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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

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ABSTRACT

Objectives: To evaluate whether a general practitioner (GP)-initiated phone call to patients with a chronic cardiovascular disease (CVD) or mental health disorder (MHD) during the covid-19 lockdown could reduce hospitalisations within 1 month.

Design: A cluster randomised controlled trial.

Setting: Primary care; Clusters were 149 GPs from 8 French regions.

Participants: Patients ≥ 70 years old with chronic CVD (COVIQuest_CV subtrial) or ≥ 18 years old with an MHD (COVIQuest_MH subtrial) were selected. A total 4724 patients completed the study.

Interventions: An immediate standardized GP-initiated phone call aiming to evaluate patients' need for urgent healthcare. The control group benefited from usual care.

Primary and secondary outcome measures: Hospital admission within 1 month after the phone call was the primary outcome. Secondary outcomes included mortality and proportion of patients called back by the GP within 1 month.

Results: In the COVIQuest_CV subtrial, 1834 and 1510 patients were included in the intervention and control groups respectively. Overall, 65 (3.54%) patients were hospitalised in the intervention group versus 69 (4.57%) in the control group (odds ratio 0.82, 95% confidence interval [CI] 0.56 to 1.20; crude difference -0.77, 95% CI -2.28 to 0.74). In the intervention group, 670/1622 (41.3%) patients were recalled by their GP. In the COVIQuest_MH subtrial, 832 and 548 patients were included in the intervention and control groups respectively. Overall, 27 (3.25%) patients were hospitalised in the intervention group versus 12 (2.19%) in the control group (odds ratio 1.52, 95% CI 0.82 to 2.81; crude difference 1.38, 95% CI 0.06 to 2.70). In the

intervention group, 188/621 (30.3%) patients were recalled by their GP. There was no difference of mortality rate between intervention and control groups in both subtrials.

Conclusions: A GP-initiated phone call may have been associated with more hospitalisations within 1 month for MHD patients, but results lack robustness.

Trial registration: NCT04359875 (ClinicalTrials.gov)

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ARTICLE SUMMARY : STRENGTHS AND LIMITATIONS OF THE STUDY

COVIQuest was an opportunity to combine both optimising access to primary care and research by mobilising general practitioners and medical students during the first COVID-19 lockdown period.

COVIQuest mobilised 149 research-naïve general practitioners who included 4624 patients in a few weeks between the start of the COVID-19 lockdown on March 17, 2020 and the start of the trial on April 30, 2020, thus demonstrating the strong potential for responsiveness of primary care actors.

The COVIQuest protocol allowed all included patients to benefit from the intervention by randomising not the patients, but the order in which the intervention was allocated to the patients.

The start of COVIQuest a few days before the lockdown's end on May 11, 2020 and the short 1-month delay of the intervention between patients in the intervention and control groups may have decreased the effect of the intervention.

The significant number of missing data linked to the data collection method will be compensated by the subsequent recovery of data from the National Health Insurance.

Introduction

The covid-19 pandemic grew exponentially in Europe since 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 March 17, 2020, as the epidemic curve for the period February 23 to March 9, 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 March 23, 2020 that only travel for "urgent care or care that respond to a summons from a doctor" were allowed[4].

Following this announcement, the number of consultations with general practitioners (GPs) was 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 over age 75 years, 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. Teleconsultations were generalized but were at the time scarcely used because of lack of such practice by the general population, especially for 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]. Underuse of care induced by strict lockdown measures may have led to ignoring symptoms possibly indicating a major cardiovascular event. Second, 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 favour 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.

In France, patients with a chronic CVD or MHD are regularly followed by the 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 chronic disease to prevent decompensation[10]. However, the average number of patients with a chronic disease regularly followed by their GP is approximately 150 per GP[11], which questioned the feasibility of this recommendation. Furthermore, choosing which patients to contact first was ethically challenging.

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 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.

Methods

Study design

The COVIQuest trial consisted of two simultaneous subtrials (although only one randomisation took place; see *Randomisation and masking* section): the COVIQuest_CV for patients with a CVD and COVIQuest_MH for patients with an 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 April 8, 2020[10], the COVIQuest study used a wait-list control design with GPs randomised to call their CVD patients first (group A) or their MHD patients first (group B). With such a procedure, each 8GP participated in the two subtrials: those allocated to the intervention group for the subtrial focusing on CVD patients actually formed the control group for the subtrial focusing on MHD patients and vice versa (Figure 1).

Figure 1. COVIQuest design

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

Figure 2: Timeline of the COVIQuest_CV and COVIQuest_MH sub-trials

Participants: GPs and patients

Eligible GPs were volunteer GPs practising as training supervisors from 8 different administrative regions in France (see Appendix 1) who had medical trainees and a dedicated time to call patients.

CVD patients were ≥ 70 years old with a chronic CVD as referenced in the long-term illness list (*Affection longue durée* [ALD], i.e.. with ALD no. 1, 3, 5, 12, 13; details in Appendix 2) and regularly followed by their GP (i.e., in the list of patients followed by a GP as referenced in the French health insurance database). MHD patients were ≥ 18 years old with an MHD referenced as no. 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 (CVD patients called first) or group B (MHD patients called first). After screening their eligible patients (both CVD and MHD patients) 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 because of 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 by the GP or his/her medical trainee as a representative of the GP. This phone call was standardized 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) Would you like an appointment with your doctor? (response Yes/No) (see 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 re-contacted by their GP if deemed necessary. Therefore, the COVIQuest study was a wait-list trial.

Procedures *(Figure 2)*

GPs were asked to identify eligible CVD and MHD patients 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 CVD patients first at the beginning of the trial and then call their MHD patients after 1 month at the same time they collected the primary outcome (see *Outcomes* section). For GPs allocated to group B, MHD patients were called first, then CVD patients 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 CVD and MHD patients were called to assess the primary outcome (see *Outcomes* section). Again, both for CVD and MHD patients, 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 MHD patients; and for GPS allocated to group B, the intervention was also delivered to CVD patients.

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.

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.

Secondary outcomes at 6 months were collected from electronic health records (national health insurance data; Système National des Données de Santé [SNDS]): mortality over the 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: nonfatal stroke, nonfatal myocardial infarction, cardiovascular death and hospitalisation for heart failure); and psychotropic drug consumption for the COVIQuest_MH subtrial. Because of a data collection time interval, these data are not collected yet and will be reported subsequently.

Statistical analyses

There were no data available to formulate hypotheses for the sample size. Therefore, all eligible GPs volunteering to participate were recruited (i.e., 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 CVD patients and 30 for MHD patients[13], approximately 16,000 CVD and

6,000 MHD participants were possible. With such sample sizes, we expected to detect a difference of 5% versus 3% of events with power of 90% for CVD patients and 78% for MHD patients, 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 (i.e., 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 because of 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 generalized 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 embeded in GPs only. A risk difference was also estimated by using an identity link function. Of note, for MHD patients, the logistic model did not take into account the stratification variable because of convergence problems. ICCs were estimated per group by using the ANOVA 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 confidence interval 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.

Ethics and dissemination

The study protocol was approved by the ethics committee of CPP Sud-Méditerranée 3, no. 2020.04.21 ter_ 20.04.17.42325. The French committee for data handling (CNIL) approved the study (no. 920185 dated 30 of April 2020). This trial was registered with ClinicalTrials.gov (NCT04359875).

Patient and Public Involvement

Unfortunately, patients and public could not be involved due to an extremely tight COVIQuest timeframe.

Results

Trial profiles

Of 267 selected GPs across 8 different French areas, 149 from 125 practices identified 10,275 patients: 6873 CVD patients and 3402 MHD patients. A total of 3,344 CVD patients and 1,380 MHD patients were included (Figure 3).

Figure 3: Trial flow chart for the COVIQuest_CV and COVIQuest_MH subtrials

Physicians and patients baseline characteristics *(Table 1)*

GPs were younger in group B than group A. They were more frequently practicing medicine in multidisciplinary healthcare centres (49.3% and 39.0% in group B and A) and/or territorial professional health communities (49.3% and 41.7%, respectively) and/or with the help of an advanced health nurse (24.7% and 16.7%, respectively).

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

Complete baseline data for GPs are in supplementary files (Appendix 4).

Table 1. Baseline general practitionners and patients characteristics

Baseline characteristics of general practitioners (GPs) by group*		
	Group A	**Group B**

	(n_1=72)	**(n_2=77)**
Mean (standard deviation); median (interquartile range) age (years)	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 CVD and MHD patients by group: intervention or control		
	Intervention group (phone call) (n=1834)	**Control group (n=1510)**
CVD patients		
Mean (standard deviation); median (interquartile range) age (years)	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)
MHD patients		
Mean (standard deviation); median (interquartile range) age (years)	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)

*Group A (cardiovascular disease [CVD] patients called first); group B (mental health disorder [MHD] patients called first).

Values are numbers (percentages) unless stated otherwise.

Results for CVD patients

Timeline adherence

In 80.4% of cases, 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 April 30, 2020 and the intervention phone call was 12 days (interquartile range 5 to 15). Then, pooling the two groups, the median time between April 30, 2020 and date of outcome assessment was 47 days (interquartile range 41 to 53). Results per group are in supplementary files (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% (611/1828) and 20.5% (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 in supplementary files (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 for 348 participants in the intervention group and 39 in the control group. Overall, 65 (3.54%) patients from the intervention group had a hospital admission within 1 month after randomisation versus 69 (4.57%) in the control group (odds ratio 0.82, 95% confidence interval (CI) 0.56 to 1.20; crude difference -0.77, 95% CI -2.28 to 0.74) (Table 2).

Table 2. COVIQuest_CV subtrial comparison of hospitalisations within 1 month

	Hospitalisations n (%)		**OR** (95%CI)* p-value	**Crude difference** (95%CI)* p-value	**ICC** (95%CI)	
	A – Intervention group (phone call) (n_1 = 1834)	B – Control group (n_2 = 1510)			A – Intervention group (phone call)	B – Control group
Full dataset	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

OR, odds ratio; 95% CI, 95% confidence interval; ICC, intraclass correlation coefficient

Among hospitalisations, 14 were for a cardiovascular cause in the intervention group versus 23 in the control group. Details on causes of hospitalisations are in supplemental files (Appendix 5, table 5). The number of deaths were 3/1523 (0.2%) in the intervention group and 0/1510 in the control group (no statistical test performed). Finally, in the intervention group, 670/1622 (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 715/814 (87.8%) of 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 (interquartile range 5 to 14). The median time from April 30, 2020 to the first phone call in the control group (i.e., the outcome assessment phone call after a 1-month delay) was 49 days (interquartile range 42 to 56). Results per group are in supplementary files (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 health status was similar in the intervention and the 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% (302/826) and 29.1% (158/542) of patients in the intervention and control groups sought an appointment with their GP. Details on information gathered by the intervention phone call are in supplementary files (Appendix 6, tables 2, 3 and 4).

Primary and secondary 1-month outcomes

Missing information on the primary outcome was imputed for 282 participants in the intervention group and 48 in the control group. The primary outcome occurred in 27 (3.25%) and 12 (2.19%) patients in the intervention and control groups (odds ratio 1.52, 95% CI 0.82 to 2.81; crude difference 1.38 95% CI 0.06 to 2.70).

Table 3. COVIQuest_MH subtrial comparison of hospitalisations within 1 month.

	Hospitalisations n (%)		**OR (*)** (95%CI) p-value	**Crude difference (*)** (95%CI) p-value	**ICC** (95%CI)	
	A – Control group (n_1 = 548)	B – Intervention group (phone call) (n_2 = 832)			A – Control group	B – Intervention group (phone call)
Full dataset	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

OR, odds ratio; 95% CI, 95% confidence interval; ICC, intraclass correlation coefficient

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

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

Discussion

For CVD patients, patients 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 MHD patients, the intervention effect expressed as an odds ratio was not statistically significant, but the crude difference in hospitalisations revealed a modest but statistically significant higher rate of hospitalisations in the intervention than control group. This apparent discrepancy is probably due to the inability to consider the region stratification variable when estimating the odds ratio, which may have reduce the power of the statistical analysis.

