PROTOCOL

Title: COVID-19: Determining trustworthiness and safety of REmote Consulting in primary Healthcare for chronic disease populations in Africa using a stepped wedge design – The REaCH Trial

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Introduction

Background and rationale

Emerging communicable diseases, such as COVID-19, poses risks for health workers and citizens during face-to-face healthcare delivery. Communicable diseases can deter people with existing health conditions from attending health facilities for their routine medications, examinations, and investigations for fear of becoming infected[1]. Compounded by fragile health systems, this context means that it is challenging for Africa to cope with existing and increasing health needs during communicable disease outbreaks if face-to-face consultations remain the main form of healthcare delivery.

The WHO advocates remote delivery of healthcare, such as using mobile phones, wherever and whenever possible to reduce risks of cross-infection. This reduces risks of transmission within populations and to health workers [2]. Importantly, it keeps health systems functioning for routine care. In high income countries (HIC) this has been rapidly deployed in such times. In low/middle income countries (LMIC), digital and telecommunication infrastructure hold the potential to deliver remote consulting even in contexts where only 2G is available. However, in most African countries, especially within marginalised communities, face-to-face healthcare remains the norm. Little is known about how to rapidly develop and deploy remote consulting systems in ways that are fit for available infrastructure and resources. Our previous research on remote consulting in HIC and LMIC indicates that trust in remote healthcare provision is an important mechanism [3,4]. It determines whether citizens concord with the consultation outcome, ignore it, or subsequently travel to the health facility to consult face-to-face. There is a clear need to develop remote consulting services however no trial evidence exists, anywhere in the world, to understand its impact on the quality or safety of healthcare.

Transitioning from face-to-face to remote consulting is not straightforward [3-5]. In both HIC and LMIC uncertainties for patients include trust, confidentiality, and privacy. For health professionals it includes patient safety, duty of care, boundaries, and workload. In LMIC, access to health records and cost of airtime/data are problematic. These issues are not insurmountable. In 2018 and building on our previous research [4], we developed remote consulting training and delivered and evaluated it with two face-to-face cohorts of medical officers. Renamed as REaCH training, between April and July 2020, REaCH was digitised, delivered, and evaluated by 14 Tanzanian medical officers from five primary care facilities [6]. In response we adapted the Moodle app for stronger/weaker network capacities and made curriculum revisions.

REmote Consulting in Healthcare (REaCH) training has a remote knowledge cascade process and has been piloted, evaluated and upscaled within parts of rural Tanzania. REaCH training is delivered in English and cascaded in local languages [7]. REaCH is scalable across LMIC countries with limited/variable digital infrastructures. Trained primary care health workers can replace 10 face-to-face consultations with remote consultations daily. Cascading to 50 others results in 510 remote consultations daily. During the project, existing in-country stakeholder groups will work to influence health policy at government levels regarding airtime and professional regulation [3,5].

Novel evidence for health workers' ability to deliver trustworthy and safe remote healthcare that patients report as non-inferior to face-to-face care, will both protect communities and their health workers during times of need. It will sustainably strengthen health systems in LMIC. We progress the UN sustainable goals 3.1-3.5, 3C and 3D in achieving good health and well-being [8].

A scoping review of Medline, Google Scholar and recent special issues of Journal of Medical Internet Research for 2020 research on remote consulting identified literature from high income countries and China which included commentaries on its role (e.g. for cancer care, diabetes), reports of how it has been implemented, what it has been used for and by whom (e.g. in Western China, US) and,

surveys of healthcare providers on how they are delivering remote consulting and of patients on their preferences. There was no evidence on whether rapid change to remote consulting in these countries resulted in healthcare that was trustworthy and safe.

Our own 2020 published review and framework focused on delivery of remote consulting to marginalised communities of low-middle-income countries [3]. We found published evidence of effectiveness of specific projects providing remote consulting for specific health conditions alongside traditional face-to-face care and evidence that some health workers used their own phones informally. There were no studies that reported on trustworthiness and safety in replacing face-to-face with remote consulting.

The 2019 World Health Organization recommendations on digital interventions for health system strengthening, have little to say about remote consulting for poor marginalised communities, being largely based on evidence from well-resourced settings. Our 2020 published review [3] draws on socio/economic/behavioural/medical evidence to identify the potential benefits and hazards of remote consulting including change in patient/provider trust and thresholds for diagnostic/treatment action depending on how it is delivered. There is a gap in the evidence relating to how remote consulting can be delivered in LMIC. There is no international evidence on its impact on indicators of quality in healthcare delivery.

Research hypothesis

REaCH training will increase the rate of remote consulting. This remote consulting will not affect patient trust in, and the safety of, primary care consultations for long-term conditions.

Objectives

We aim to deliver internationally unique evidence on a remote consulting training scheme, whether it is effective in increasing remote consulting, whether it affects face to face consulting, and whether it changes patient reports of trustworthiness and changes specified indicators of safety of healthcare consultations in primary health care in Tanzania and Nigeria. Alongside runs south-south collaboration with Uganda and Kenya. We propose two trials to deliver evidence for different African contexts. A process evaluation will inform implementation across East and West Africa.

Trial research questions

To what extent does REaCH training affect:

1. Patient consultation rates delivered face-to-face and remote?
2. Patient perceptions of the trustworthiness of health workers providing consultations?
3. The medication prescription issue rate?
4. Missed appointment rate?
5. Medical investigation issue rate?
6. Patient health activation levels?

Process evaluation research questions

1. What is the impact of REaCH training on patient and health worker experience with healthcare?
2. What enables and hinders health workers in deploying remote consulting?

Trial design

The evaluation consists of two stepped-wedge cluster randomised trials running concurrently in Nigeria and Tanzania. The REaCH intervention will be rolled out to all clusters over the course of the trial in a staggered fashion and the order that clusters receive the intervention will be randomised. The evaluation will comprise both the quantitative trial outcomes and a process evaluation. The

evaluation in each country will be conducted independently; comparisons between results will be predominantly qualitative. As a secondary analysis we will estimate the between country difference in treatment effects, although the trials are not designed for this purpose.

Methods: Participants, interventions, and outcomes

Study setting

We propose two identical trials in contrasting countries with marginalised populations: 1) Rural/remote, low income Tanzania in East Africa and 2) Urban and peri-urban in middle income Nigeria in West Africa.

Participants

Health workers and patients receiving healthcare from participating primary care facilities. Tier 1 trainees are doctors/nurses/ medical officers who speak, read and write in English, tier 2 are other cadres e.g. community health workers, pharmacy assistants, receptionists etc who may communicate in English or in local languages. The tier 1 and tier 2 trainees work as a team within the facility.

Eligibility criteria

Primary care facilities

Recruited primary care facilities will individually, or in collaboration with other smaller facilities, become a research cluster. We will recruit 20 clusters which must have 1) a minimum of 100 active patients with one of the eligible long-term conditions attending for healthcare three times per year. Active patients are those for whom there is record of a consultation within the previous five months. 2) paper-based or electronic record keeping of patient names, phone number, age, sex, appointments attended and with whom and pharmacy/investigation records 3) employ a minimum of five health workers. At least one must be tier 1 with the remainder a mix of tier 1 and 2 providing healthcare to citizens 4) Facility managers consent to all parts of the study including process evaluation.

Health workers

Tier 1 trainees must own a smart phone and commit to cascading their training to ≥5 tier 2 health workers. Tier 2 health workers must own a feature phone as a minimum. Whatever the existing gender balance of health workers in each health facility, we will require health facilities to nominate the same ratio of trainee places to women health workers.

Patients

Adults ≥ 18yrs receiving treatment and/or monitoring for at least one of Type 2 diabetes, Hypertension, Chronic Obstructive Pulmonary Disease or Coronary Heart Disease. These conditions are common, patients are vulnerable to poor outcomes from communicable diseases and they require contact with health facilities three times per year.

