP or his/her medical trainee as a representative of the GP. This phone call was standardised with three questions: how are you doing? (response on a Likert scale from 0 'very bad' to 10 'very well'); would you have made an appointment with your GP if there had not been COVID-19 epidemic and lockdown? (response yes/no); and would you like an appointment with your doctor? (response yes/no) (see online supplemental appendix 3). In view of the answers to these three questions, the GP decided whether to propose a consultation or teleconsultation to the patient, taking into account the patient's medical background.

Patients in the control group initially benefited from usual care. When they were called to report the primary outcome within 1 month after the initiation of the trial (see Outcomes section), they also benefited from the intervention because they were asked the same three questions as for the intervention group, and once again were recontacted by their GP if deemed necessary. Therefore, the COVIQuest study was a wait-list trial.



1 **Identification**
General practitioners (GPs) are identified

2 **Recruitment**
GPs agreed to participate

3 **Randomisation**
GPs are randomized. In case several GPs work within the same practice, randomization is forced such that all GPs from a common practice are allocated to the same group. This comes down to randomize practices. Randomization is stratifed on geographical areas.

4 **Identification**
Patients are identified by GPs looking at their health record

5a **Recruitment**
In the experimental group, GPs or their students phoned to patients and asked them whether they agree to be involved in the trial.

6a **Intervention delivery**
In the same phone call during which patients' consent is obtained, patients are asked 3 questions by the GP or his/her student

7a **Outcome assessment**
One month after their recruitment, patients are contacted again either by the GP or his/her student. Patients are asked whether they have been hospitalized.

5b **Recruitment**
One month after the beginning of the study, patients are contacted by their GP or a student, and asled whether they would agree to be included in the study.

6b **Outcome assessment**
In the same phone call during which patients' consent is obtained, patients are asked whether they have been hospitalized.

7b **Intervention delivery**
In the same phone call as the one during which patients agreed and are assessed, the intervention (i.e. asking 3 short questions) is delivered.

Figure 2 Timeline of the COVIQuest_CV and COVIQuest_MH subtrials.

Procedures

GPs were asked to identify eligible patients with CVD and MHD and to alphabetically order them. Then GPs were randomised all at once to group A or B. GPs allocated to group A had to call their patients with CVD first at the beginning of the trial and then call their patients with MHD after 1 month at the same time they collected the primary outcome (see Outcomes section). For GPs allocated to group B, patients with MHD were called first, then patients with CVD 1 month later. When GPs were allocated to groups A and B, they were also randomly allocated to one of the 26 alphabet letters. They had to phone patients on the list, beginning with the letter to which they had been allocated. One month later, all patients with CVD and MHD were called to assess the primary outcome (see Outcomes section). Again, both for patients with CVD and patients with MHD, the order by which these patients were called was alphabetic, starting at the letter to which the GP had been randomly allocated. During the same phone call, for GPs allocated to group A, the intervention was also delivered to patients with MHD; and for GPS allocated to group B, the intervention was also delivered to patients with CVD (figure 2).

Outcomes

The primary outcome was the occurrence of at least one hospitalisation within 1 month after GP randomisation. It was patient self-reported and assessed by a phone call from the GP or his/her medical trainee to the patient 1 month after the practice had been randomised. Hospitalisation details (date, location, length and reason, if available) were collected. The primary outcome was the same for the two subtrials.

The secondary outcomes at 1 month were the proportion of patients for whom the practitioner had to call back after the medical trainee had phoned (in the intervention group only) and mortality (with cause of death) over the 1-month period after randomisation.

The secondary outcomes at 6 months were collected from electronic health records (national health insurance data; Système National des Données de Santé (SNDS)): mortality over 6 months; number and date of GP consultations and teleconsultations; number and date of consultations with another specialist; number of prescriptions related to the chronic disease that were dispensed by the pharmacy; number, date and reason for hospitalisations; cardiovascular events for COVIQuest_CV subtrial (MACE4 or Massive Adverse Cardiovascular Events or Major adverse cardiovascular events).