These COVIQuest first 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, as medical trainees changed internship June 1, 2020 and the lockdown ended on May 11, 2020. Therefore, fewer control than 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 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 *Système National des Données de Santé* (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 April 30, 2020, and therefore we expected that all day-1 phone calls would have been completed before May 7, 2020. As a result, month-1 phone calls were expected to take place before June 4, 2020. However, day-1 phone calls took place between April 30, 2020 and June 8, 2020 for CVD patients and between April 30, 2020 and May 25, 2020 for MHD patients. Therefore, the last month-1 phone call took place on July 2, 2021 for CVD patients,and on July 3, 2021 for MHD patients. 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 April 30, 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 because of 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. We could not totally avoid this risk. However, this performance bias, if present, may have resulted in an underestimation of the intervention effect.

Beyond these limitations, 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.[10].

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 because of 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 under-use of care for CVD patients. 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 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 a 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 a chronic MHD during the covid-19 pandemic[18-19]. Data on mortality, hospitalisations, and recourse of care analyses using the SNDS system at 6 months could give some answers.

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 MHD patients. Conversely, this phone call had no significant impact on number of hospitalisations within 1 month in CVD patients.

Contributorship statement

Each author participated to 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.

Dibao-Dina Clarisse, Léger Julie, Boussageaon Rémy, Pouchain Denis and Giraudeau Bruno conceived the study.

Ettori-Ajasse Isabelle, 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 and the COVIQuest group participated to the acquisition of the data.

Léger Julie and Giraudeau Bruno analysed the data. Data were then interpreted with Dibao-Dina Clarisse.

Dibao-Dina Clarisse, Léger Julie and Giraudeau Bruno drafted the work.

Competing interests

The COVIQuest study was funded by the University Hospital of Tours Endowment Funds. We confirm that the sponsor had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. We also confirm the independence of researchers from funders and that all authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Funding

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Data sharing statement

Technical appendix, statistical code, and dataset are available on request.

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Ethics approval

The COVIQuest study obtained ethics approval from CPP Sud-Méditerranée 3 (no. 2020.04.21 ter_ 20.04.17.42325).

Participants gave oral consent to the medical trainee/general practitioner team before taking part in the study. Consents were recorded in the general practitioner's files.

Transparency declaration

As a lead author, Clarisse Dibao-Dina affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

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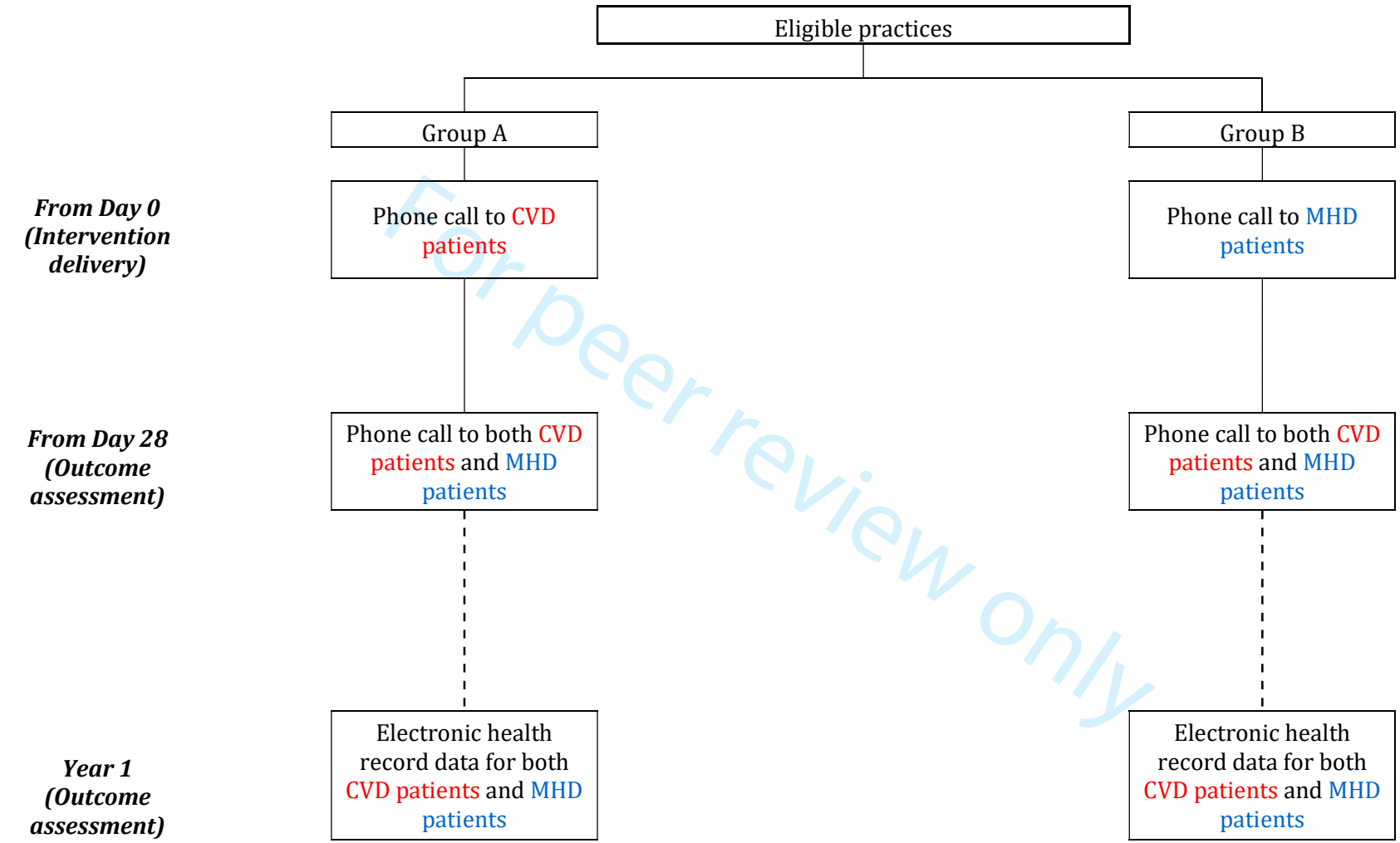
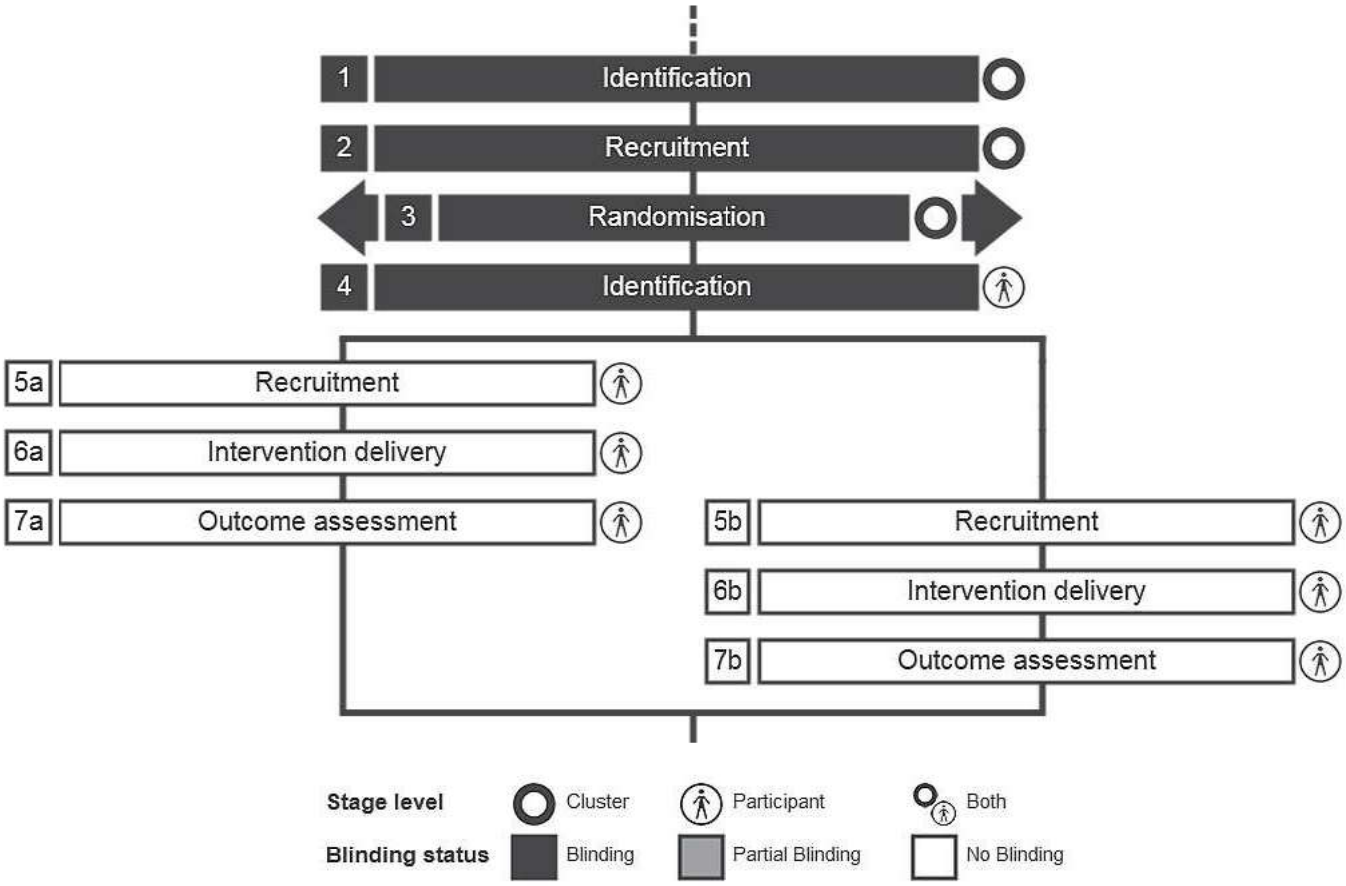
Julien Andouard, Hadrien Payen, Marie Blois, Guillemette Boyer, Marie Conte, David Hassan, Céline Terrasse, Lucile Ruin, Rachid Setaihi, Gaëlle Schoch, Cindy Filly, Valéria Zizolfi, Marie Quantin, Marine Barbier, Hulot Guillaume, Sara Da mota Pereira, Anaïs Wagenheim, Loren Audia, Simonnet Elisa, Raissa Wanyou, Laure Patturel, Houari Kaid Ali, Marie Citounadin, Tang Vu Tuong Van, Xavier Bolla, Claire Le Lièvre de la Morinière, François Pettinotti, Agathe Edeline, Céline Duchossoir, Marianne Dufournier, Agathe Pinot, Clément Bertrand, Guillaume Rioult, Cynthia Delauneay Belleville.



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



1 Identification
General practitioners (GPs) practising as training supervisors from 8 different French administrative regions are identified

2 Recruitment
GPs who agree to participate are recruited

3 Randomisation
GPs are randomised. In case several GPs work within the same practice, randomisation is forced such that all GPs from a common practice are allocated to the same group. This comes down to randomise practices. Randomisation is stratified on administrative regions.

4 Identification
In the COVIQuest_CV subtrial, patients ≥ 70 years old with a chronic cardiovascular disease (CVD patients) are identified. In the COVIQuest_MH subtrial, patients ≥ 18 years old with a mental disorder (MHD patients) are identified. Patients with both a cardiovascular disease and a mental health disorder are not eligible. GPs are not informed of their randomised allocation while identifying patients.

5a Recruitment
In the intervention group, GPs or their students phone to patients and ask them whether they agree to be included in the trial.