Exclusion criteria are no access to a mobile phone or fixed phone in their community; those identified by health workers as nearing end of life or currently severely ill, carers consulting on a another person's behalf and those unable to provide informed consent.

Informed Consent

Consent on behalf of each cluster

The country principle investigator (PI) is responsible, with the research team, for approaching health facilities to determine their interest in participating. The country PI will verbally inform them of the

study, share the research protocol and discuss their eligibility. When a facility confirms interest and eligibility, a partnership contract will be developed between the host university and the facility management. This contract will document the responsibilities of each partner and the financial details of the contract. The REaCH trial offers each facility funding for each facility manager and administrator to supply the required data, airtime support for the trainees to deliver remote consultations and for their time to engage in training and cascading. Once the contract is signed the trial can commence.

From the facility records we will be provided with pseudonymised data on the active, eligible patient population from each clinic. These data include the age and sex of each patient, but no identifiable information such as contact details or name. A table linking patient IDs to patient records will be kept by each clinic. For each patient ID the clinics will record the number of visits each month by mode of delivery; patients with at least one visit will constitute the 'numerator' population. The data are pseudonymised and no personal data will be transferred out of the clinic, so its disclosure represents minimal risk to the research participants, and we will not seek informed consent from the patients for the use of this data. To obtain informed consent would require the disclosure of contact information to research staff, which would be an unnecessary transfer of identifiable data, and require a larger number of field staff than are available to the study. See Appendix 1 for flow diagram of management of open cohort pseudonymised data.

Patient participant informed consent

From the numerator population above we will sample 30 patients per month to complete our surveys and these participants will give informed consent. They will be contacted by mobile phone by health facility staff, offered brief study information and asked if they would be happy for a researcher to contact them. They may also have seen posters raising awareness of our research that we will put up in the facilities and they may also have previously asked questions. If they consent to name and telephone number being given to the study team, they will be contacted by a researcher to undertake the informed consent process. Written and verbal study information will be offered to patients and the opportunity to provide written or verbal, audio-recorded consent. Potential participants will be offered the choice of whether they undertake informed consent in English or in local languages. Informed consent processes include information that potential participants will be offered up to five days to decide whether they wish to participate. They will be informed that their decision to participate, or not, will not affect their current or future care and that there will be no remuneration offered for their participation. Exemplar participant information sheets and consent forms are found in appendices 2 & 3. The information sheet and consent form will ask these potential participants to give consent to the research team to access their health records. Where this consent is provided, it will enable the linking of facility level pseudonymised data with the survey data. See Appendix 1 for flow diagram of management of identifiable patient participant data.

Facility staff informed consent

Facility staff will be provided with written study information in English or local languages as required in each country. They will be asked to provide informed consent to undertake REaCH training and to cascade it to tier 1 and 2 colleagues, to contribute REaCH learning data from the Moodle, to participate in interviews and to answer survey questions about implementation of REaCH training and remote consulting. Consent will be signed or taken verbally with an audio recorded record.

<u>Participant timeline in the trial</u>

Primary care facilities will be in the study for 14 months. Month 1 to recruit and set up training and procedures on trial methods and pilot data collection methods and data quality assurance methods. Months 2-13 to provide pseudonymised open cohort data and support REaCH training and patient

recruitment. Month 14 will be for the collection of missing data, final data quality checks and closing the trial site down.

Health workers will be in the trial for between one and six months depending upon when they receive REaCH training and whether they take part in the process evaluation.

Patient participants will remain in the trial for the time it takes to complete two questionnaires which we estimate to be less than 60 minutes. If they offer consent to be interviewed they will remain in the study for a further six weeks from the point of conducting the survey to give sufficient time for the sampling framework to be consulted and an interview to be set up and completed.

Interventions

Experimental Intervention: REaCH training is designed to increase the use and quality of remote consulting [7] that meets ethical and professional regulation standards. Our definition of remote consulting is when a person with a perceived health need consults a healthcare provider using a mobile phone [3,5]. They will use the internet or telecommunications infrastructure and will use SMART phones or feature phones to communicate. Our LMIC definition includes consultations using non-mobile technology (e.g. a computer in a community centre or a shared fixed telephone line in a remote rural village).

REaCH training uses a blended learning Moodle app and cascade process which support the delivery of trustworthy, safe and scalable remote primary healthcare [7]. REaCH trainees are doctors/nurses/medical officers who work for primary healthcare facilities in Tanzania and Nigeria (tier 1 trainees). They subsequently cascade training in local languages to five health workers in their team (tier 2 trainees). Tier 1 training consists of 20 hours of self-directed learning plus local tutor/peer time over 2/3 weeks using a smart phone. Tier 2 training is cascaded remotely via feature phone or through locally established team meetings/training with prescribed social distancing. REaCH is informed by the TRAIN framework for optimising sustainability of changes in healthcare delivery following a cascaded learning process in LMIC [9].

REaCH curriculum

Module	Learning Outcome
Introduction: *Why is remote consulting important?*	Develop and strengthen motivation for engagement
1: *What devices and platforms are used in Remote Consulting?*	Analyse different forms of digital communication, understanding how they are supported and funded, and the changing patterns of use by citizens
2: *How does my role change and the care I provide my patients?*	Discuss how digital communication changes the nature of the health professional and patient roles, and their interactions
3: *What new issues arise in remote consulting that are different to face to face care?*	Summarise the enablers and barriers to implementing a digital communication service about clinical issues, including but not limited to: technical issues, communication skills, ethics, patient safety, cost, and sustainability
4: *What patient outcomes can I expect?*	Explain how digital communication with patients and between health professionals about clinical issues is likely to have benefit for patient care and health outcomes
5: *What health behaviours will help or hinder the successful transition to remote consulting?*	Analyse the opportunities and choices available for using digital communication for healthcare, considering capability, opportunity, and motivation

6: *What is my plan for delivering my work remotely (and that of my team/colleagues)?*	Develop a plan for a digital communication service about a health need identified from one's own practice, either with patients or between health professionals
7: *How can I evaluate my own remotely delivered healthcare practice (and that of my team/colleagues)?*	Reflect on how digital communications services has the potential to transform health
8: *How can I influence others to change to remote consulting?*	Reflect on the leadership qualities required to bring about change

For each module there is a narrated presentation and between 1-3 short assignments for each trainee to undertake and upload onto the Moodle platform. Within each module there is a reflective exercise on planning the cascading of that particular topic to others. Trainees work in virtual cohorts of approximately 12. Each cohort has four peer group/facilitator WhatsApp chats during the three weeks of study. Trainees upload completed module assignments onto the Moodle which their facilitator reviews. These reviewed assignments are the basis for the certificate of attendance awarded at course completion.

Comparison intervention: Usual care delivered in the routine way for each facility. Our stakeholder consultation indicates that this will be face to face care for most patients with occasional informally provided remote telephone consultations for friends and family members of the health worker.

Training procedure

Once the participants give their consent, they are given orientation about the course and offered the trainee's course guide with an overview about the course and the duration, mode of delivery and the learning process, the learning support they can expect, and how the course will be evaluated. In addition, they are given a Moodle guide to enable them to register and access the materials in the Moodle platform. During the learning process the participants can interact and exchange their views through the Moodle forum. The facilitator also has a guide i.e. facilitator guide, to assist him/her in delivering the course. Trainees are informed that they will be required to undertake a short interview at the end of their training with their facilitator to assess their learning. This structure serves the purpose of motivating trainees to engage with the training, self-directed learning activities and the peer-discussion and it provides a quality assurance process to assess and confirm their learning prior to being permitted to deliver cascade training. Trainees have to satisfactorily complete to receive their certificate. The award of the certificate is required to continue cascade learning to colleagues and to continue participation in the trial.