Statistical analyses

There were no data available to formulate hypotheses for the sample size. Therefore, all eligible GPs volunteering to participate were recruited (ie, at least 200 GPs were expected to be recruited). However, considering that the mean number of eligible patients per GP was expected to be about 80 for patients with CVD and 30 for patients with MHD,[13] approximately 16 000 participants with CVD and 6000 participants with MHD were possible. With such sample sizes, we expected to detect a difference of 5% vs 3% of events, with power of 90% for patients with CVD and 78% for patients with MHD, considering a two-sided type I error rate of 5%, a 0.5 coefficient of variation for cluster size and an intraclass correlation coefficient (ICC) of 0.03 (ie, the median value observed in Campbell *et al*[14]).

Statistical analyses were conducted by keeping all patients who agreed to be included in the group to which their GP had been allocated to. For the primary outcome, missing data were considered as no hospitalisation, whatever the study group. A multiple imputation strategy was considered impossible due to the absence of participant baseline data (except for age and sex). A sensitivity analysis was conducted for participants without a missing primary outcome (completers analysis). Another sensitivity analysis was performed, adjusting on sex and age. The level of statistical significance was set to 5%.

For the primary outcome analysis, a marginal approach was used by fitting a logistic regression model within a generalised estimating equation framework with a robust variance estimator and considering a compound symmetry correlation structure. This model accounted for clustering at the GP level. All analyses were adjusted on region (stratification variable). Clustering at the practice level was not taken into account, which limited our models to two-level hierarchical models with patients embedded in GPs only. A risk difference was also estimated by using an identity link function. Of note, for patients with MHD, the logistic model did not take into account the stratification variable due to convergence problems. ICCs were estimated per group by using the analysis of variance estimator.

For the secondary outcome analysis, the proportion of patients for whom the GP had to call back after the medical trainee call (in the intervention group) was estimated. The CI was corrected to take into account clustering. For that, a corrected variance was used, taking into account the ICC estimate associated with the intervention group.[15] Mortality rates were reported without any statistical analysis owing to the small number of events.

All analyses were conducted with SAS V.9.4.

This trial was registered with ClinicalTrials.gov (NCT04359875).