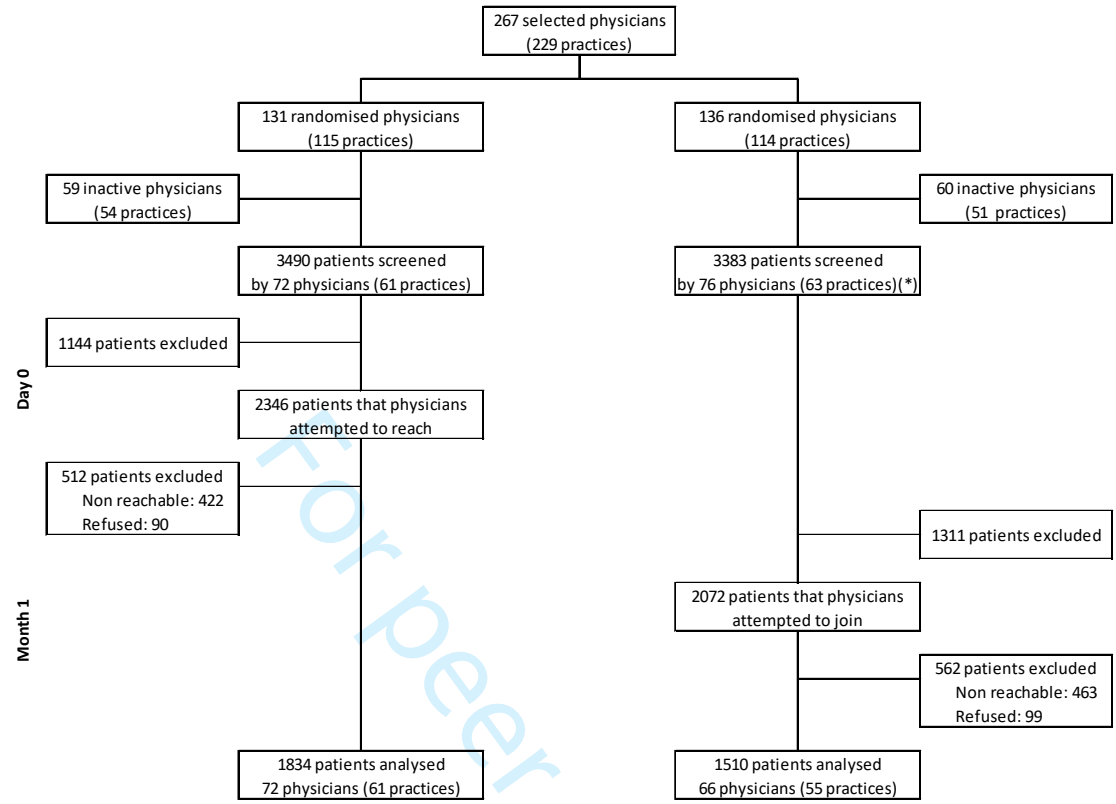
6a Intervention delivery
In the same phone call during which patients' consent is obtained, patients are asked 3 questions by the GP or his/her student: 1) How are you doing? 2) Would you have made an appointment with your GP if there had not been Covid 19 epidemic and lockdown? 3) Would you like an appointment with your doctor?

7a Outcome assessment
One month after their recruitment, patients are contacted again by their GP or his/her student, and asked wheter they have been hospitalised.

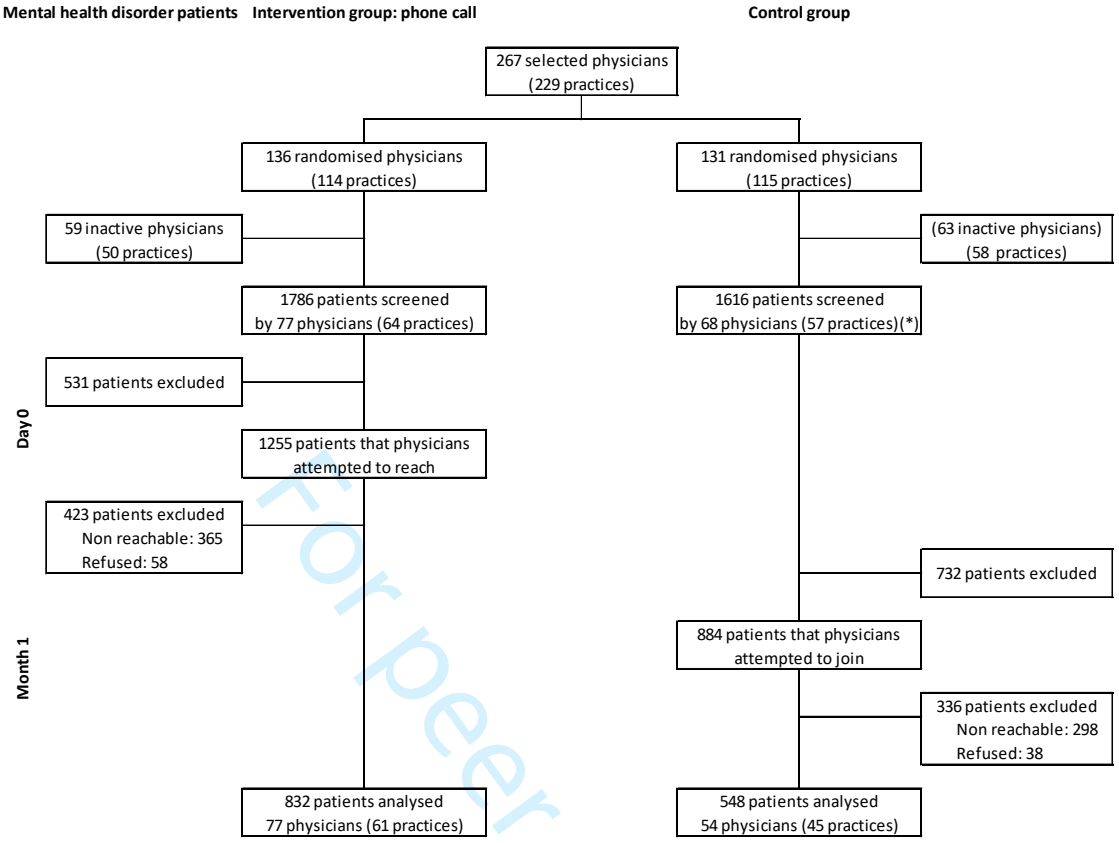
5b Recruitment
One month after the beginning of the study, patients are contacted by their GP or his/her student, and asked whether they agree to be included in the trial.

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

7b Intervention delivery
Still during the same phone call, the intervention (i.e. asking the 3 short questions) is delivered.



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



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

Supplementary files

Appendix 1. List of study sites, coordinators and general practitioners from the COVIQuest group

Name	Academic general practice department	Administrative area	General Practitioners
Ettori-Ajasse Isabelle	Tours	Centre-Val de Loire	SAMKO BORIS, DIBAO-DINA CLARISSE, GONZALES ANNE-MARIE, GAY-LAUNAY KARINE, MOLIMART FRANCOIS, BADEY-MEURISSE ALEXANDRA, THOMAS MARIE, PHILIPPE LAURENCE, LEROUX FARRUGIA DELPHINE, LEFEVRE RÉMI, LANG VIRGINIE, LIZE SOPHIE, DUGUE DURET MARIE-LOUISE, BAGOURD EMMANUEL, RICOIS AMÉLIE, CUVILLIER OLIVIER, DE LA PORTE DES VAUX CÉDRIC, BROUX HÉLÈNE, BACHELIER JEAN-YVES, ROBERT JEAN, BORDEAUX SAMUEL, CHALEIX LYSIANE, GABERT MARTINE, GRISON XAVIER, SIMONEAU CORINNE, PÈRE DOMINIQUE, BOURDU STÉPHANIE, DUMAS ADRIEN, LAUVERJAT FLORENCE, MAUPERTUIS QUENTIN, NOE LAGRANGE ANAIDE, TIERCIN SYLVIE, DUMOT PIERRE, AUMARECHAL ALAIN, MOLINA VALÉRIE, RIVOAL BERNARD, GROSSE JULIE, GALY VINCENT, DESRUES PATRICE, YVON-PETRAULT BLANDINE, VIEILLE ROGER, WITTKE LAURENCE, RUBE DELPHINE, BAUSSANT ALEXANDRE, MONTPERT-BOUVIER LUCIE, CONSTANT MARIE-VÉRONIQUE, TEN KET KIAN FRANÇOIS, PERRAIN ALICE
Sun Sophie	Lyon	Auvergne-Rhône-Alpes	JACQUIOT DENIS, MUZELLE VÉRONIQUE, PIGACHE CHRISTOPHE, LAMORT BOUCHE MARION, MANGOT CLAIRE, BENEDINI ELISE, LAVILLE AGNÈS, POTENCIER BENJAMIN, FOSSIER BENOIT, VALLE FLORIAN, FAY ISABELLE, CHAMBION PIERRE, BRYS VERONIQUE, SUN SOPHIE, BELLECOSTE VINCENT, FLORI MARIE
Jego Maeva	Marseille	Occitanie	DE TADDEO CHRISTINE, THERY DIDIER, CORDEL ANNE CATHERINE , GUERCIA OLIVIER, BARGIER JACQUES, TUDOSE IRINA, NUSSLI NICOLAS
Motte Baptise	Lille catholique	Hauts de France	NGUYEN BRUNO, MORIN PIERRE-ETIENNE, DURAND-CHEVAL CLOTILDE, MOTTE BAPTISTE, DANCHIN FREDERIC

Bruel Sébastien	Saint Etienne	Auvergne-Rhône-Alpes	FRUMUSELU RUXANDRA, DELEBARRE AMANDINE, FAVIE JULIEN
Chiron Benoit	Brest	Bretagne	GELINEAU THOMAS, LE GOFF DELPHINE, VERBEQUE MORVAN, MANON DARABAN TUDOR, PENIN GAELLE, LUCAS ALDRIC, LOPIN CÉLINE, FONSECA JÉROME, LE GUENNEC ANGÉLIQUE
Chambe Juliette	Strasbourg	Grand Est	GHALI-DEBUS ISABELLE, MAGINOT HÉLÈNE, ZUMSTEIN CARINE, ROOS-BERNARD SÉVERINE, RUXER SERGE, PLAUM MANUELA, GUIHENEUF CHARLINE, LENERTZ JOHN, ERNST MYRIAM, CHAMBE JULIETTE, DE CHAZELLES GRÉGOIRE, BUCHLIN FRANÇOIS, HILD PHILIPPE, VONAU PHILIPPE, DUMAS BREITWILLER CLAIRE, BERTHOU ANNE, CHARTON LÉA, LÉPINE CAMILLE
Sidorkiewicz Stéphanie	Paris Descartes	Ile de France	OLESKER SOPHIE, MALMARTEL ALEXANDRE, GHASAROSSIAN CHRISTIAN, RUSSO PATRICK, ANDERSON MARGUERITE, RICHEMOND MICHÈLE, SIDORKIEWICZ STÉPHANIE, ECOLLAN MARIE, JAURY PHILIPPE, BENAINOUS OLIVIER, MSIKA RAZON MARIE, CATU-PINAULT ANNIE
Khau Cam-Anh	Paris Nord La Sorbonne	Ile de France	KHAU CAM-ANH, BERKAI RANIA, MERCIER ALAIN, GRUNBERG PHILIPPE, PHAM LAN-ANH, RENAULT ALAINE, BACH LORENE, COUDERC AUDREY, CHEVALLIER FREDERIC, CHABANNES AUDREY
Bouchez Tiphanie	Nice	Provence-Alpes-Côte d'Azur	MELLERIN IANIS, BOUCHEZ TIPHANIE, GARSON SANDRINE, GARDON GILLES, PASCUCCI-ZAKARIAN SANDRINE, GUERVILLE VÉRONIQUE, MOUILLE BLANC CECILE, MUNCK STEPHANE, GUERVILLE MARC-ANDRÉ
Ghali Maria	Angers	Pays de la Loire	JUDALET ILLAND GHISLAINE, PY THIBAUT, TESSIER CAZENEUVE CHRISTINE, RAMOND ROQUIN ALINE, GALLOT EMMANUEL, LOSSON DAUSSY GAELLE, LACOMBE ANTOINE, GABARD CATHERINE, DEVAUD BERTRAND, BUFFARD PASCAL, PLESSIS ANNE, BOURGEOIS CÉCILE

Appendix 2. List of 30 long-term illnesses (ALD 30) that are exempt from user fees

ALD no. 1 - Invalid stroke

ALD no. 2 - Bone marrow failure and other chronic cytopenias

ALD no. 3 - Chronic arteriopathies with ischemic manifestations

ALD no. 4 - Complicated bilharziasis

ALD no. 5 - Severe heart failure, severe arrhythmia, severe valvular heart disease; Graves congenital heart disease

ALD no. 6 - Chronic active diseases of the liver and cirrhosis

ALD no. 7 - Severe primary immune deficiency, prolonged treatment, infection with human immunodeficiency virus

ALD no. 8 - Type 1 diabetes and type 2 diabetes

ALD no. 9 - Severe form of neurological and muscular disorders (including myopathy), severe epilepsy

ALD no. 10 - Hemoglobinopathies, hemolysis, chronic constitutional and acquired severe

ALD no. 11 - Hemophilia and constitutional disorders of severe hemostasis

ALD no. 12 - Severe hypertension

ALD no. 13 - Coronary disease

ALD no. 14 - Severe chronic respiratory failure

ALD no. 15 - Meadow

ALD no. 16 - Parkinson disease

ALD no. 17 - Hereditary metabolic diseases a prolonged specialized treatment

ALD no. 18 - Cystic fibrosis

ALD no. 19 - Severe chronic nephropathy and primary nephrotic syndrome

ALD no. 20 - Paraplegia

ALD no. 21 - Periarthritis nodosa, acute systemic lupus erythematosus, progressive generalized scleroderma

ALD no. 22 - Progressive rheumatoid arthritis

ALD no. 23 - Psychosis, severe personality disorder, mental retardation

ALD no. 24 - Ulcerative colitis and progressive Crohn's disease

ALD no. 25 - Multiple sclerosis

ALD no. 26 - Progressive structural scoliosis (with an angle equal to or greater than 25 degrees) until spinal maturation

ALD no. 27 - Fall from ankylosing spondylitis

ALD no. 28 - Organ transplant suites

ALD no. 29 - Active tuberculosis

ALD no. 30 - Malignant tumor, malignant disease of lymphatic or hematopoietic tissue.