<u>Outcomes</u>

We propose four primary outcomes, detailed below, to test our research hypothesis. Multiple primary outcomes are recommended against by some guidance for cluster trials (e.g. CONSORT) [10] as it "incurs the problems of interpretation associated with multiplicity of analyses". However, we opt for multiple primary outcomes here as the intervention is multi-faceted and may affect different aspects of patient care and their interaction with the health system in different ways. Appropriate inferences about the functioning of REaCH cannot be made on the basis of any singular outcome. We ensure appropriate correction for multiple testing for all our test statistics (see Statistical methods). Furthermore, we will not be using 'statistical significance' to make inferences about the effectiveness or not of the intervention, given the importance of including the full range of qualitative and quantitative evidence to make conclusions about the effectiveness of REaCH, which also limits the risk of faulty inferences made through the use of multiple primary outcomes. Our unit of analysis for all outcomes is at the individual level.

Primary outcomes:

1) Trust in healthcare provider: Physician Humanistic Behaviour Questionnaire (PHBQ) [11] determines the degree to which healthcare providers communicate humanistically with their patients. Humanistic communications engender trust between the patient and the healthcare worker. The PHBQ has face and content validity with patients and health workers for assessing these behaviours during remote consultations [12].

2) Face to face consultation rate: the number of visits per month for the eligible patient population where the patient is seen in person by the consulting health worker.

3) Remote consultation rate: the number of visits per month for the eligible patient population conducted using a telephone.

4) Prescribing rate: the number of prescriptions issued and collected to the eligible patient population per month. This outcome is a proxy for patient safety as a change in this outcome is an indicator of changes in safety and confidence. The meaning and impacts of changes in this indicator will be explored in the process evaluation.

Secondary outcomes:

5) Patient engagement with their health: Patient Activation Measure (PAM-13) aims to understand the knowledge, beliefs and skills required by people to enable them to manage their long-term conditions [13]. It has been successfully used in African populations [14]. Our previous research found that patient activation increases with remote consulting [4]. Also that the PAM-13 [12] has face and content validity for assessing the impact of remote consulting.

6) Patient safety is assessed by counting the number of investigations processed by the facility monthly and matching these to the patient's consultation type. An increase may indicate a higher safety threshold when the person cannot be examined. A decrease may indicate missed health needs. The meaning and impacts of changes in this indicator will be explored in the process evaluation.

Evidence from the secondary outcomes will be explored in the process evaluation.

Sample size

The trials in Nigeria and Tanzania will take place independently, but with identical designs. We plan to recruit 20 clusters in each country for the trial and we expect there to be an average of 100 active eligible patients at any one time in each cluster. We describe each of these active patients in each cluster as an open cohort- patients will leave the cohort if they are not seen for >5 months and newly diagnosed patients meeting the eligibility criteria can join the cohort. The trial has both non-inferiority and superiority inferential goals: we hypothesise the intervention will increase the remote consultation but not affect consultation trust, for example. We therefore opt to determine "minimum detectable effect" sizes rather than power to indicate the precision of the trial and the likely sizes of effect for which we can provide strong evidence of superiority or non-inferiority. Our calculations are based on the statistical models reported below and a power of 80%, a type I error rate of 5%, an ICC of 0.05, and a CAC of 0.8. The assumptions about each outcome and minimum detectable effect sizes are reported in the Table below.

Outcome	**Baseline assumed**	**Denominator population**	**Treatment effect**	**Lower minimum**	**Upper minimum**

				detectable effect	**detectable effect**
Face to face consultation/prescription rate	0.25 consults/prescriptions per person-month	All active patients (n=100)	Incidence rate ratio	0.84	1.20
Remote consultation rate	0.02 consults per person-month	All active patients (n=100)	Incidence rate ratio	0.77	1.56
Patient trust	3.5 (sd=0.5)	Sampled patients (n=20)	Absolute effect	-0.07	0.07

A change in either consultation rate of an equivalent of one visit per person-year is considered "clinically significant", which is well outside our minimum detectable range. Similarly, we will be able to identify reasonably small changes (~0.15 standard deviations) in patient trustworthiness score, although we do not hypothesise a change in this outcome.

Patient participant recruitment and sampling

At the study commencement each cluster provides the study with a pseudonymised list of active patients, giving us a patient ID and the basic information, we need from each patient (age, sex and eligible diagnosis). At the clinic they will have a link to patient ID with the patient's record but we will not have access to the patient personal data. This is the open cohort for each cluster.

Each month we collect from each clinic a record of the consultations conducted and prescriptions and investigations ordered by the clinic, all they need to provide is the number of visits by type, prescriptions, investigations and any other information we need linked to a patient ID (e.g. patient 1234 had one remote visit, 2 prescriptions). Any additional patients can join the open cohort if they become eligible during the trial period.

Using the information, the research team can calculate outcomes, remove patients that are no longer active/who default, and sample for participation in the trust and patient activation outcomes and the process evaluation interviews. We will return the list of sampled patient identification number to the clinic for them to contact the potential participant so the research team can commence the informed consent processes.

This method of recruitment and sampling limits the amount of information to be collected each month, enables the tracking of patients each month to maintain the open cohort within each clinic, it simplifies the sampling process, and maintains patient confidentiality.

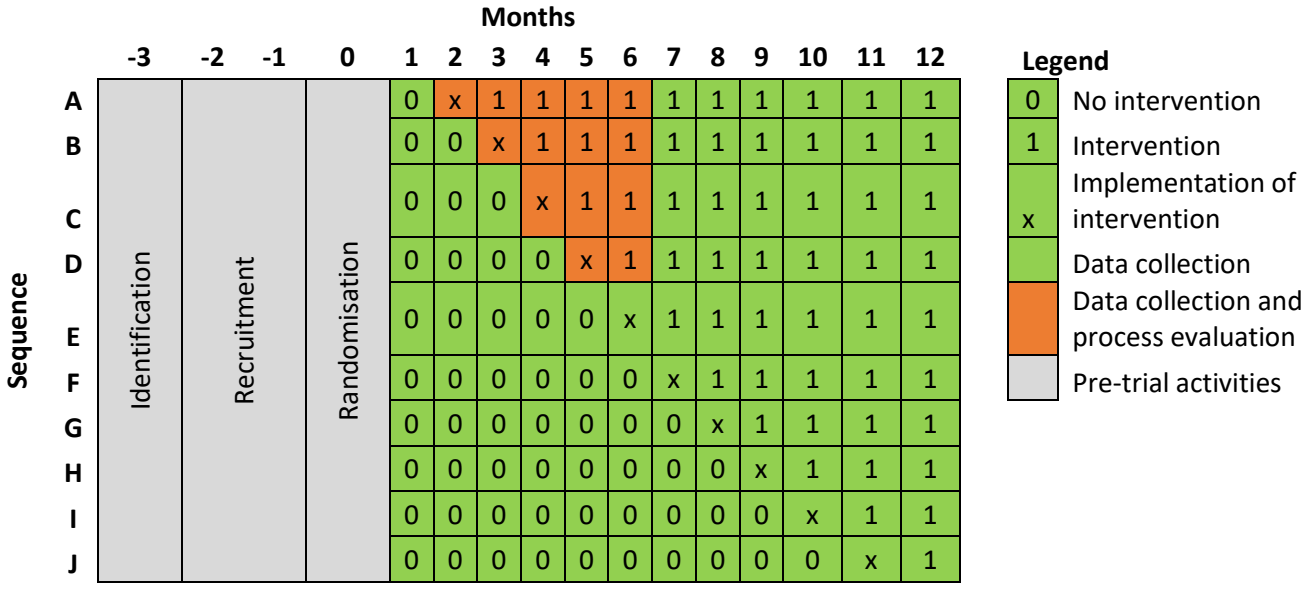
The research participation response rate experienced by our partners range from 60-80% and we will sample 30 patients each month to achieve our target sample of 20 per month.