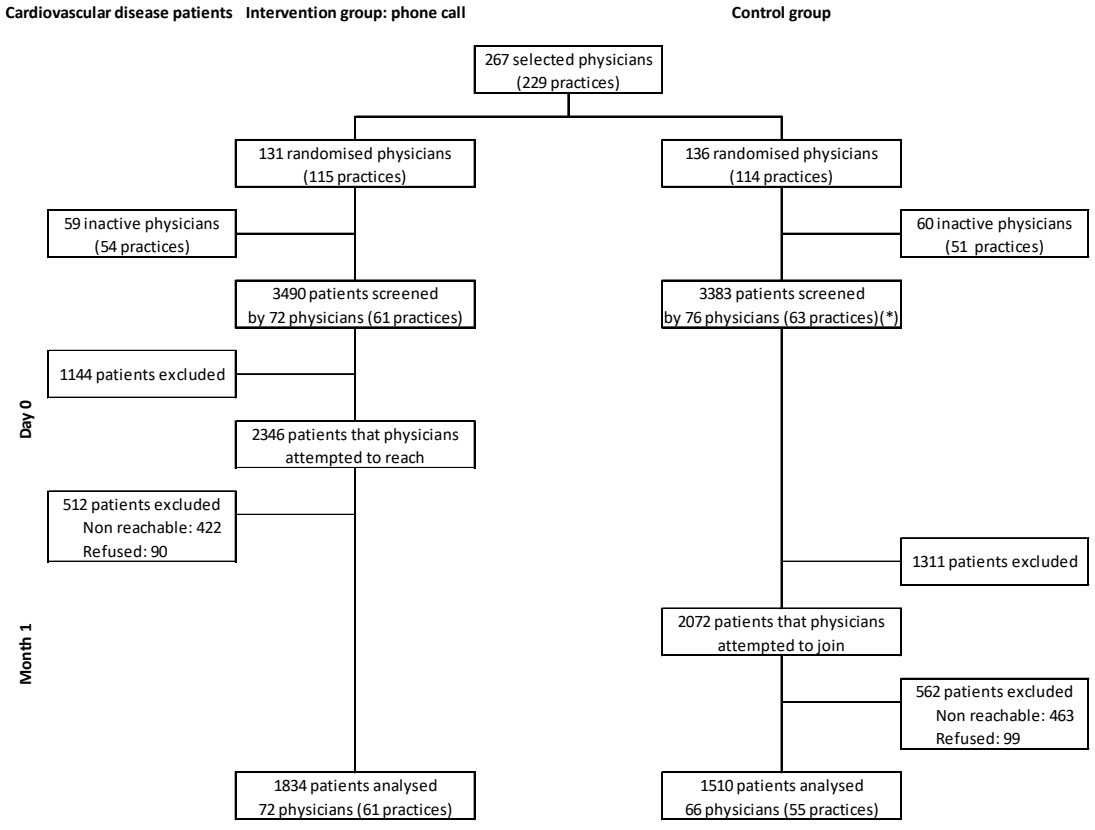
RESULTS

Trial profiles

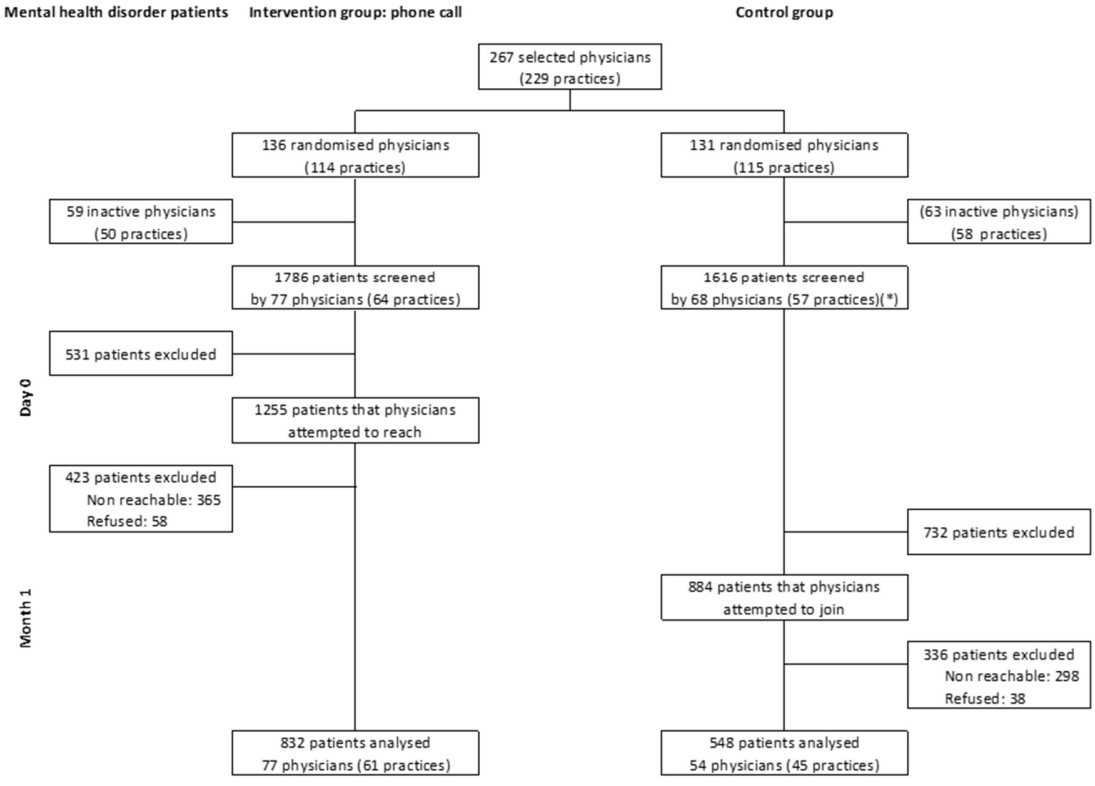
Of 267 selected GPs across eight different French areas, 149 from 125 practices identified 10 275 patients: 6873 patients with CVD and 3402 patients with MHD. A total of 3344 patients with CVD and 1380 patients with MHD were included (figure 3).