Appendix 3. Interview guide

Information and oral consent of the patient:

I am Mr/Mrs X, a student in my Nth year of medical school at Dr Y's practice. I am calling you at the request of your GP Dr Y to ask you three short questions. The answers you give me will enable Dr Y to know how you are doing and to offer you appropriate care during lockdown if necessary. Your answers will be used anonymously in the COVIQUEST study in which Dr Y is participating. The aim of this study is to find out what impact this call has on your care. (Only for patients in the intervention group: If you agree to your answers being used in this study, you should know that you will be contacted again in 1 month time to hear from you in the same way). If you do not want your answers to be used for the study, please note that this will not affect your treatment by Dr Y. Do you accept that I ask you questions? I would like to remind you that your answers will be completely anonymous and that you can say at any time that you no longer wish your answers to be collected in the framework of COVIQUEST, without any impact on your care. If you have any questions to ask me or would like to discuss them with Dr Y, please do not hesitate.

Intervention:

How are you doing? (using a Likert scale of 1 = very bad to 10 = very good)

Would you have made an appointment with your GP if there had not been a lockdown related to the COVID19?

Would you like an appointment with your GP?

Appendix 4. Baseline characteristics of general practitioners (GPs) by group*.

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**A** (n_1 = 72)	**B** (n_2 = 77)
Age (years)	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)
Work organisation		
Practice, only physicians	39 (54.2)	32 (41.6)
Alone	5 (6.9)	7 (9.1)
Practice, multidisciplinary healthcare centre	28 (39.0)	38 (49.3)
Territorial professional health community	30 (41.7)	38 (49.3)
Advanced public health nurse	12 (16.7)	19 (24.7)

*Group A (cardiovascular disease [CVD] patients called first); group B (mental health disorder [MHD] patients called first)

Appendix 5. COVIQuest_CV results

Table 1. Process evaluation of the intervention and outcome assessment

mean ± standard deviation, median [Q1 ; Q3] & {Min ; Max} for quantitative variables *n (%) for qualitative variables*	**A - Intervention group - Phone call** (n_1 = 1834)	**B - Control group** (n_2 = 1510)
Who phoned (intervention phone call)? - n_1 = 1801		
Physician	236 (13.1)	
Student	1448 (80.4)	
Other person (e.g. secretary)	117 (6.5)	
Time between April 30th 2020 and phone call (days)	11.7±8.0 12.0 [5.0 ; 15.0] {0 ; 39}	
Time between the phone call and the outcome assessment (days) - n_1 = 1508	34.1±7.0 33.0 [29.0 ; 39.0] {12 ; 58}	
Time between April 30th 2020 and the outcome assessment (days) - n_1 = 1508, n_2 = 1510	45.6±8.7 47 [40 ; 53] {26 ; 64]	48.7±7.8 48 [42 ; 56] {26 ; 63]

Table 2. Patient health status when phoned (intervention group)

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**A - Intervention group - Phone call** (n_1 = 1834)
Had consultations with his/her physician since the beginning of the lockdown period - n_1 = 1825	851 (46.6)
Number of consultations - n_1 = 845	1.5±0.9 1 [1 ; 2]
Had a contact with his/her physician since the beginning of the lockdown period - n_1 = 1811	500 (27.6)
Health status perception - n_1 = 1820 (*)	7.4±1.8 8 [6 ; 9]
Would have made an appointment - n_1 = 1828	856 (46.8)
Would like an appointment - n_1 = 1828	611 (33.4)

(*) 0-10 Likert scale

Table 3. Symptoms (for patients who declared they would like an appointment)

n (%) for qualitative variables	**A - Intervention group - Phone call - Patients who wanted an appointment** (n = 611)
Number of symptoms - n_1 = 459	
1	374 (81.5)
2	62 (13.5)
3	23 (5.0)
Symptoms (*)	
General, non specific	304 (53.6)
Blood system, immunology	2 (0.3)
Digestive	35 (6.2)
Ocular	5 (0.9)
Ear	4 (0.7)
Cardiovascular	60 (10.6)
Osteoarticular	64 (11.3)
Neurological	6 (1.1)
Psychological	22 (3.9)
Respiratory	22 (3.9)
Skin	15 (2.6)
Metabolism, nutrition	11 (1.9)
Urology	8 (1.4)
Pregnancy	0
Reproductive system, female	2 (0.3)
Reproductive system, male	0
Social	7 (1.2)

(*) One patient may have two or three symptoms

Table 4. Patient health status when assessed

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**A - Intervention group - Phone call** (n_1 = 1834)	**B - Control group** (n_2 = 1510)
Had COVID-19 disease - n_1 = 1586, n_2 = 1409		
Yes (TR-PCR test)	4 (0.2)	7 (0.5)
May-be	72 (4.5)	61 (4.3)
Do not know	1510 (95.2)	1341 (95.2)
Health status perception - n_1 = 1457, n_2=1488 (*)	7.4±1.8	7.3±1.9
	8 [6 ; 9]	8 [6 ; 8.5]
Had consultations with his/her physician since the beginning of the lockdown period - n_2 = 1417		1159 (81.8)
Number of consultations - n_2 = 1155		1.9±1.3
		1 [1 ; 2]
Had a contact with his/her physician since the beginning of the lockdown period - n_2= 1454		580 (39.9)
Would like an appointment - n_2 = 1500		308 (20.5)

(*) 0-10 Likert scale

Table 5. Causes of hospitalisations

n (%) for qualitative variables	**A - Intervention group - Phone call**	**B - Control group**
Cause of hospitalization - $n_1 = 64$, $n_2 = 70$ (*)		
UCV: Cardiovascular emergency	14 (21.9)	23 (32.9)
TS: Suicide attempt	0	0
USM: Mental health emergency (except suicide attempt)	0	0
UAM: Other medical emergency	30 (46.9)	18 (25.7)
UAC: Other surgical emergency	10 (15.6)	15 (21.4)
PCV: Planned cardiovascular hospitalisation	2 (3.1)	0
PSM: Planned mental health hospitalisation	0	0
PAM: Planned other medical reason hospitalisation	1 (1.6)	7 (10.0)
PAC: Planned other surgical reason hospitalisation	7 (10.9)	7 (10.0)

(*) Units of analysis are hospitalisations not patients

Appendix 6. COVIQuest_MH results

Table 1. Process evaluation of the intervention and outcome assessment

mean ± standard deviation, median [Q1 ; Q3] & {Min ; Max} for quantitative variables *n (%) for qualitative variables*	**A - Control group** (n_1 = 548)	**B - Intervention group - Phone call** (n_2 = 832)
Who phoned (intervention phone call)? n_2 = 814		
Physician		85 (10.4)
Student		715 (87.8)
Other person (e.g. secretary)		14 (1.7)
Time between April 30th 2020 and phone call (days)		10.6±7.5 7.0 [5.0 ; 14.0] {0 ; 29}
Time between the phone call and the outcome assessment (days) - n_2 = 560		37.3±9.2 35.0 [29.0 ; 45.5] {12 ; 56}
Time between April 30th 2020 and the outcome assessment (days) - n_1 = 548, n_2 = 560	48.3±9.0 49 [42 ; 56] {20 ; 64]	47.3±9.3 48 [41 ; 55.5] {14 ; 63]

Table 2. Patient health status when phoned (intervention group)

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**B - Intervention group - Phone call** (n_2 = 832)
Had consultations with his/her physician since the beginning of the lockdown period - n_2 = 819	393 (48.0)
Number of consultations - n_2 = 392	2.1±1.4 2 [1 ; 3]
Had a contact with his/her physician since the beginning of the lockdown period - n_2 = 817	211 (25.8)
Health status perception - n_2 = 819 (*)	6.9±2.2 7 [5 ; 9]
Would have made an appointment - n_2 = 826	401 (48.5)
Would like an appointment - n_2 = 826	302 (36.6)

(*) 0-10 Likert scale

Table 3. Symptoms (for patients who declared they would like an appointment)

n (%) for qualitative variables	**B- Intervention group - Phone call - Patients who wanted an appointment n=302**
Number of symptoms - n_2 = 246	
1	190 (77.2)
2	41 (16.7)
3	15 (6.1)
Symptoms (*)	
General, non specific	131 (41.3)
Blood system, immunology	1 (0.3)
Digestive	21 (6.6)
Ocular	2 (0.6)
Ear	1 (0.3)
Cardiovascular	8 (2.5)
Osteoarticular	39 (12.3)
Neurological	12 (3.8)
Psychological	57 (18.0)
Respiratory	12 (3.8)
Skin	7 (2.2)
Metabolism, nutrition	5 (1.6)
Urology	5 (1.6)
Pregnancy	0
Reproductive system, female	2 (0.6)
Reproductive system, male	2 (0.6)
Social	12 (3.8)

(*) One patient may have two or three symptoms

Table 4. Patient health status when assessed

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**A - Control group** (n_1 = 548)	**B - Intervention group - Phone call** (n_2 = 832)
Had COVID-19 disease - n_1 = 538, n_2 = 584		
Yes (TR-PCR test)	5 (0.9)	0
May-be	51 (9.5)	42 (7.2)
Do not know	482 (89.6)	542 (92.8)
Health status perception - n_1 = 544, n_2=544 (*)	7.1±2.0 7 [6 ; 8]	7.1±2.2 7 [6 ; 9]
Had consultations with his/her physician since the beginning of the lockdown period - n_1 = 546	367 (67.2)	
Number of consultations - n_1 = 366	2.1±1.5 1 [1 ; 3]	
Had a contact with his/her physician since the beginning of the lockdown period - n_1= 534	247 (46.2)	
Would like an appointment - n_1 = 542	158 (29.1)	

(*) 0-10 Likert scale

Table 5. Causes of hospitalisations

n (%) for qualitative variables	**A - Control group**	**B - Intervention group - Phone call**
Cause of hospitalization - $n_1 = 13$, $n_2 = 26$ (*)		
UCV: Cardiovascular emergency	0	0
TS: Suicide attempt	0	1 (3.8)
USM: Mental health emergency (except suicide attempt)	4 (30.8)	7 (26.9)
UAM: Other medical emergency	3 (23.1)	10 (38.5)
UAC: Other surgical emergency	4 (30.8)	4 (15.4)
PCV: Planned cardiovascular hospitalisation	0	0
PSM: Planned mental health hospitalisation	0	0
PAM: Planned other medical reason hospitalisation	1 (7.7)	4 (15.4)
PAC: Planned other surgical reason hospitalisation	1 (7.7)	0

(*) Units of analysis are hospitalisations not patients

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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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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 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 and MHD patients during the COVID-19 lockdown could reduce the number of hospitalisation(s) over a 1-month period.

Design: A cluster randomised controlled trial. Clusters were GPs from 8 French regions.