Methods: Assignment of interventions

A number of outcomes will be collected by interviewing a random sample of 20 patients who have received a consultation in the previous month. To reduce the transfer of patient identifiable data and their contact details, we specify the following sampling protocol. On the first calendar day of each month the list of patients who have had at least one consultation in the preceding month will be aggregated within each cluster site by the facility representative. The list will be pseudonymised by redacting identifiable information including patient name and contact details but keeping unique IDs, such as row numbers, and other basic data to permit comparisons between sampled and interviewed

groups for quality control. The list will be photographed and sent to the trial statistician, who will send back a random sample. Data collection from the selected patients can then proceed.

Figure 1: Cluster randomisation sequencing



Allocation

Within each country the 20 participating clusters will be randomised to one of ten sequences (see figure 1) with two per sequence. A random number will be generated for each cluster and then clusters assigned to each sequence in ascending order of the generated number. The randomisation will be conducted by the trial statistician who will be blinded to cluster name. The intervention implementers and clinics will not be blinded to allocation sequence as this is impractical given the need to plan and prepare training.

Blinding

In each local trial delivery team, one investigator and 1 research assistant will remain blinded to the month during which REaCH training was delivered to each cluster. Each facility is given a unique identification number consisting of 4 digits. We use four digits to make it more difficult for the research team to recall cluster IDs when discussing with the unblinded education team. This will reduce bias when monthly data collection is undertaken. When education and research teams meet together, clusters will be referred to by identification number only. At the beginning of every data collection activity the researcher will remind the health worker or patient participant not to reveal whether the facility has undertaken REaCH training. Data entry will be undertaken by a database assistant who will be blinded to whether the data is from a cluster in the intervention or the control. At the bi-weekly trial team meetings we will have an agenda item to check with every blinded member whether they think they have been unblinded in relation the identity of a randomised cluster during the previous two weeks. All UK investigators will be blind to cluster randomisation except the Birmingham trial statistician.

Methods: Data collection, management, and analysis

Trial data collection methods

At trial set up each cluster will provide the research team with a pseudonymised whole facility population of eligible patients. This is the open cohort. On the same day/date of every month the clinic will provide the research team with four lists:

1) A list of pseudonymised patients who had face to face consultations since the last data period
2) A list of pseudonymised patients who had remote consultations since the last data period
3) A list of pseudonymised patients who had prescriptions ordered and collected since the last data period
4) A list of pseudonymised patients who had investigations ordered since the last data period

From the combined monthly lists of 1 and 2, the research team will generate a random order list of 30 pseudonymised patients to sample for completion of the patient reported outcome data. Once informed consent procedures are completed, the researcher will undertake a structured interview with the participant by telephone to complete the two questionnaires.

Table 1: Complete listing of the trial data collected

Study set up (t=-2 to -1)	**Every month during active trial (t=1 to 13)**	**Sampled patients (n=20) (t=1 to 13)**	**Study endline (t=13)**
1) Dataset with each row a unique patient with the following information with be collected from the participating clinics at study setup: -Patient study ID -Age -Sex -Primary eligible diagnosis 2) Clinics will generate a unique patient identifier that will be attached to each patient record	1) Dataset of consultations from the previous month with variables: - Patient study ID - Mode and data of consultation/s - Prescriptions ordered - Investigations ordered 2) Dataset of repeat prescriptions ordered without health consultation 3) Dataset of missed appointment	1) Dataset of 20 completed surveys	1) Missing data from months 1-12

Survey outcome measures will be translated into local languages. Participants will complete the questionnaires over the telephone or in person with trained fieldworkers. In person visits to facilities for the purpose of data collection will occur only if necessary, to problem solve and if it is safe to do so. Local health guidelines will be followed in relation to observing social distancing and/or wearing PPE as appropriate. The trained fieldworker will ask the survey questions and record their responses[15]. The data will be recorded by the researcher directly onto survey monkey software.

Appendix 1 shows the data flow for patient participants through the trial.

Statistical methods

The data from each trial will be analysed using a generalised linear mixed model framework standard for stepped-wedge cluster designs[16]. Data from each time point are considered a repeated cross-section given the difficulty linking observations between patients in different time periods. The primary outcomes are of two types: count data (the number of consultations by mode of delivery and the number of prescriptions) and a continuous score (the patient trust outcome). For the former we

specify the following log-linear model, for patient $i = 1, \dots, N$ in cluster $j = 1, \dots, J$ at time period $t = 1, \dots T$ with number of events y_{ijt}^{1}:

$$y_{ijt}^{(1)} \sim Poisson\left(\lambda_{ijt}\right)$$

$$\lambda_{ijt} = N_{jt} \exp\left(\eta_{ijt}^{(1)}\right)$$

where N_{jt} is the denominator population (i.e. the number of active patients in cluster j at time t) and η_{ijt} is the linear predictor. For the continuous outcome y_{ijt}^{2} we specify:

$$y_{ijt}^{(2)} \sim N\left(\eta_{ijt}^{(2)}, \sigma^2\right)$$

The specification of the linear predictor in both models takes the form:

$$\eta_{ijt} = x_{ijt}'\beta + z_{jt}'\gamma + \delta D_{jt} + \alpha_j + \psi_{jt}$$

where x_{ijt} is a vector patient-level covariates, z_{jt} is a vector of cluster-level covariates, D_{jt} is an indicator equal to one if cluster j has the intervention at time t and zero otherwise, and $\alpha_j \sim N(0, \sigma_\alpha^2)$ and $\psi_{jt} \sim N\left(0, \sigma_\psi^2\right)$ are cluster, cluster-time and individual random effects respectively. The treatment effect of interest from the Poisson model is an incidence rate ratio, although we will also provide absolute treatment effects for context, and from the linear model we will report only absolute treatment effects.

Inference

All models will be estimated using restricted maximum likelihood using the R package lme4. We will report point estimates, confidence intervals, and p-values but not make any claims of "statistical significance" given recent strong arguments against doing so[17]. P-values will be based on the null hypotheses $H_0: \delta = 0$ versus the two-sided alternatives $H_1: \delta \neq 0$ in each of the models. Given there are multiple primary outcomes we will adjust reported p-values for multiple testing using a stepdown method, which provides an efficient means of controlling the family-wise error rate[18]. We will derive the exact distributions of the test statistics to perform the stepdown procedure using a permutation test approach, by re-randomising clusters to different sequences in the stepped-wedge design[19]. This method ensures appropriate control of the family-wise error rate and avoids potential biases resulting from small numbers of clusters.

Data management

Each country team will store consent forms and raw data on their own university secure password protected server or if paper-based, such as consent forms, in a locked filing cabinet. The data will be electronic in an email attachment, or a photo of a list, or entered into a survey software, on the REaCH Moodle or a digital recording. The exact nature of the raw data will depend on the available infrastructures of individual clusters and their geographical proximity to the university. Data will be translated as necessary and transcribed locally. We will ensure a confidentiality agreement is in place for all transcribers. Two members of the local country team (one unblinded) will have access to a list which links a patient identifier to their identity and their informed consent forms. For REaCH trainees this will be three people because the facilitators will also know their identity and have access to their Moodle data. These will remain stored locally throughout the trial and not leave the country.

In Tanzania, data will be stored virtually in a server at Commission for Science and Technology (COSTECH) P.O. Box 4302, Ali Hassan Mwinyi Road, Kijitonyama (Sayansi) COSTECH Building, Dar es Salaam, Tanzania. Email: dg@costech.or.tz Research Registry Office Phone number: +255 22 2700749

Physical data will be stored at St. Francis University College of Health and Allied Sciences, Ifakara Health Institute (IHI), Box 53, Ifakara, Tanzania.

In Nigeria, physical and electronic data will be stored at College of Medicine, University of Ibadan, University College Hospital Campus, Queen Elizabeth II Road, Oritamefa, Ibadan, Nigeria.