Physician and patient baseline characteristics

GPs were younger in group B than in group A. They were more frequently practising medicine in



(*) One physician (1 practice) screened patients with mental health disorders but no patient with cardiovascular disease



(*) Four physicians (4 practices) screened patients with mental health disorder but no patients with cardiovascular disease

Figure 3 Trial flow chart for the COVIQuest_CV and COVIQuest_MH subtrials. COVIQuest_CV, patients with cardiovascular disease; COVIQuest_MH, patients with mental health disorder.

Table 1 Baseline general practitioner and patient characteristics

Baseline characteristics of GPs by group*		
	Group A (n_1=72)	Group B (n_2=77)
Age (years), mean (SD); median (IQR)	49.9 (11.9); 49.0 (38.0–60.5)	43.3 (10.3); 39.0 (35.0–53.0)
Sex: male	32 (44.4)	30 (39.0)
Baseline characteristics of patients with CVD and MHD by group: intervention and control		
	Intervention group (phone call)	Control group
Patients with CVD, n	1834	1510
Age (years), mean (SD); median (IQR)	79.9 (6.9); 80.0 (74.0–85.0)	79.8 (7.2); 80.0 (74.0–85.0)
Sex: male	1056 (57.6)	878 (58.1)
Patients with MHD, n	832	548
Age (years), mean (SD); median (IQR)	53.2 (14.2); 53.0 (44.0–63.0)	53.4 (16.1); 54.0 (41.0–64.5)
Sex: male	298 (35.8)	203 (37.0)

Values are numbers (percentages) unless stated otherwise.
*Group A: patients with CVD called first; group B: patients with MHD called first.
CVD, cardiovascular disease; GP, general practitioner; MHD, mental health disorder.

multidisciplinary healthcare centres (n=38, 49.3% and n=28, 39.0% in groups B and A) and/or territorial professional health communities (n=38, 49.3% and n=30, 41.7%, respectively) and/or with the help of an advanced health nurse (n=19, 24.7% and n=12, 16.7%, respectively).

Patients' baseline data from the COVIQuest_CV and COVIQuest_MH subtrials were comparable between the intervention and the control group (table 1).

Complete baseline data for GPs are shown in online supplemental appendix 4.

Results for patients with CVD

Timeline adherence

In 80.4% of cases (n=1448/1834), the medical trainee initiated the intervention phone call as a representative of the GP. In the intervention group, the median time between the beginning of the trial on 30 April 2020 and the intervention phone call was 12 days (IQR 5–15). Then, pooling the two groups, the median time between 30 April 2020 and date of outcome assessment was 47 days (IQR 41–53). The results per group are shown in online supplemental appendix 5, table 1.

Information gathered by phone calls

The proportion of patients who had a consultation with their physician since the beginning of the lockdown was 46.6% (n=851/1825) and 81.8% (n=1159/1417) in the intervention and control groups. The perceived health status was similar in the intervention and control groups, with a mean (SD) score on the 0–10 Likert scale of 7.4 (1.8) and 7.3 (1.9), respectively. At the end of the phone call, 33.4% (n=611/1828) and 20.5% (n=308/1500) of patients in the intervention and control groups wanted an appointment with their GP. Details on information gathered by the intervention phone call are shown in online supplemental appendix 5, tables 2, 3 and 4.