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

Interventions: A standardized GP-initiated phone call aiming to evaluate patients' need for urgent healthcare. The control group benefited 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 versus 69 (4.57%) in the control group (odds ratio 0.82, 95% confidence interval [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 versus 12 (2.19%) in the control group (odds ratio 1.52, 95% CI 0.82 to 2.81; risk difference 1.38, 95% CI 0.06 to 2.70).

Conclusions: 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.

Trial registration NCT04359875 (ClinicalTrials.gov)

Funding The University Hospital of Tours Endowment Fund

SUMMARY BOXES

Strengths and limitations of this study

There was a lot of missing data on the primary outcome because of 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 GPs 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 since 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 March 17, 2020, as the epidemic curve for the period February 23 to March 9, 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 March 23, 2020 that only travel for "urgent care or care that respond to a summons from a doctor" were allowed[4]. This measure significantly reduced patients' access to care. Indeed, in France, access to care (except for serious emergencies) is primarily through the GP, especially access to specialists.

Following this announcement, the number of consultations with general practitioners (GPs) was 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 over age 75 years, 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 generalized but were at the time scarcely used because of lack of such practice by the general population, especially for 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]. 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. 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 a chronic CVD or MHD are regularly followed by the 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 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.

Methods

Study design

The COVIQuest trial consisted of two simultaneous subtrials (although only one randomisation took place; see *Randomisation and masking* section): the COVIQuest_CV for patients with a CVD and COVIQuest_MH for patients with an 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 April 8, 2020[11], the COVIQuest study used a wait-list control design with GPs randomised to call their CVD patients first (group A) or their MHD patients first (group B). With such a procedure, each 9GP participated in the two subtrials: those allocated to the intervention group for the subtrial focusing on CVD patients actually formed the control group for the subtrial focusing on MHD patients and vice versa (Figure 1).

Figure 1. COVIQuest design

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

Figure 2: Timeline of the COVIQuest_CV and COVIQuest_MH sub-trials

Participants: GPs and patients

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. 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.

CVD patients were ≥ 70 years old with a chronic CVD as referenced in the long-term illness list (*Affection longue durée* [ALD], i.e.. with ALD no. 1, 3, 5, 12, 13; details in Appendix 2) and regularly followed by their GP (i.e., in the list of patients followed by a GP as referenced in the French health insurance database). MHD patients were ≥ 18 years old with an MHD referenced as no. 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 (CVD patients called first) or group B (MHD patients called first). After screening their eligible patients (both CVD and MHD patients) 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 because of 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 by the GP or his/her medical trainee as a representative of the GP. This phone call was standardized 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) Would you like an appointment with your doctor? (response Yes/No) (see 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 re-contacted by their GP if deemed necessary. Therefore, the COVIQuest study was a wait-list trial.

Procedures *(Figure 2)*

GPs were asked to identify eligible CVD and MHD patients 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 CVD patients first at the beginning of the trial and then call their MHD patients after 1 month at the same time they collected the primary outcome (see *Outcomes* section). For GPs allocated to group B, MHD patients were called first, then CVD patients 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 CVD and MHD patients were called to assess the

primary outcome (see *Outcomes* section). Again, both for CVD and MHD patients, 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 MHD patients; and for GPS allocated to group B, the intervention was also delivered to CVD patients.

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.

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.

Secondary outcomes at 6 months were collected from electronic health records (national health insurance data; Système National des Données de Santé [SNDS]): mortality over the 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: nonfatal stroke, nonfatal myocardial infarction, cardiovascular death and hospitalisation for heart failure); and psychotropic drug consumption for the COVIQuest_MH subtrial. Because of a data collection time interval, these data are not collected yet and will be reported subsequently.

Statistical analyses

There were no data available to formulate hypotheses for the sample size. Therefore, all eligible GPs volunteering to participate were recruited (i.e., 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 CVD patients and 30 for MHD patients[13], approximately 16,000 CVD and 6,000 MHD participants were possible. With such sample sizes, we expected to detect a difference of 5% versus 3% of events with power of 90% for CVD patients and 78% for MHD patients, 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 (i.e., 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 because of 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 generalized 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 embeded in GPs only. A risk difference was also estimated by using an identity link function. Of note, for MHD patients, the logistic model did not take into account

the stratification variable because of convergence problems. ICCs were estimated per group by using the ANOVA 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 confidence interval 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 9.4.

Ethics and dissemination

The study protocol was approved by the ethics committee of CPP Sud-Méditerranée 3, no. 2020.04.21 ter_ 20.04.17.42325. The French committee for data handling (CNIL) approved the study (no. 920185 dated 30 of April 2020). This trial was registered with ClinicalTrials.gov (NCT04359875).

Results

Trial profiles

Of 267 selected GPs across 8 different French areas, 149 from 125 practices identified 10,275 patients: 6873 CVD patients and 3402 MHD patients. A total of 3,344 CVD patients and 1,380 MHD patients were included (Figure 3).

Figure 3: Trial flow chart for the COVIQuest_CV and COVIQuest_MH subtrials

Physicians and patients baseline characteristics *(Table 1)*

GPs were younger in group B than group A. They were more frequently practicing medicine in multidisciplinary healthcare centres (n=38, 49.3% and n=28, 39.0% in group 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 groups (Table 1).

Complete baseline data for GPs are in supplementary files (Appendix 4).

Table 1. Baseline general pracitionners and patients characteristics

Baseline characteristics of general practitioners (GPs) by group*		
	Group A (n_1=72)	**Group B** (n_2=77)
Mean (standard deviation); median (interquartile range) age (years)	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 CVD and MHD patients by group: intervention or control		
	Intervention group (phone call)	**Control group**
CVD patients	(n=1834)	(n=1510)
Mean (standard deviation); median (interquartile range) age (years)	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)
MHD patients	(n=832)	(n=548)
Mean (standard deviation); median (interquartile range) age (years)	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)

*Group A (cardiovascular disease [CVD] patients called first); group B (mental health disorder [MHD] patients called first).

Values are numbers (percentages) unless stated otherwise.

Results for CVD patients

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 April 30, 2020 and the intervention phone call was 12 days (interquartile range 5 to 15). Then, pooling the two groups, the median time between April 30, 2020 and date of outcome assessment was 47 days (interquartile range 41 to 53). Results per group are in supplementary files (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 in supplementary files (Appendix 5, tables 2, 3 and 4).

Primary and secondary 1-month outcome results (Table 2)

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 dataset, overall, 65/1834 (3.54%) patients from the intervention group had a hospital admission within 1 month after randomisation versus 69/1510 (4.57%) in the control group (odds ratio 0.82, 95% confidence interval (CI) 0.56 to 1.20; risk difference -0.77, 95% CI -2.28 to 0.74) (Table 2).

Table 2. COVIQuest_CV subtrial comparison of hospitalisations within 1 month

	Hospitalisations n (%)		**OR** (95%CI)* p-value	**Risk difference** (95%CI)* p-value	**ICC** (95%CI)	
	A – Intervention group (phone call) (n_1 = 1834)	B – Control group (n_2 = 1510)			A – Intervention group (phone call)	B – Control group
Full dataset	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

OR, odds ratio; 95% CI, 95% confidence interval; ICC, intraclass correlation coefficient

Among hospitalisations, 14/64 (21.9%) were for a cardiovascular cause in the intervention group versus 23/70 (32.9%) in the control group. Details on causes of hospitalisations are in supplemental files (Appendix 5, table 5). The number of deaths were 3/1523 (0.2%) in the intervention group and 0/1510 in the control group (no statistical test performed). Finally, in the intervention group, 670/1622 (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 715/814 (87.8%) of 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 (interquartile range 5 to 14). The median time from April 30, 2020 to the first phone call in the control group (i.e., the outcome assessment phone call after a 1-month delay) was 49 days (interquartile range 42 to 56). Results per group are in supplementary files (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 health status was similar in the intervention and the 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% (302/826) and 29.1% (158/542) of patients in the intervention and control groups sought an appointment with their GP. Details on information gathered by the intervention phone call are in supplementary files (Appendix 6, tables 2, 3 and 4).

Primary and secondary 1-month outcomes (Table 3)

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 dataset, the primary outcome occurred in 27/832 (3.25%) and 12/548 (2.19%) patients in the intervention and control groups (odds ratio 1.52, 95% CI 0.82 to 2.81; risk difference 1.38 95% CI 0.06 to 2.70) (Table 3).

Table 3. COVIQuest_MH subtrial comparison of hospitalisations within 1 month.

	Hospitalisations n (%)		**OR (*)** (95%CI) p-value	**Risk difference (*)** (95%CI) p-value	**ICC** (95%CI)	
	A – Control group (n_1 = 548)	B – Intervention group (phone call) (n_2 = 832)			A – Control group	B – Intervention group (phone call)
Full dataset	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

OR, odds ratio; 95% CI, 95% confidence interval; ICC, intraclass correlation coefficient

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

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

Discussion

For CVD patients, patients 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 MHD patients, the intervention effect expressed as an odds ratio was not statistically significant, but the risk difference in hospitalisations revealed a modest but statistically significant higher rate of hospitalisations in the intervention than control group. This apparent discrepancy is probably due to the inability to consider the region stratification variable when estimating the odds ratio, which may have reduce the power of the statistical analysis.

These COVIQuest first 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 June 1, 2020, so some did not know the GP or the COVIQuest study and did not participate in the study. Some GPs no longer had a medical trainee from June 1, 2020, which led to a lack of time to call patients. The lockdown ended on May 11, 2020. Therefore, fewer control than 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 *Système National des Données de Santé* (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 April 30, 2020, and therefore we expected that all day-1 phone calls would have been completed before May 7, 2020. As a result, month-1 phone calls were expected to take place before June 4, 2020. However, day-1 phone calls took place between April 30, 2020 and June 8, 2020 for CVD patients and between April 30, 2020 and May 25, 2020 for MHD patients. Therefore, the last month-1 phone call took place on July 2, 2021 for CVD patients,and on July 3, 2021 for MHD patients. 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 April 30, 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 because of 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 because of 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 under-use of care for CVD patients. 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 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 a 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 a 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 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 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 MHD patients. Conversely, this phone call had no significant impact on number of hospitalisations within 1 month in CVD patients.

Ethics approval

The COVIQuest study obtained ethics approval from CPP Sud-Méditerranée 3 (no. 2020.04.21 ter_ 20.04.17.42325).

Participants gave oral consent to the medical trainee/general practitioner team before taking part in the study. Consents were recorded in the general practitioner's files.

Transparency declaration

As a lead author, Clarisse Dibao-Dina affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

Patient and Public Involvement statement

Not concerned

Contributorship statement

Each author participated to 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. CDD and BG conceived, planned and conducted the study, interpreted and reported the data. RB and DP participated to the conception of the study and interpretation of the data and critically revised

the paper. JL participated to the conception of the study, analysed the data with BG and drafted the work with CDD and BG. IEA, JC, KAMF, SoS, MJ, BM, BC, StS, CAK, TB, MG, SB and the COVIQuest group critically discussed the design, participated to the acquisition of data and reporting of results. EB, JPL, VC, WEH, DA, AC, LGG, EL, OSL participated to the study design and gave their approval to the interpretation of the data and reporting of the results.

Competing interest statement

No competing interest.

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University Hospital of Tours Endowment Funds

Role of the study sponsor

The COVIQuest study was funded by the University Hospital of Tours Endowment Funds. We confirm that the sponsor had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. We also confirm the independence of researchers from funders and that all authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Data availability statement

Data are available upon reasonable request.