To reduce data entry errors, range checks and other quality control measures will be put in place during database design. Data cleaning and validation will be done monthly.

Data transfer

Participant identifiable data will be transferred from the health facility to the university-based research team electronically or by telephone. Electronic transfer will be in the form of encrypted emails, online survey or photographs of paper lists sent via end-to-end encrypted WhatsApp from named recipient to named recipient. Once the photo or email has been downloaded onto the university secure server it will be deleted from the mobile device. All devices used will be password protected. Data will be pseudonymised once at the university with a local copy of patient identifiable data linked to pseudonym stored securely in locked filing cabinet.

Pseudonymised trial data will be transferred from health facility to local secure storage, electronically and finally onto a trial database hosted by the Clinical Trial Unit at the Medical School, University of Ibadan, Nigeria. Trial teams from Nigeria, Tanzania, Birmingham and KCL will have access to the database for the purpose of data input, cleaning, monitoring and analysis.

Process evaluation data will be transferred from local secure storage, electronically onto a secure storage area hosted by the Clinical Trial Unit at the Medical School, University of Ibadan, Nigeria. Evaluation teams from Warwick, Nigeria, Tanzania and KCL will have access to the data for the purposes of data entry, quality monitoring and analysis. All electronically stored research data will be both password protected and encrypted.

See uploaded participant data flow in Appendix 1 illustrating data flow and secure repositories.

Methods: Monitoring

Trial monitoring

We will develop a single Trial Steering Committee (TSC) to oversee both trials. Members will be drawn from the country networks, our broader collaborators in other LMIC and our existing project advisory groups for earlier projects [3,5]. The TSC will meet virtually on three occasions during the project life in months 3, 9 and 16. At each meeting a risk assessment paper will be completed and presented to the TSC for scrutiny and discussion.

Data monitoring

University of Ibadan will host an independent Data Monitoring and Ethics Committee (DMEC). The Committee comprises experienced researchers and community stakeholders and an independent statistician. The DMEC will liaise with the study statisticians at Birmingham and Ibadan to review unblinded patient safety data. The DMEC will meet during project months 2, 8 and 16 and report to the chair of the TSC. Interim analyses will be undertaken at trial month 6 specifically to monitor participant safety.

Harms

One unblinded co-investigator in each country will hold responsibility for monitoring prescriptions and investigation rates monthly by consultation type across all cluster data. Differences by consultation type of greater than 40% (i.e. equivalent to one visit per patient year) across each cluster will trigger a consideration of whether there could be a participant safety issue. Any such

difference will be investigated with the facility manager to identify and report any adverse or serious adverse events at an individual participant and/or cluster level. Where such events are revealed, this will be reported to the KCL PI, the country PIs and the chair of the DMEC.

Process evaluation

The process evaluation will a) explore patient and health-worker experience of remote consulting b) its impact on healthcare and c) enablers/impediments of remote consulting. It will be informed by:

1. MRC framework for complex intervention process evaluation [20] to understand how REaCH training impacts on health workers and in turn how remote consulting impacts healthcare experience.
2. TRAIN framework to assess how well the train-the-trainer approach works [9].
3. Consolidated implementation framework [21] to understand what enables/hinders implementation of remote consulting.

Participants and sampling

From all trial clusters we will collate data on the REaCH training: number and roles of tier 1 and tier 2 trainees, their sex, their engagement with each part of the training/cascading, and their text written during the REaCH training.

In all trial clusters we will survey facility managers and tier 1 trainees on implementation one month after completion of the REaCH training for the cluster. The timing allows them time to have reflected on the training and start planning delivery. The questionnaire provides the participant opportunity to reflect on implementation. We will collect information on how facilities distributed the airtime allowance across tier 1 and tier 2 trainees.

Observation, interview and prescription data will be collected in each country, from a random sample of five facilities (clusters) who receive the intervention during the first 6 months of the trial, to allow time for implementation prior to data collection.

Consent to process evaluation data collection will be taken along with consent to trial participation.

Training data (all clusters)

Prior to each REaCH training the facilitator will confirm consent to the use of aggregate data about the trainees/training and to the use of trainees' text for analysis in the study process evaluation clarifying that all personal identifiers will be removed before it is shared with the research team. This will be repeated at the end of the training. Trainees will be able to confidentially inform the facilitator if they do not wish their text to be included.

Survey of facility manager and trainees (all clusters)
All tier 1 trainees and the facility manager in all clusters will be invited to complete a questionnaire about implementation of remote consulting.

Observation (2x5 clusters)
We will observe two tier 1 and two tier 2 training sessions. Each REaCH facilitator will provide us with their timetable for training delivery. We will take a stratified random sample of planned training sessions to ensure observation of the range of modules within the training. Where individuals scheduled to attend observed training sessions have not given consent to be observed we will discuss with them their options. They may choose to attend but remain silent or they may choose not to attend. They will be offered a briefing session with the facilitator after the session so they are able to catch up on learning.

Semi-structured telephone interviews (2x5 clusters)

We will interview 3-4 months after training
- the facility manager
- the REaCH facilitator
- two tier 1 and two tier 2 health workers
- four patient trial participants
Within each cluster and each tier, from among health workers/patients consenting to participate in interviews will take a random sample.

Prescription data (2x5 clusters)
Prior to training and three months after training is complete, we will ask the facility managers to provide us with the timetable of sessions/clinics run at the facility including remote consulting, and identify those where prescriptions may be issued (e.g. we will exclude child immunisation sessions). We will stratify sessions/clinics by mostly remote consulting/mostly face to face and take a random sample of four sessions with a 1-2-week timeframe at each time point (prior to training and three months after training). We will collect prescription data on consecutive patients from each session.

Survey of facility manager and trainees
All tier 1 trainees and the facility manager in each cluster will be invited to complete three brief questionnaires 1) The four item Intervention Acceptability Measure (AIM), the four item Intervention Appropriateness Measure (IAM) and the four item Feasibility of Intervention Measure (FIM)[22]. We will aim to obtain a minimum of two completed questionnaires from each cluster. The REaCH facilitator will ask the tier 1 trainees for permission to give their name and phone number to the research team. Once informed consent is completed the researcher will ask the trainee to complete the four questions by paper, telephone or via email.

Data collection
All data will be collected via the internet or phone or using social distancing at primary care facilities. Appendix 4 contains a participant distress protocol for anyone feeling uncomfortable during an interview.

Training data
Data on number and roles of trainees and engagement with each part of the training/cascading will be collated by facilitators and passed to the research team as aggregate data. Facilitators will extract student text and remove identifiers before passing it to the research team.

Survey of facility managers and Tier 1 trainees
Four brief surveys will be used to assess the feasibility of implementation of remote consulting. The surveys are 1) The four item Intervention Acceptability Measure (AIM), the four item Intervention Appropriateness Measure (IAM) and the four item Feasibility of Intervention Measure (FIM)[22]. Items are measured on a 5-point Likert scale, Completely Disagree to Completely Agree. The REaCH facilitators will send a link to the questionnaire, in English, to all participants one month after the training completion. Where necessary, in discussion with the facilitator, we will consider other approaches to this data collection including paper questionnaires and email. Survey data will be given a study ID with only the facilitator knowing which ID corresponds to which facility manager/trainee. The research team will be informed of whether the ID corresponds to a facility manager or trainee, whether the participant received REaCH training and in which three-month timeframe the training was received.

Observation
The researcher will be a non-participant observer, listening to discussion and reading posts related to the session. They will take field notes throughout the session. The fieldnotes will follow the sequence

of the session and note what is discussed, who participates in the discussion, and how the participants relate to each other in narrative form. Field notes will not include any identifiers. At the start of every observation we will remind participants about the study and verbally confirm consent.

Interviews
At the start of every interview we will remind participants about the study and verbally confirm consent. Interviews will be audio-recorded and transcribed/translated into English. All identifiers will be removed during transcription/translation. Transcripts will be checked against audio-recordings and then the audio-recording will be destroyed. All data will be labelled with a study ID.