Primary and secondary 1-month outcome results

In the COVIQuest_CV subtrial, missing information on 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 data set, overall, 65 of 1834 (3.54%) patients from the intervention group had a hospital admission within 1 month after randomisation vs 69 of 1510 (4.57%) in the control group (OR 0.82, 95% CI 0.56 to 1.20; risk difference −0.77, 95% CI −2.28 to 0.74) (table 2).

Among hospitalisations, 14 of 64 (21.9%) were for a cardiovascular cause in the intervention group vs 23 of 70 (32.9%) in the control group. Details on causes of hospitalisations are shown in online supplemental appendix 5, table 5. The number of deaths was 3 out of 1523 (0.2%) in the intervention group and 0 out of 1510 in the control group (no statistical test performed). Finally, in the intervention group, 670 of 1622 (41.3%) patients were recalled by their GP after the trainee intervention phone call to adapt their care.

COVIQuest_MH subtrial results

Timeline adherence

In 715 of 814 (87.8%) cases, the intervention phone call was made by the medical trainee as a representative of the GP. The median time from the beginning of the trial to the intervention phone call in the intervention group was 7 days (IQR 5–14). The median time from 30 April 2020 to the first phone call in the control group (ie, the outcome assessment phone call after a 1-month delay) was 49 days (IQR 42–56). The results per group are shown in online supplemental appendix 6, table 1.

Information gathered by phone calls

The proportion of patients who already had a consultation with their physician after the beginning of the lockdown was 48.0% (n=393/819) and 67.2% (367/546) in the intervention and control groups. The perceived

Table 2 COVIQuest_CV subtrial comparison of hospitalisations within 1 month

	Hospitalisation, n (%)				ICC (95% CI)	
	A: intervention group (phone call) (n_1=1834)	B: control group (n_2=1510)	OR (95% CI)*, p value	Risk difference (95% CI)*, p value	A: intervention group (phone call)	B: control group
Full data set	65 (3.54)	69 (4.57)	0.82 (0.56 to 1.20), 0.310	−0.77 (−2.28 to 0.74), 0.319	−0.004 (−0.011 to 0.009)	0.012 (−0.017 to 0.035)
Adjusted analysis†			0.82 (0.56 to 1.20), 0.308	−0.77 (−2.28 to 0.74), 0.315		
Completers‡	65/1486 (4.37)	69/1471 (4.69)	0.99 (0.68 to 1.43), 0.943	−0.06 (−1.66 to 1.54), 0.941	−0.003 (−0.011 to 0.014)	0.011 (−0.002 to 0.035)

*Adjustment on region.
†Adjustment on region, age and sex.
‡Missing data were considered as no hospitalisation.
COVIQuest_CV, patients with cardiovascular disease; ICC, intraclass correlation coefficient.

health status was similar in the intervention and control groups, with a median (SD) score on the 0–10 Likert scale at 1 month of 7.1 (2.2) and 7.1 (2.0), respectively. At the end of the phone call, 36.6% (302 of 826) and 29.1% (158 of 542) of patients in the intervention and control groups sought an appointment with their GP. Details on information gathered by the intervention phone call are shown in online supplemental appendix 6, tables 2, 3 and 4.

Primary and secondary 1-month outcomes

In the COVIQuest_MH subtrial, missing information on 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 data set, the primary outcome occurred in 27 of 832 (3.25%) and 12 of 548 (2.19%) patients in the intervention and control groups (OR 1.52, 95% CI 0.82 to 2.81; risk difference 1.38, 95% CI 0.06 to 2.70) (table 3).