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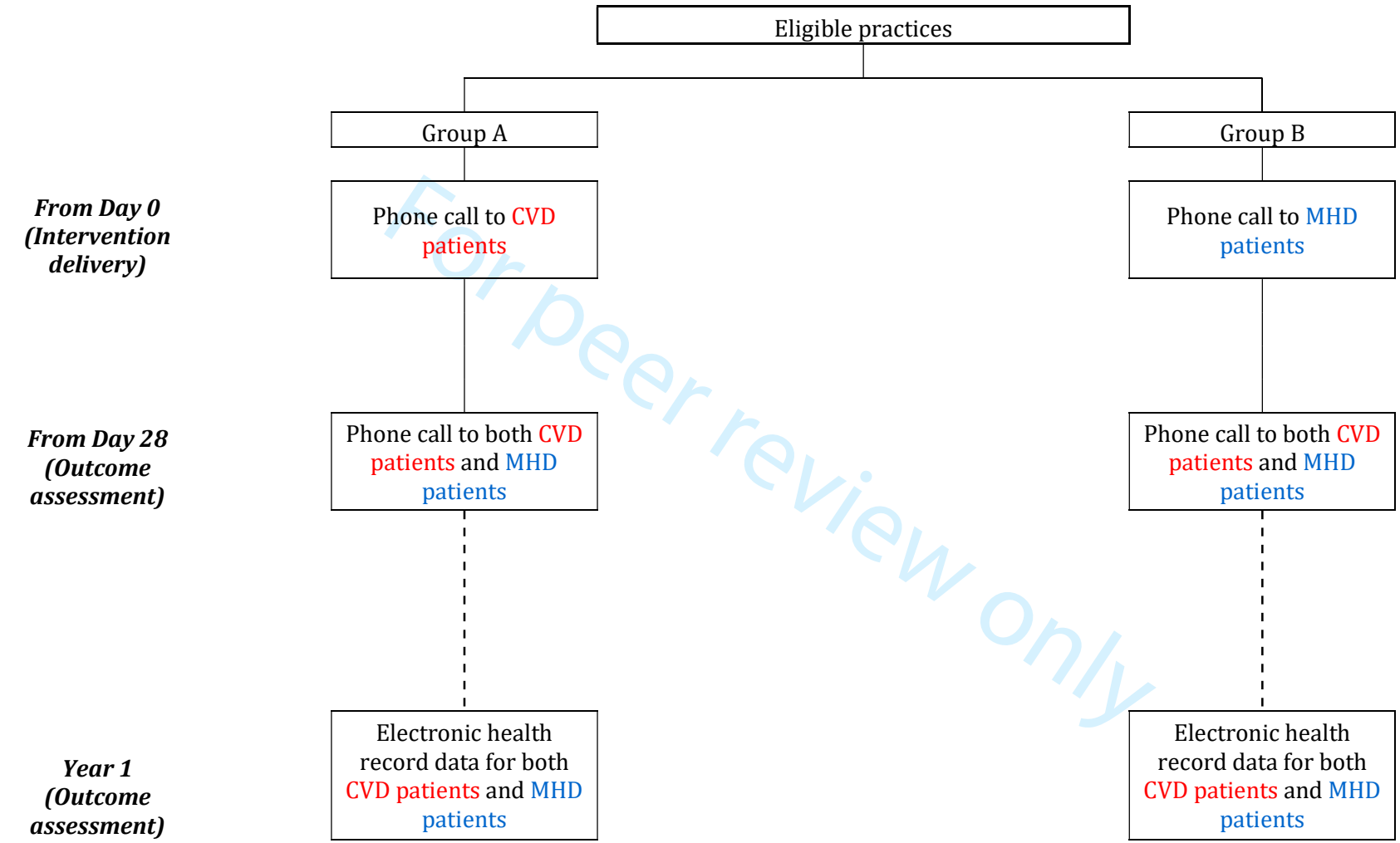
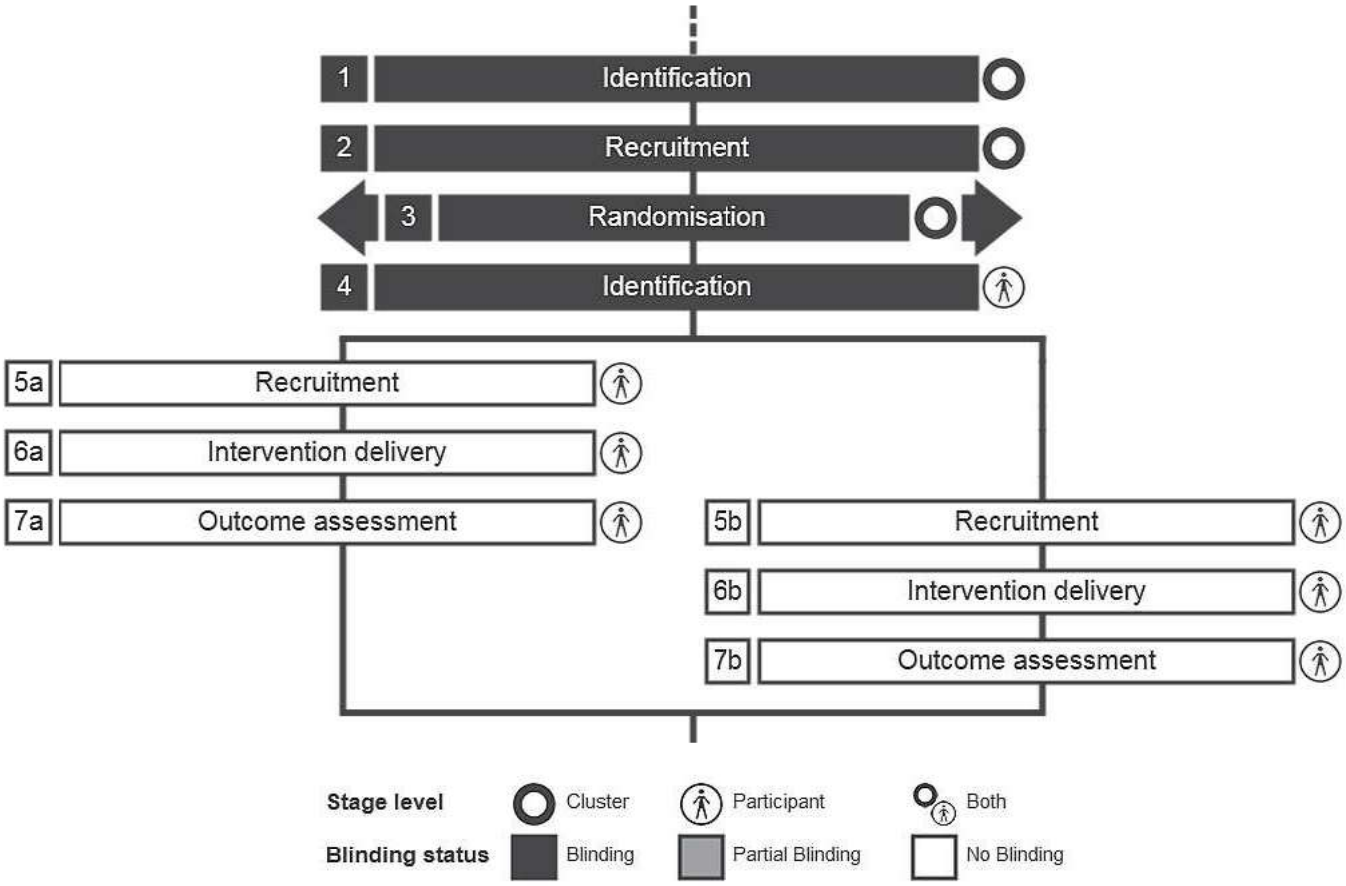


CVD patients: patients with a cardiovascular disease - MHD patients: patients with a mental health disorder



1 Identification
General practitioners (GPs) practising as training supervisors from 8 different French administrative regions are identified

2 Recruitment
GPs who agree to participate are recruited

3 Randomisation
GPs are randomised. In case several GPs work within the same practice, randomisation is forced such that all GPs from a common practice are allocated to the same group. This comes down to randomise practices. Randomisation is stratified on administrative regions.

4 Identification
In the COVIQuest_CV subtrial, patients ≥ 70 years old with a chronic cardiovascular disease (CVD patients) are identified. In the COVIQuest_MH subtrial, patients ≥ 18 years old with a mental disorder (MHD patients) are identified. Patients with both a cardiovascular disease and a mental health disorder are not eligible. GPs are not informed of their randomised allocation while identifying patients.

5a Recruitment
In the intervention group, GPs or their students phone to patients and ask them whether they agree to be included in the trial.

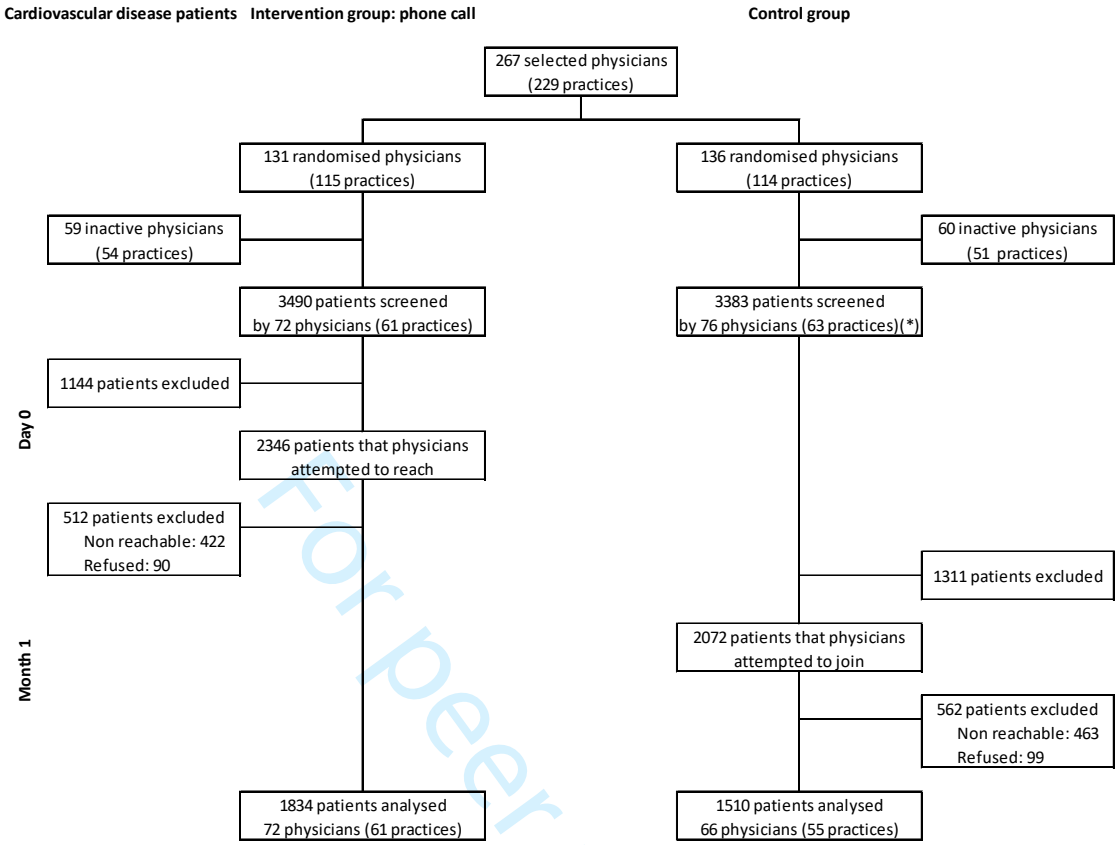
6a Intervention delivery
In the same phone call during which patients' consent is obtained, patients are asked 3 questions by the GP or his/her student: 1) How are you doing? 2) Would you have made an appointment with your GP if there had not been Covid 19 epidemic and lockdown? 3) Would you like an appointment with your doctor?

7a Outcome assessment
One month after their recruitment, patients are contacted again by their GP or his/her student, and asked wheter they have been hospitalised.