District/facility manager and health workers
We will explore the experience of REaCH training, support and cascade and of undertaking remote consulting, how they have deployed remote healthcare themselves and within the facility, what impact this has on their working patterns, facility organisation and the experience of patients, what is working or not and why, and changes needed or made to enable remote consulting (e.g. facility expenditure on airtime, phones, appointment system, guidelines, policy). We will use initial analysis of survey data to inform how we probe during interviews.

REaCH facilitators
We will explore the experience of REaCH training, support and cascade, their understanding of how their trainees planned to or have deployed remote healthcare, what worked well or not in the training and adaptations they made to the training in response to the need of their trainees. We will ask them what enables the Tier 1 trainees to cascade training successfully and what hinders this, and how this cascade fits within other team activities.

Patient trial participants
We will explore their experience of remote consulting and its impact on their healthcare including what is working or not and why, expenditure on airtime and changes needed or made to enable remote consulting.

Prescription data
We will work with each of the clinics on how we collect this to avoid disrupting the clinic and ensuring patient confidentiality. We aim to collect the drug details from each prescription issued in the sampled sessions. We expect this will involve taking a photograph, ensuring the patient's name is not included in the photograph. There may be a step where a carbon copy is made when the prescription is issued which is then photographed.

<u>Analysis</u>

Training data
Data on trainee engagement will be summarised using descriptive statistics. Trainee text data obtained from the Moodle will be uploaded into NVivo for data management. Meaningful chunks of data will be coded based on its content. Through team discussion we will identify themes related to our objectives and move these into a framework of themes [21, 23] and training cohort. We will undertake within cohort comparison and cross cohort comparison. We will pay attention to how trainees consider remote consulting and its implementation and, how they plan to problem solve. From comparing data from cohorts implementing earlier and later in the trial we will gain insights into what external changes impact on the trainee's approach to mobile consulting and its implementation.

Survey data
We will use descriptive statistics for analysis. Each section of the questionnaire will be analysed separately as they relate to different implementation constructs[22]. The mean score is calculated for

each section [24]. We will examine the variation of scores by a number of parameters including role of participant (facility manager/trainee), receipt of REaCH training or not and in which 3-month timeframe the REaCH training was received. This analysis will assist with interpretation of our trial results.

Observation and interview data
Data from each cluster will be analysed together, to enable comparison of account between different methods of data collection and between different types participants within the same setting. We will then undertake comparison between clusters including across countries.

Data will be uploaded into NVivo for data management. Meaningful chunks of data will be coded based on its content. Through team discussion we will identify themes related to our objectives and move these into a framework [21,23] of themes and participants for each cluster. We will undertake within cluster comparison and then cross cluster comparison. We will pay particular attention to impact on healthcare as this will assist with interpretation of our trial results, how challenges are problem-solved as this provides applied learning, and the barriers that demand organisational or policy change as we will take these to decision makers.

Ethics

Stakeholder engagement

Through ongoing projects [3,5], local project advisory groups in Nigeria, Tanzania, Kenya, Uganda, Bangladesh, Pakistan have met 3-4 monthly each comprising 6-10 representatives from marginalised communities in urban and rural settings including:

- community residents, leaders, local women's/disability group representatives
- local healthcare workers and managers in these communities
- local/national government departments, NGOs, academic/research institutions and commercial companies (e.g. mHealth service providers, mobile companies)

Advice actioned from Nigeria and Tanzania has been to recognise the importance of context, understand and seek to integrate plans with existing services; and explore reasons for failure as well as success.

Empirically we have undertaken fieldwork with >300 community residents, 60 health workers and 50 local/national decision-makers about the availability, use and perceptions of remote consulting, its impact on users/healthcare workers and potential to strengthen access to health care(4,7). Community members saw value in remote consulting for sensitive and long-term conditions/requiring chronic care but emphasised the importance of establishing trust and ensuring communication about wider treatment pathways.

We will continue to engage key beneficiaries through our project advisory groups and as part of our process evaluation. Partners include the East African Science and Technology Commission (EASTECO) and Society for Telemedicine and eHealth, (Nigeria). Through our participation in ministerial working groups and committees, we reach decision-making bodies such as Digital Health Nigeria; the Tanzanian Ministry of eHealth Working Group; Kenya National mHealth and eHealth forum; Uganda Health Information, Innovation and Research (HIIRE) Technical Working Group. We have applied to list our REaCH Training through the World Health Organization Digital Clearing House.

Ethics approval

As sponsor, King's College London will provide ethical approval initially and, in accord with good ethical practices in LMIC research [25], this will be followed by applications for approval to St

Frances University College of Health and Applied Sciences, Tanzania and University of Ibadan, Nigeria.

In Nigeria we will seek approval from:

Oyo State Health Research Ethics Review Committee
Oyo State Ministry of Health
Department of Planning, Research & Statistics
Government Secretariat, Agodi, PMB 5027,
Ibadan, Nigeria.

In Tanzania we will seek approval from:

National Health Research Ethics Review Committee
National Institute for Medical Research
2448 Ocean Road
P.O. Box 9653
Dar es Salaam, Tanzania
Tel: +255 22 2121400
Fax: 255 22 2121360
Email: ethics@nimr.or.tz ; nimrethics@gmail.com

Exemplar participant informed consent documentation can be found in Appendices 2 and 3. The project has been peer-reviewed by the UKRI/GCRF/Newton Fund funding panel prior to making an award.

Ethical Issues

Privacy and confidentiality
The intervention promotes remote health consultations by mobile phone or fixed communal landlines by both patient and health care worker. This presents issues of privacy for both parties when engaging in a confidential health communication. The REaCH intervention training covers the issue of privacy for both partners. Health workers are trained to both ensure that the conversation is confidential at their end of the phone call. They are also requested to ask the patient at the other end of the phone whether they are receiving the call in a sufficiently private place to meet their needs. Our process evaluation will seek to understand how this is experienced in reality for both partners and the stepped wedge design affords us the opportunity to strengthen messages around privacy if we detect concerns.

Sex-based equality
In Tanzania and Nigeria more men than women own a mobile phone. The difference in ownership differs by country and across Africa as a whole, the difference is 8% fewer women owning mobile phones [26]. The potential impact of this is that women may have less access to remote consultations. If they have less access they may travel to health centres for face to face health care which puts them and their health workers at risk. Whilst fewer women own a mobile phone the majority have access either to a family phone or a fixed landline in the community [27]. To ensure that our research does not disadvantage women we will monitor recruitment within each cluster by sex. Where we find a difference in the sex of participants of greater than 10% this will trigger an over sampling in the process evaluation of the sex least represented so that we can understand the issue for women. The stepped-wedge trial designs means that we can monitor this and make changes to our trial procedures as we deliver REaCH trainng to subsequent health facilities to try and understand and address any sex imbalance that we find. However, the breadth of women's phone use is also narrower. REaCH training is intended to result in people having a trustworthy and safe experience of remote consulting with health workers and such experience may expand women's often self-restricted use of mobile services in general [26].

Protocol amendments

Protocol amendments with ethical implications will be subject to approval by all three ethical committees approving the trial. The proposed protocol amendments will not be implemented without prior ethical approval.

Consent or assent

All participants will undertake an informed consent process with information provided in written and spoken local languages and consent recorded in writing or verbally audio-recorded.

Confidentiality

Each participant's personal details will be linked to their study identifier in an excel spreadsheet that five members of the investigator team will have access to. This document will be password protected and encrypted. Responsibility for managing this database will be held with the Ibadan Trial manager and the database will be held on a secure Ibadan server. All data collection and recording will be GDPR compliant.

Declaration of interests

All investigators will register any conflicts of interest with the KCL PI and the KCL Trial Manager.