Hospitalisations were for a mental health emergency (including suicide attempt): 8 of 26 (30.8%) vs 4 of 13 (30.8%) in the intervention and control groups. Details on causes of hospitalisations are shown in online supplemental appendix 6, table 5. The number of deaths was 2 out of 570 (0.35%) and 0 out of 548 in the intervention and control groups (no statistical test performed).

Finally, in the intervention group, 188 of 621 (30.3%) patients were recalled by their GP after the trainee's intervention phone call to adapt their care.

DISCUSSION

For patients with CVD, those who were called immediately (intervention group) and those who were called at 1 month (control group) did not differ in number of hospitalisations within 1 month. For patients with MHD, the intervention effect expressed as an OR was not statistically significant, but the risk difference in hospitalisations revealed a modest but statistically significant higher rate of hospitalisations in the intervention than in the control group. This apparent discrepancy is probably due to the inability to consider the region stratification variable when estimating the OR, which may have reduced the power of the statistical analysis.

These COVIQuest's primary results must be interpreted with caution. First, some randomised GPs did not screen any patients (119 for the COVIQuest_CV subtrial and 122 for the COVIQuest_MH subtrial). These empty clusters were discarded from all statistical analyses, which remains a limitation for data interpretation.[16] Other GPs screened control patients but finally did not include them, which led to 10 more empty clusters in the COVIQuest_CV subtrial and 14 in the COVIQuest_MH subtrial. Patients were included at day 0 in the intervention group and at month 1 in the control group. Reaching out to patients was more difficult at month 1 than at day 0. Indeed, medical trainees changed internship 1 June 2020, so some did not know the GP or the COVIQuest study and did not participate in the study. Some GPs no longer had

Table 3 COVIQuest_MH subtrial comparison of hospitalisations within 1 month

	Hospitalisation, n (%)				ICC (95% CI)	
	A: control group (n_1=548)	B: intervention group (phone call) (n_2=832)	OR* (95% CI), p value	Risk difference* (95% CI), p value	A: control group	B: intervention group (phone call)
Full data set	12 (2.19)	27 (3.25)	1.52 (0.82 to 2.81), 0.180	1.38 (0.06 to 2.70), 0.040	0.014 (–0.017 to 0.067)	0.002 (–0.018 to 0.036)
Adjusted analysis†			1.52 (0.82 to 2.81), 0.179	1.38 (0.07 to 2.68), 0.038		
Completers‡	12/500 (2.40)	27/550 (4.91)	2.14 (1.15 to 3.99), 0.017	2.79 (0.80 to 4.78), 0.006	0.012 (–0.020 to 0.068)	0.018 (–0.016 to 0.074)

*Adjustment on region.
†Adjustment on region, age and sex.
‡Missing data were considered as no hospitalisation.
COVIQuest_MH, patients with mental health disorder; ICC, intraclass correlation coefficient.

a medical trainee from 1 June 2020, which led to a lack of time to call patients. The lockdown ended on 11 May 2020. Therefore, fewer control patients compared with intervention patients had been recruited, which led to a possible risk of selection bias occurring in both subtrials. 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. All these elements may have biased the intervention effect estimates, which is the main limitation of the trial. However, missing data will be completed by the SNDS data collection performed by the National Health Insurance Caisse Nationale d'Assurance-Maladie, provider of the SNDS data, and published in an upcoming paper (data not available yet for administrative delays).

Second, the 1-month period between the first (day 1) phone call in the intervention group and the second (month 1) phone call in the control group was not always respected. When designing the study, GPs were expected to phone their patients allocated to the intervention group during the week after the initiation of the study. The study started on 30 April 2020, and therefore we expected that all day 1 phone calls would have been completed before 7 May 2020. As a result, month 1 phone calls were expected to take place before 4 June 2020. However, day 1 phone calls took place between 30 April 2020 and 8 June 2020 for patients with CVD and between 30 April 2020 and 25 May 2020 for patients with MHD. Therefore, the last month 1 phone call took place on 2 July 2021 for patients with CVD and on 3 July 2021 for patients with MHD. Hence, considering the 1-month period after randomisation as the observational period of interest would not be sensible. We decided to consider, for each patient, an observational period defined as the period between 30 April 2020 and the date of their month 1 phone call. This led to variations in observational period length between patients. However, there is no reason to consider that the distributions of these lengths would differ between groups.