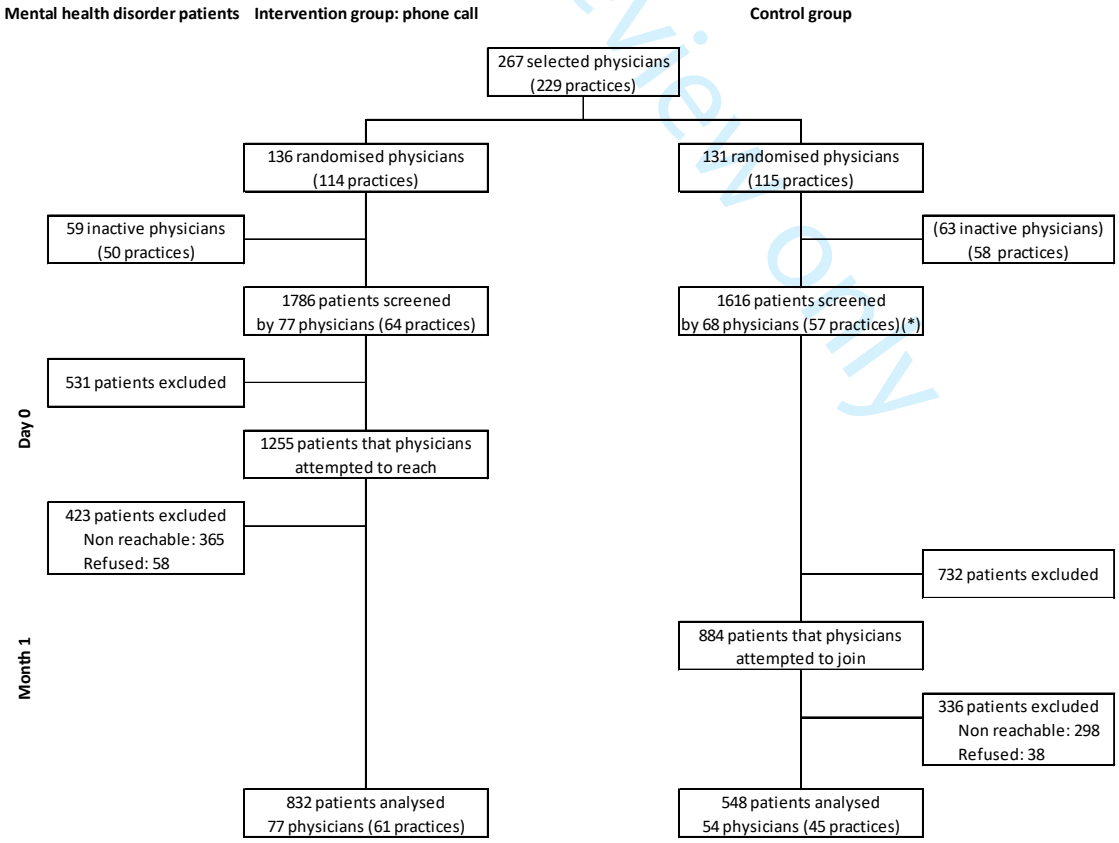
5b Recruitment
One month after the beginning of the study, patients are contacted by their GP or his/her student, and asked whether they agree to be included in the trial.

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

7b Intervention delivery
Still during the same phone call, the intervention (i.e. asking the 3 short questions) is delivered.



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



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

Supplementary files

Appendix 1. List of study sites, coordinators and general practitioners from the COVIQuest group

Name	Academic general practice department	Administrative area	General Practitioners
Ettori-Ajasse Isabelle	Tours	Centre-Val de Loire	SAMKO BORIS, DIBAO-DINA CLARISSE, GONZALES ANNE-MARIE, GAY-LAUNAY KARINE, MOLIMART FRANCOIS, BADEY-MEURISSE ALEXANDRA, THOMAS MARIE, PHILIPPE LAURENCE, LEROUX FARRUGIA DELPHINE, LEFEVRE RÉMI, LANG VIRGINIE, LIZE SOPHIE, DUGUE DURET MARIE-LOUISE, BAGOURD EMMANUEL, RICOIS AMÉLIE, CUVILLIER OLIVIER, DE LA PORTE DES VAUX CÉDRIC, BROUX HÉLÈNE, BACHELIER JEAN-YVES, ROBERT JEAN, BORDEAUX SAMUEL, CHALEIX LYSIANE, GABERT MARTINE, GRISON XAVIER, SIMONEAU CORINNE, PÈRE DOMINIQUE, BOURDU STÉPHANIE, DUMAS ADRIEN, LAUVERJAT FLORENCE, MAUPERTUIS QUENTIN, NOE LAGRANGE ANAIDE, TIERCIN SYLVIE, DUMOT PIERRE, AUMARECHAL ALAIN, MOLINA VALÉRIE, RIVOAL BERNARD, GROSSE JULIE, GALY VINCENT, DESRUES PATRICE, YVON-PETRAULT BLANDINE, VIEILLE ROGER, WITTKE LAURENCE, RUBE DELPHINE, BAUSSANT ALEXANDRE, MONTPERT-BOUVIER LUCIE, CONSTANT MARIE-VÉRONIQUE, TEN KET KIAN FRANÇOIS, PERRAIN ALICE
Sun Sophie	Lyon	Auvergne-Rhône-Alpes	JACQUIOT DENIS, MUZELLE VÉRONIQUE, PIGACHE CHRISTOPHE, LAMORT BOUCHE MARION, MANGOT CLAIRE, BENEDINI ELISE, LAVILLE AGNÈS, POTENCIER BENJAMIN, FOSSIER BENOIT, VALLE FLORIAN, FAY ISABELLE, CHAMBION PIERRE, BRYS VERONIQUE, SUN SOPHIE, BELLECOSTE VINCENT, FLORI MARIE
Jego Maeva	Marseille	Occitanie	DE TADDEO CHRISTINE, THERY DIDIER, CORDEL ANNE CATHERINE , GUERCIA OLIVIER, BARGIER JACQUES, TUDOSE IRINA, NUSSLI NICOLAS
Motte Baptise	Lille catholique	Hauts de France	NGUYEN BRUNO, MORIN PIERRE-ETIENNE, DURAND-CHEVAL CLOTILDE, MOTTE BAPTISTE, DANCHIN FREDERIC

Bruel Sébastien	Saint Etienne	Auvergne-Rhône-Alpes	FRUMUSELU RUXANDRA, DELEBARRE AMANDINE, FAVIE JULIEN
Chiron Benoit	Brest	Bretagne	GELINEAU THOMAS, LE GOFF DELPHINE, VERBEQUE MORVAN, MANON DARABAN TUDOR, PENIN GAELLE, LUCAS ALDRIC, LOPIN CÉLINE, FONSECA JÉROME, LE GUENNEC ANGÉLIQUE
Chambe Juliette	Strasbourg	Grand Est	GHALI-DEBUS ISABELLE, MAGINOT HÉLÈNE, ZUMSTEIN CARINE, ROOS-BERNARD SÉVERINE, RUXER SERGE, PLAUM MANUELA, GUIHENEUF CHARLINE, LENERTZ JOHN, ERNST MYRIAM, CHAMBE JULIETTE, DE CHAZELLES GRÉGOIRE, BUCHLIN FRANÇOIS, HILD PHILIPPE, VONAU PHILIPPE, DUMAS BREITWILLER CLAIRE, BERTHOU ANNE, CHARTON LÉA, LÉPINE CAMILLE
Sidorkiewicz Stéphanie	Paris Descartes	Ile de France	OLESKER SOPHIE, MALMARTEL ALEXANDRE, GHASAROSSIAN CHRISTIAN, RUSSO PATRICK, ANDERSON MARGUERITE, RICHEMOND MICHÈLE, SIDORKIEWICZ STÉPHANIE, ECOLLAN MARIE, JAURY PHILIPPE, BENAINOUS OLIVIER, MSIKA RAZON MARIE, CATU-PINAULT ANNIE
Khau Cam-Anh	Paris Nord La Sorbonne	Ile de France	KHAU CAM-ANH, BERKAI RANIA, MERCIER ALAIN, GRUNBERG PHILIPPE, PHAM LAN-ANH, RENAULT ALAINE, BACH LORENE, COUDERC AUDREY, CHEVALLIER FREDERIC, CHABANNES AUDREY
Bouchez Tiphanie	Nice	Provence-Alpes-Côte d'Azur	MELLERIN IANIS, BOUCHEZ TIPHANIE, GARSON SANDRINE, GARDON GILLES, PASCUCCI-ZAKARIAN SANDRINE, GUERVILLE VÉRONIQUE, MOUILLE BLANC CECILE, MUNCK STEPHANE, GUERVILLE MARC-ANDRÉ
Ghali Maria	Angers	Pays de la Loire	JUDALET ILLAND GHISLAINE, PY THIBAUT, TESSIER CAZENEUVE CHRISTINE, RAMOND ROQUIN ALINE, GALLOT EMMANUEL, LOSSON DAUSSY GAELLE, LACOMBE ANTOINE, GABARD CATHERINE, DEVAUD BERTRAND, BUFFARD PASCAL, PLESSIS ANNE, BOURGEOIS CÉCILE

Appendix 2. List of 30 long-term illnesses (ALD 30) that are exempt from user fees

ALD no. 1 - Invalid stroke

ALD no. 2 - Bone marrow failure and other chronic cytopenias

ALD no. 3 - Chronic arteriopathies with ischemic manifestations

ALD no. 4 - Complicated bilharziasis

ALD no. 5 - Severe heart failure, severe arrhythmia, severe valvular heart disease; Graves congenital heart disease

ALD no. 6 - Chronic active diseases of the liver and cirrhosis

ALD no. 7 - Severe primary immune deficiency, prolonged treatment, infection with human immunodeficiency virus

ALD no. 8 - Type 1 diabetes and type 2 diabetes

ALD no. 9 - Severe form of neurological and muscular disorders (including myopathy), severe epilepsy

ALD no. 10 - Hemoglobinopathies, hemolysis, chronic constitutional and acquired severe

ALD no. 11 - Hemophilia and constitutional disorders of severe hemostasis

ALD no. 12 - Severe hypertension

ALD no. 13 - Coronary disease

ALD no. 14 - Severe chronic respiratory failure

ALD no. 15 - Meadow

ALD no. 16 - Parkinson disease

ALD no. 17 - Hereditary metabolic diseases a prolonged specialized treatment

ALD no. 18 - Cystic fibrosis

ALD no. 19 - Severe chronic nephropathy and primary nephrotic syndrome

ALD no. 20 - Paraplegia

ALD no. 21 - Periarthritis nodosa, acute systemic lupus erythematosus, progressive generalized scleroderma

ALD no. 22 - Progressive rheumatoid arthritis

ALD no. 23 - Psychosis, severe personality disorder, mental retardation

ALD no. 24 - Ulcerative colitis and progressive Crohn's disease

ALD no. 25 - Multiple sclerosis

ALD no. 26 - Progressive structural scoliosis (with an angle equal to or greater than 25 degrees) until spinal maturation

ALD no. 27 - Fall from ankylosing spondylitis

ALD no. 28 - Organ transplant suites

ALD no. 29 - Active tuberculosis

ALD no. 30 - Malignant tumor, malignant disease of lymphatic or hematopoietic tissue.

Appendix 3. Interview guide

Information and oral consent of the patient:

I am Mr/Mrs X, a student in my Nth year of medical school at Dr Y's practice. I am calling you at the request of your GP Dr Y to ask you three short questions. The answers you give me will enable Dr Y to know how you are doing and to offer you appropriate care during lockdown if necessary. Your answers will be used anonymously in the COVIQUEST study in which Dr Y is participating. The aim of this study is to find out what impact this call has on your care. (Only for patients in the intervention group: If you agree to your answers being used in this study, you should know that you will be contacted again in 1 month time to hear from you in the same way). If you do not want your answers to be used for the study, please note that this will not affect your treatment by Dr Y. Do you accept that I ask you questions? I would like to remind you that your answers will be completely anonymous and that you can say at any time that you no longer wish your answers to be collected in the framework of COVIQUEST, without any impact on your care. If you have any questions to ask me or would like to discuss them with Dr Y, please do not hesitate.

Intervention:

How are you doing? (using a Likert scale of 1 = very bad to 10 = very good)

Would you have made an appointment with your GP if there had not been a lockdown related to the COVID19?

Would you like an appointment with your GP?

Appendix 4. Baseline characteristics of general practitioners (GPs) by group*.