Ancillary and post-trial care

Any arising concerns about the conduct of the research during or following completion will be notified to one or more of the following:

The Secretary
Oyo State Health Research Ethics Review Committee
Oyo State Ministry of Health
Department of Planning, Research & Statistics
Government Secretariat, Agodi, PMB 5027,
Ibadan, Nigeria.

Secretariat
National Health Research Ethics Review Committee
National Institute for Medical Research
2448 Ocean Road
P.O. Box 9653
Dar es Salaam, Tanzania
Tel: +255 22 2121400
Fax: 255 22 2121360
Email: ethics@nimr.or.tz ; nimrethics@gmail.com

The Chair
Psychiatry, Nursing and Midwifery Research Ethics
Research Ethics Office
Franklin Wilkins Building
5.9 Waterloo Bridge Wing
Waterloo Road
London SE1 9NH
Email: rec@kcl.ac.uk

Dissemination and Outputs

Dissemination

We will publish manuscripts in open access peer review journals, present our findings at conferences and engage with policy makers in partner countries and the UK including governments, NGOs and digital health and telecommunications companies. We will undertake stakeholder activities within each country building on our existing stakeholder communities and engaging with the local facilities to interpret and extend the impact of our findings.

Research deliverables

1) Month 3: Digitally optimised REaCH training on royalty-free license ideal for LMIC organisations where digital infrastructures are limited/variable. This prepares for ongoing communicable disease peaks such as COVID-19 peaks and strengthens health care systems.
2) Month 14: Realisation of first international trial evidence on quality and safety of remote health consulting informing policy briefs. These influence delivery of sustainable resources/regulation to enable adaption as technological infrastructures strengthen.
3) Commencing month 2: Populations offered greater protection from communicable diseases such as COVID-19 impacts. Women mobile users have strengthened/broadened confidence in remote/digital services.
4) Commencing Month 3: Strengthened clinical trial capability in Tanzania and Nigeria.

Training and capacity building in collaborating countries

The proposed research has training and capacity development as its central focus. It will deliver REaCH training to 80 tier 1 doctors, nurses and clinical medical officers across Tanzania and Nigeria. These 80 learners will each cascade to at least four other tier 2 learners resulting in education spreading to a further 320 learners across the two countries. If each of these 400 health workers deliver five remote consultations per day this leads to 2,000 consultations with patients every day. This will have an impact on how citizens see alternative uses for mobile technology including employment, finances, nutrition and wellbeing.

Additionally, we deliver capacity building beyond REaCH as follows:

1) Raising awareness and experiential learning on the use of Moodle on online learning infrastructures and techniques by the senior tier 1 trainees.

2) Developing knowledge, skills and confidence in successfully cascading learning to tier 2 trainees. New knowledge includes use of the TRAIN framework (Talent, Resources, Alignment, Implementation and Nurture) as key criteria when determining who to cascade any learning to and how to support these learners.

3) Tier 2 trainees, who have limited access to training support and digital resources are able to develop a new skill in remote consulting, have support in practicing it and develop a confidence in learning which may have wider implications for the tier 2 learner.

4) University of Ibadan has clinical trials capability but not a networked capacity. Our trial will bring individuals from across the university together to develop a clinical trials team. This develops trials leadership capacity within Africa.

5) The team at St Francis have never taken part in a clinical trial. Their role in delivering our trial locally will develop knowledge and skills in trial designs.

Policy relevant outcomes:

- Evidence of how citizens experience the safety and trustworthiness of remotely delivered

healthcare compared to face to face care.
- The airtime costs of delivering remote care to inform national resourcing decisions.
- How the implementation of remote healthcare is operationalised in different LMIC settings.
- The efficacy of medical and health worker training using Moodles, SMART phones and Feature phones which will inform healthcare education providers in LMIC.

Our pathways to impact will ensure that these outcomes lead to realised health and welfare improvements in rural and urban marginalised communities.

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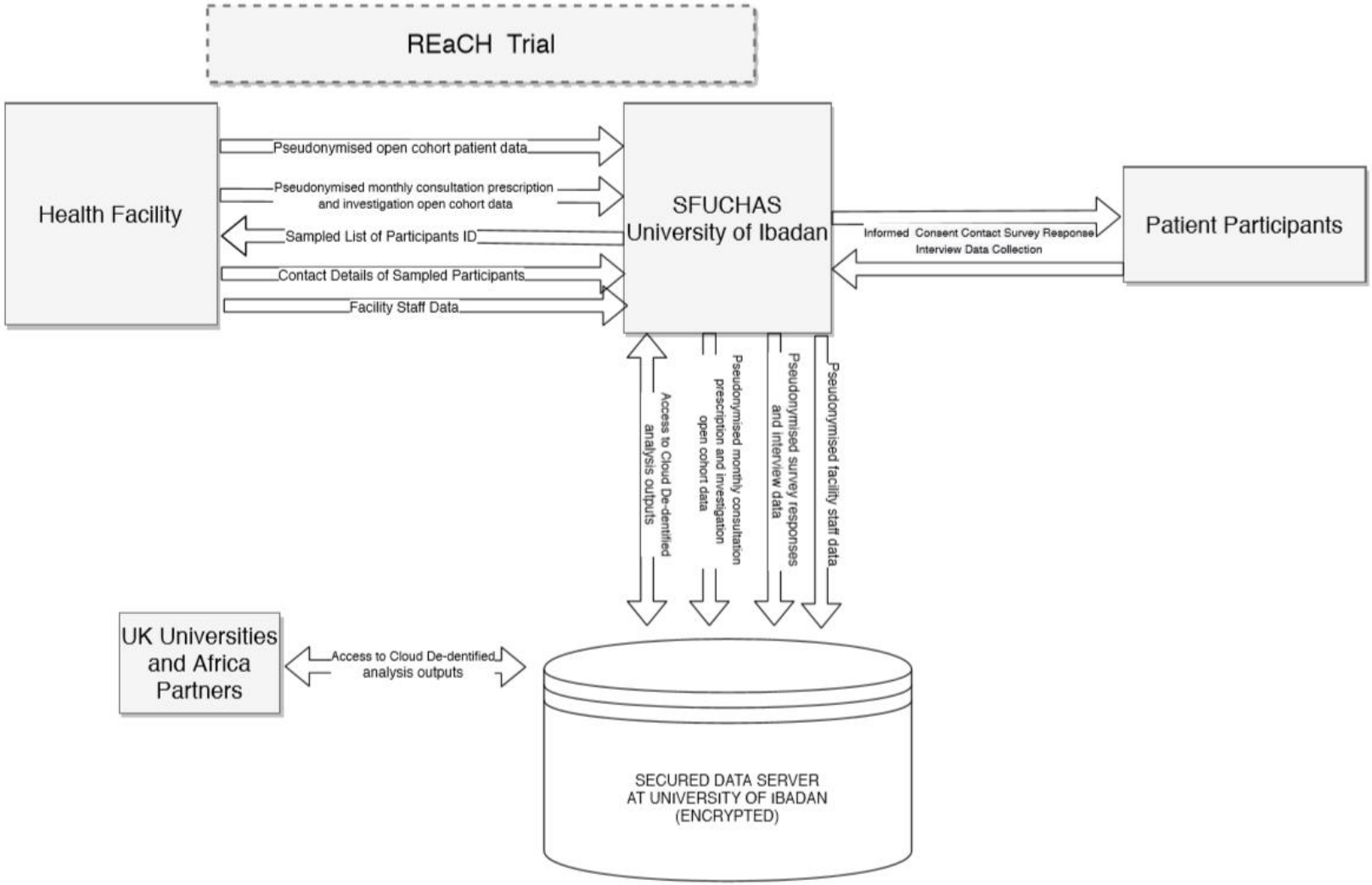
Appendix 1 REaCH Trial Data Flow Diagram for Participants



Appendix 2 Information sheet for patient participation in the survey

University of Ibadan

KING'S College LONDON

INFORMATION SHEET V1 30/10/2020

PATIENT INFORMATION SHEET FOR TAKING PART IN SURVEYS

King's College Research Ethics Committee Ref: XXX

National Institute for Medical Research, Tanzania Ref: XXX

National Health Research Ethics Committee of Nigeria Ref: XXX

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET IF YOU WISH TO TAKE PART

Determining trustworthiness and safety of Remote Consulting in primary Healthcare for chronic illness.