Third, blinding was not possible in the present trial due to the nature of the intervention. There is a risk of performance and contamination bias, with GPs allocated to a control group calling their patients before the planned 1-month delay. 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.

Beyond these limitations, including the limited data collected at inclusion for feasibility reasons in the emergency context, the strength of COVIQuest trial was as both a healthcare and a research project. This opportunity to conjugate a strategy to detect decompensations in

patients with chronic disease during the lockdown and an evaluation of this strategy with a high level of evidence motivated 149 GPs to participate with their medical trainees. GPs were all new to research and signed up for free as investigators, which demonstrates their strong motivation to improve care and research during the COVID-19 pandemic. Another strength was the design of the protocol allowing all trial participants to benefit from the intervention while maintaining the experimental design. With a protocol randomising not patients to be called but rather the order of the patients to be called, each patient participating in the trial received a GP-initiated phone call to assess their state of health, which agreed with government recommendations.[11]

Considering the results of the primary outcome for both the COVIQuest_CV and COVIQuest_MH subtrials, the reasons for those early hospitalisations at 1 month are not fully known. In the COVIQuest_CV subtrial, the intervention and control groups did not differ in 1-month hospitalisation number. This lack of difference could be explained by a lack of power of the study because the sample size had not been reached particularly due to GP withdrawals. It could also be explained by an unexpected reduction in incidence of myocardial infarction during the lockdown period, which led to lack of impact of an underuse of care for patients with CVD. Hypotheses for a truly reduced incidence of myocardial infarction include reduced triggers such as physical activity or air pollution.[17] The COVIQuest_MH subtrial showed a higher 1-month hospitalisation rate in the intervention than in the control group. This result was the opposite of the hypothesis that the intervention phone call would result in a reduced hospitalisation rate. This increase in early hospitalisations for patients with chronic MHD may have avoided more complicated or critical issues such as suicides, psychiatric decompensations or substance/drug abuse that were particularly frequent in patients living with chronic MHD during the COVID-19 pandemic.[18 19] Data on mortality, hospitalisations and recourse of care analyses using the national health insurance at 6 months could give some answers.

The lack of differences in hospitalisation at 1 month for patients with CVD does not allow us to draw any useful conclusions for practice. For patients with MHD, 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 people at 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.

CONCLUSION

A GP-initiated phone call during the first COVID-19 lockdown in France may have been associated with increased number of hospitalisations within 1 month in patients with MHD. Conversely, this phone call had no significant impact on number of hospitalisations within 1 month in patients with CVD.

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Contributors Each author participated in the study design, revised the work critically for important intellectual content, gave his/her final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. CD-D and BG conceived, planned and conducted the study, and interpreted and reported the data. RB and DP participated in the conception of the study and interpretation of the data and critically revised the paper. JL participated in the conception of the study, analysed the data with BG and drafted the work with CD-D and BG. IE-A, JC, KA-M-F, SSu, MJ, BM, BC, SSi, C-AK, TB, MG, SB and the COVIQuest group critically discussed the design and participated in the acquisition of data and reporting of the results. EB, JP-L, VC, WE-H, DA, AC, LG-G, EL and OS-L participated in the study design and gave