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**A** (n_1 = 72)	**B** (n_2 = 77)
Age (years)	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)
Work organisation		
Practice, only physicians	39 (54.2)	32 (41.6)
Alone	5 (6.9)	7 (9.1)
Practice, multidisciplinary healthcare centre	28 (39.0)	38 (49.3)
Territorial professional health community	30 (41.7)	38 (49.3)
Advanced public health nurse	12 (16.7)	19 (24.7)

*Group A (cardiovascular disease [CVD] patients called first); group B (mental health disorder [MHD] patients called first)

Appendix 5. COVIQuest_CV results

Table 1. Process evaluation of the intervention and outcome assessment

mean ± standard deviation, median [Q1 ; Q3] & {Min ; Max} for quantitative variables *n (%) for qualitative variables*	**A - Intervention group - Phone call** (n_1 = 1834)	**B - Control group** (n_2 = 1510)
Who phoned (intervention phone call)? - n_1 = 1801		
Physician	236 (13.1)	
Student	1448 (80.4)	
Other person (e.g. secretary)	117 (6.5)	
Time between April 30th 2020 and phone call (days)	11.7±8.0 12.0 [5.0 ; 15.0] {0 ; 39}	
Time between the phone call and the outcome assessment (days) - n_1 = 1508	34.1±7.0 33.0 [29.0 ; 39.0] {12 ; 58}	
Time between April 30th 2020 and the outcome assessment (days) - n_1 = 1508, n_2 = 1510	45.6±8.7 47 [40 ; 53] {26 ; 64]	48.7±7.8 48 [42 ; 56] {26 ; 63]

Table 2. Patient health status when phoned (intervention group)

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**A - Intervention group - Phone call** (n_1 = 1834)
Had consultations with his/her physician since the beginning of the lockdown period - n_1 = 1825	851 (46.6)
Number of consultations - n_1 = 845	1.5±0.9 1 [1 ; 2]
Had a contact with his/her physician since the beginning of the lockdown period - n_1 = 1811	500 (27.6)
Health status perception - n_1 = 1820 (*)	7.4±1.8 8 [6 ; 9]
Would have made an appointment - n_1 = 1828	856 (46.8)
Would like an appointment - n_1 = 1828	611 (33.4)

(*) 0-10 Likert scale

Table 3. Symptoms (for patients who declared they would like an appointment)

n (%) for qualitative variables	**A - Intervention group - Phone call - Patients who wanted an appointment** (n = 611)
Number of symptoms - n_1 = 459	
1	374 (81.5)
2	62 (13.5)
3	23 (5.0)
Symptoms (*)	
General, non specific	304 (53.6)
Blood system, immunology	2 (0.3)
Digestive	35 (6.2)
Ocular	5 (0.9)
Ear	4 (0.7)
Cardiovascular	60 (10.6)
Osteoarticular	64 (11.3)
Neurological	6 (1.1)
Psychological	22 (3.9)
Respiratory	22 (3.9)
Skin	15 (2.6)
Metabolism, nutrition	11 (1.9)
Urology	8 (1.4)
Pregnancy	0
Reproductive system, female	2 (0.3)
Reproductive system, male	0
Social	7 (1.2)

(*) One patient may have two or three symptoms

Table 4. Patient health status when assessed

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**A - Intervention group - Phone call** (n_1 = 1834)	**B - Control group** (n_2 = 1510)
Had COVID-19 disease - n_1 = 1586, n_2 = 1409		
Yes (TR-PCR test)	4 (0.2)	7 (0.5)
May-be	72 (4.5)	61 (4.3)
Do not know	1510 (95.2)	1341 (95.2)
Health status perception - n_1 = 1457, n_2=1488 (*)	7.4±1.8	7.3±1.9
	8 [6 ; 9]	8 [6 ; 8.5]
Had consultations with his/her physician since the beginning of the lockdown period - n_2 = 1417		1159 (81.8)
Number of consultations - n_2 = 1155		1.9±1.3
		1 [1 ; 2]
Had a contact with his/her physician since the beginning of the lockdown period - n_2= 1454		580 (39.9)
Would like an appointment - n_2 = 1500		308 (20.5)

(*) 0-10 Likert scale

Table 5. Causes of hospitalisations

n (%) for qualitative variables	**A - Intervention group - Phone call**	**B - Control group**
Cause of hospitalization - $n_1 = 64$, $n_2 = 70$ (*)		
UCV: Cardiovascular emergency	14 (21.9)	23 (32.9)
TS: Suicide attempt	0	0
USM: Mental health emergency (except suicide attempt)	0	0
UAM: Other medical emergency	30 (46.9)	18 (25.7)
UAC: Other surgical emergency	10 (15.6)	15 (21.4)
PCV: Planned cardiovascular hospitalisation	2 (3.1)	0
PSM: Planned mental health hospitalisation	0	0
PAM: Planned other medical reason hospitalisation	1 (1.6)	7 (10.0)
PAC: Planned other surgical reason hospitalisation	7 (10.9)	7 (10.0)

(*) Units of analysis are hospitalisations not patients

Appendix 6. COVIQuest_MH results

Table 1. Process evaluation of the intervention and outcome assessment

mean ± standard deviation, median [Q1 ; Q3] & {Min ; Max} for quantitative variables *n (%) for qualitative variables*	**A - Control group** (n_1 = 548)	**B - Intervention group - Phone call** (n_2 = 832)
Who phoned (intervention phone call)? n_2 = 814		
Physician		85 (10.4)
Student		715 (87.8)
Other person (e.g. secretary)		14 (1.7)
Time between April 30th 2020 and phone call (days)		10.6±7.5 7.0 [5.0 ; 14.0] {0 ; 29}
Time between the phone call and the outcome assessment (days) - n_2 = 560		37.3±9.2 35.0 [29.0 ; 45.5] {12 ; 56}
Time between April 30th 2020 and the outcome assessment (days) - n_1 = 548, n_2 = 560	48.3±9.0 49 [42 ; 56] {20 ; 64]	47.3±9.3 48 [41 ; 55.5] {14 ; 63]

Table 2. Patient health status when phoned (intervention group)

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**B - Intervention group - Phone call** (n_2 = 832)
Had consultations with his/her physician since the beginning of the lockdown period - n_2 = 819	393 (48.0)
Number of consultations - n_2 = 392	2.1±1.4 2 [1 ; 3]
Had a contact with his/her physician since the beginning of the lockdown period - n_2 = 817	211 (25.8)
Health status perception - n_2 = 819 (*)	6.9±2.2 7 [5 ; 9]
Would have made an appointment - n_2 = 826	401 (48.5)
Would like an appointment - n_2 = 826	302 (36.6)

(*) 0-10 Likert scale

Table 3. Symptoms (for patients who declared they would like an appointment)

n (%) for qualitative variables	**B- Intervention group - Phone call - Patients who wanted an appointment n=302**
Number of symptoms - n_2 = 246	
1	190 (77.2)
2	41 (16.7)
3	15 (6.1)
Symptoms (*)	
General, non specific	131 (41.3)
Blood system, immunology	1 (0.3)
Digestive	21 (6.6)
Ocular	2 (0.6)
Ear	1 (0.3)
Cardiovascular	8 (2.5)
Osteoarticular	39 (12.3)
Neurological	12 (3.8)
Psychological	57 (18.0)
Respiratory	12 (3.8)
Skin	7 (2.2)
Metabolism, nutrition	5 (1.6)
Urology	5 (1.6)
Pregnancy	0
Reproductive system, female	2 (0.6)
Reproductive system, male	2 (0.6)
Social	12 (3.8)

(*) One patient may have two or three symptoms

Table 4. Patient health status when assessed

mean ± standard deviation & median [Q1 ; Q3] for quantitative variables *n (%) for qualitative variables*	**A - Control group** (n_1 = 548)	**B - Intervention group - Phone call** (n_2 = 832)
Had COVID-19 disease - n_1 = 538, n_2 = 584		
Yes (TR-PCR test)	5 (0.9)	0
May-be	51 (9.5)	42 (7.2)
Do not know	482 (89.6)	542 (92.8)
Health status perception - n_1 = 544, n_2=544 (*)	7.1±2.0 7 [6 ; 8]	7.1±2.2 7 [6 ; 9]
Had consultations with his/her physician since the beginning of the lockdown period - n_1 = 546	367 (67.2)	
Number of consultations - n_1 = 366	2.1±1.5 1 [1 ; 3]	
Had a contact with his/her physician since the beginning of the lockdown period - n_1= 534	247 (46.2)	
Would like an appointment - n_1 = 542	158 (29.1)	

(*) 0-10 Likert scale

Table 5. Causes of hospitalisations

n (%) for qualitative variables	**A - Control group**	**B - Intervention group - Phone call**
Cause of hospitalization - $n_1 = 13$, $n_2 = 26$ (*)		
UCV: Cardiovascular emergency	0	0
TS: Suicide attempt	0	1 (3.8)
USM: Mental health emergency (except suicide attempt)	4 (30.8)	7 (26.9)
UAM: Other medical emergency	3 (23.1)	10 (38.5)
UAC: Other surgical emergency	4 (30.8)	4 (15.4)
PCV: Planned cardiovascular hospitalisation	0	0
PSM: Planned mental health hospitalisation	0	0
PAM: Planned other medical reason hospitalisation	1 (7.7)	4 (15.4)
PAC: Planned other surgical reason hospitalisation	1 (7.7)	0

(*) Units of analysis are hospitalisations not patients

Table 1: CONSORT 2010 checklist of information to include when reporting a cluster randomised trial

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No *
Title and abstract				
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[1,2]	See table 2	3 + See table 2
Introduction				
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	6-7
	2b	Specific objectives or hypotheses	Whether objectives pertain to the the cluster level, the individual participant level or both	7-8
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	9
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		**/**
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	9-10
	4b	Settings and locations where the data were collected		**11-12**
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	11-12

Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Whether outcome measures pertain to the cluster level, the individual participant level or both	12
	6b	Any changes to trial outcomes after the trial commenced, with reasons		/
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or *k*), and an indication of its uncertainty	13-14
	7b	When applicable, explanation of any interim analyses and stopping guidelines		/
Randomisation:				10 + protocol
Sequence generation	8a	Method used to generate the random allocation sequence		**10**
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	10
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the individual participant level or both	10
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	10
	10a		Who generated the random allocation sequence, who	10

			enrolled clusters, and who assigned clusters to interventions	
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling)	10
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	10
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		**/**
	11b	If relevant, description of the similarity of interventions		**10**
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	13-14
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		**/**
Results				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	For each group, the numbers of clusters that were randomly assigned, received intended treatment, and were analysed for the primary outcome	15 + fig 3

	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	Fig 3
Recruitment	14a	Dates defining the periods of recruitment and follow-up		**17-21 + appendix 5-6**
	14b	Why the trial ended or was stopped		**/**
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Baseline characteristics for the individual and cluster levels as applicable for each group	16 + table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	18-20 + 22-24 + fig 3
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	18-20 + 22-24
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		**17-21**
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		**/**
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[3])		**/**
Discussion				
Limitations	20	Trial limitations, addressing sources of potential bias,		**25-26**

		imprecision, and, if relevant, multiplicity of analyses		
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	/
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		**27**
Other information				
Registration	23	Registration number and name of trial registry		**4, 14**
Protocol	24	Where the full trial protocol can be accessed, if available		**/**
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		**33**

** Note: page numbers optional depending on journal requirements*

Table 2: Extension of CONSORT for abstracts[1,2] to reports of cluster randomised trials

Item	Standard Checklist item	Extension for cluster trials
Title	Identification of study as randomised	**Identification of study as cluster randomised**
Trial design	Description of the trial design (e.g. parallel, cluster, non-inferiority)	
Methods		
Participants	Eligibility criteria for participants and the settings where the data were collected	**Eligibility criteria for clusters**
Interventions	Interventions intended for each group	
Objective	Specific objective or hypothesis	**Whether objective or hypothesis pertains to the cluster level, the individual participant level or both**
Outcome	Clearly defined primary outcome for this report	**Whether the primary outcome pertains to the cluster level, the individual participant level or both**
Randomization	How participants were allocated to interventions	**How clusters were allocated to interventions**
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	
Results		
Numbers randomized	Number of participants randomized to each group	**Number of clusters randomized to each group**
Recruitment	Trial status[1]	
Numbers analysed	Number of participants analysed in each group	**Number of clusters analysed in each group**
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision	**Results at the cluster or individual participant level as applicable for each primary outcome**
Harms	Important adverse events or side effects	
Conclusions	General interpretation of the results	
Trial registration	Registration number and name of trial register	
Funding	Source of funding	

[1] Relevant to Conference Abstracts

REFERENCES

1 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet* 2008, 371:281-283

2 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG at al (2008) CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration. *PLoS Med* 5(1): e20

3 Ioannidis JP, Evans SJ, Gotzsche PC, O'Neill RT, Altman DG, Schulz K, Moher D. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; 141(10):781-788.