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REFERENCES

1 Bernard Stoecklin S, Rolland P, Silue Y. Investigation team. first cases of coronavirus disease 2019 (COVID-19) in France: surveillance, investigations and control measures, January 2020. *Euro Surveill*;2020:6.
2 Hodcroft EB. Preliminary case report on the SARS-CoV-2 cluster in the UK, France, and Spain. *Swiss Med Wkly* 2020;150:9–10.
3 Yuan J, Li M, Lv G, *et al*. Monitoring transmissibility and mortality of COVID-19 in Europe. *Int J Infect Dis* 2020;95:311–5.
4 Ministère de la Santé. Prise en charge en ville PAR les Médecins de ville des patients symptomatiques en phase épidémique de covid-19, 2020. Available: https://solidarites-sante.gouv.fr/soins-et-maladies/maladies/maladies-infectieuses/coronavirus/professionnels-de-sante/article/en-ambulatoire-recommandations-covid-19-et-prise-en-charge
5 Saint-Lary O, Gautier S, Le Breton J, *et al*. How GPs adapted their practices and organisations at the beginning of COVID-19 outbreak: a French national observational survey. *BMJ Open* 2020;10:e042119.
6 Rimmer A. Covid-19: GPs can stop health checks for over 75s and routine medicine reviews. *BMJ* 2020;368:m1157.
7 Arrêté Du 23 Mars 2020 prescrivant les mesures d'organisation et de fonctionnement Du Système de santé nécessaires pour faire face l'épidémie de covid-19 dans Le cadre de l'état d'urgence sanitaire. Available: https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000041746744&dateTexte=20200403
8 An J, Zhang Y, Muntner P, *et al*. 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;9:e017310.
9 Hinton W, McGovern A, Coyle R, *et al*. Incidence and prevalence of cardiovascular disease in English primary care: a cross-sectional and follow-up study of the Royal College of general practitioners (RCGP) research and surveillance centre (RSC). *BMJ Open* 2018;8:e020282.
10 Mansfield KE, Mathur R, Tazare J, *et al*. Indirect acute effects of the COVID-19 pandemic on physical and mental health in the UK: a population-based study. *Lancet Digit Health* 2021;3:e217–30.
11 Ministère de la Santé. Prise en charge hors COVID19, 2020. Available: https://solidarites-sante.gouv.fr/IMG/pdf/soins-hors-covid-19.pdf
12 Caille A, Kerry S, Tavernier E, *et al*. Timeline cluster: a graphical tool to identify risk of bias in cluster randomised trials. *BMJ* 2016;354:i4291.
13 Données relatives l'ensemble des bénéficiaires Du dispositif des ALD une année donnée, 2021. Available: https://www.ameli.fr/l-assurance-maladie/statistiques-et-publications/donnees-statistiques/affection-de-longue-duree-ald/prevalence/prevalence-des-ald-en-2019.php
14 Campbell MK, Fayers PM, Grimshaw JM. Determinants of the intracluster correlation coefficient in cluster randomized trials: the case of implementation research. *Clin Trials* 2005;2:99–107.
15 Donner A, Klar N. Confidence interval construction for effect measures arising from cluster randomization trials. *J Clin Epidemiol* 1993;46:123–31.
16 Giraudeau B, Ravaud P. Preventing bias in cluster randomised trials. *PLoS Med* 2009;6:e1000065.
17 Mesnier J, Cottin Y, Coste P, *et al*. Hospital admissions for acute myocardial infarction before and after lockdown according to regional prevalence of COVID-19 and patient profile in France: a registry study. *Lancet Public Health* 2020;5:e536–42.
18 Czeisler Mark É, Lane RI, Petrosky E, *et al*. Mental Health, Substance Use, and Suicidal Ideation During the COVID-19 Pandemic - United States, June 24-30, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1049–57.
19 Robillard R, Daros AR, Phillips JL. Emerging new psychiatric symptoms and the worsening of pre-existing mental disorders during the COVID-19 pandemic: a Canadian multisite study: Nouveaux symptômes psychiatriques émergents et détérioration des troubles mentaux préexistants durant La pandémie de la COVID-19: une étude canadienne multisite. *Can J Psychiatry* 2021.