Place of study: Ibadan, Nigeria and Kilombero district, Morogoro, Tanzania

We would like to invite you to participate in this research project on remote consulting (consulting by mobile phone) in primary care for patients with chronic illness. You should only participate if you want to; choosing not to take part will not disadvantage you in anyway. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please feel free to ask if there is anything that is not clear or if you would like more information.

1. What is the purpose of the study?

We are undertaking a study to see if we can increase patients' access to health care by using telephone consultations/appointments. We want to know if these healthcare appointments feel safe and trusted to patients accessing health care this way. We are doing this research with patients who have one of these health conditions: Type 2 diabetes, Hypertension, Chronic Obstructive Pulmonary Disease or Coronary Heart Disease. We aim to find out if this model of care is acceptable to patients and health facilities.

We know from previous research that people with chronic illness experience pain, shortness of breath and other physical problems and concerns and may require support with psychosocial or spiritual care.

Through this study we want to find out if receiving care through telephone calls with health workers can help to manage these problems and concerns.

2. Why have I been invited to take part?

We are inviting you to take part because your health facility has told us that you are living with one of these chronic illnesses and that you have had a recent health appointment with the health facility either by telephone or face to face.

3. What will happen if I take part?

If you choose to participate in this study you will be asked to complete two questionnaires with the help of a researcher. This will take place during a telephone call of a face to face meeting on a single occasion. The first questionnaire will ask you how health care providers communicate with you. The second will ask about your knowledge, beliefs and skills and how well you feel able to manage your own condition between visits to the health facility.

The study researcher may need to access some of your medical records for the purpose of this research study, e.g. your medical diagnosis or medical prescriptions.

4. Do I have to take part?

You are free to choose if you want to take part in the research. You should only take part if you want to and choosing not to take part will not disadvantage you in anyway. Once you have read the information sheet, please contact us if you have any questions that will help you make a decision about taking part. If you decide to take part we will ask you to sign a consent form and you will be given a copy of this consent form to keep.

5. Incentives:

There are no incentives for participation in this study

6. Risks and discomforts:

There are no expected risks associated with participation in this study. If you become upset or distressed, we will offer you the chance to take some time out of the study and then either carry on or stop the study completely. The researcher will help you identify someone else to talk to if you continue to feel upset.

7. Benefits

There are no direct benefits to you, though it may have some benefits for future patients.

8. Data handling and confidentiality:

The Human Research Ethics Committee regulations at the University of Ibadan, St. Francis University College of Health and Allied Sciences, King's College London and the General Data Protection Regulation, 2016 (GDPR) will apply to all the information that you provide to this study. Information that could identify you such as your name or phone number, will be stored electronically on password protected computers and encrypted or in a locked cabinets at [*insert University of Ibadan or St. Francis University College of Health and Allied Sciences*]. This information will not leave your country. Once your information has been anonymized, it will be held on a secure cloud storage based at University of Ibadan.

The research team may use your data for future research but any such use of identifiable data would be reviewed and approved by a research ethics committee.

Your identity will not be disclosed to anybody except the Ethics committee and/or regulatory authorities during the course and after completion of the study if required. When we report the findings you will not be identifiable from the information.

Research data will be stored or accessed by the research team and securely archived for 10 years after the study has ended.

9. Data Protection Statement

The data controllers for this project will be King's College London, the University of Ibadan, and SFUCHAS. These institutions will process any data you provide for the purpose of the research outlined above in accordance with the General Data Protection Regulation 2016 (GDPR). Under GDPR, a data controller is responsible for handling personally identifiable data. They decide how and why the data is processed. At King's College London, the data controller for research data is the university itself. For each research project, the Principal Investigator takes responsibility. They have to ensure that only the relevant research team has access to your personal data. The legal basis for processing your personally identifiable data for research purposes under GDPR is a 'task in the public interest'

Researchers also have a common law duty and ethical obligation to gain explicit informed consent from you as a research participant for all aspects of the research. This includes the use of your personal data. You have the right to be informed of the following:

- What data we collect from you.
- How we will ensure the confidentiality of your data.
- How long we will keep your data for, and whether it will be shared with anyone else.

Under GDPR, you have the right of access to any information we hold about you. You can ask for it to be corrected, erased and object to how it is processed. However, this might be restricted in some circumstances. These include compliance with legal obligations. Restrictions might also be applied for scientific research purposes. For example, this might be if the deletion of your data was seriously detrimental to the research. In such circumstances, we may need to keep the information about you that we have already collected. However, the research team are required, under GDPR, to explain why these restrictions might be necessary *before* you agree to take part in the study. This is part of the informed consent process.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer, Mr Albert Chan info-compliance@kcl.ac.uk who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO) www.ico.org.uk.

10. What if I change my mind about taking part?

You are free withdraw at any point of the study, without having to give a reason. Withdrawing from the study will not affect you in any way.

You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You can ask for the information you give to be withdrawn and not used, but this will not be possible from four weeks (one month) after your final interview. If you refuse or withdraw from the study, this will not affect the treatment and care you receive from your Doctor. You will still receive care as usual from health facilities.

11. How is the project being funded?

This study is being funded by UKRI/GCRF/Newton Fund in the UK.

12. What will happen to the results of the study?

The findings of the study will be presented in a report and will be published in scientific journals and at academic meetings. A report will be displayed at the health facility and you will not be identified in the results of the study or any publication that might arise from this study. Anonymised data may also be used in future research studies by appropriately qualified researchers. We will also present the findings from this study at international and national conferences, we will use anonymised data to present these findings so that you should not be identified in anyway. We will use the findings to inform local and international policy makers.

13. Who should I contact for further information?

If you have any questions or require more information about this study, please contact the following:

Akinyinka Omigbodun
Professor of Obstetrics and Gynaecology
University of Ibadan
Email: omigbodun@yahoo.com

Professor Senga Pemba
SFUCHAS
Deputy Principal (Academic, Research and Consultancy)
Email: spemba@sfuchas.ac.tz

Jackie Sturt
Professor of Behavioural Medicine in Nursing
Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care
King's College London
James Clerk Maxwell Building
57 Waterloo Rd
London
SE18WA
Email: Jackie.sturt@kcl.ac.uk

14. What if I have further questions, what if something goes wrong?

If this study has harmed you in any way or if you wish to make a complaint about the conduct of the study you should contact;

The Secretary
Oyo State Health Research Ethics Review Committee
Oyo State Ministry of Health
Department of Planning, Research & Statistics
Government Secretariat, Agodi, PMB 5027,
Ibadan, Nigeria.

Secretariat
National Health Research Ethics Review Committee
National Institute for Medical Research
2448 Ocean Road
P.O. Box 9653
Dar es Salaam, Tanzania
Tel: +255 22 2121400

Fax: 255 22 2121360

Email: ethics@nimr.or.tz ; nimrethics@gmail.com

The Chair

Psychiatry, Nursing and Midwifery Research Ethics, Research Ethics Office, Franklin Wilkins Building, 5.9 Waterloo Bridge Wing, Waterloo Road, London SE1 9NH, Email: rec@kcl.ac.uk

THANK YOU FOR TAKING THE TIME TO READ THIS INFORMATION SHEET AND CONSIDERING WHETHER TO TAKE PART IN THIS RESEARCH.

Appendix 3 Consent form for patient participation in the survey

University of Ibadan

KING'S College LONDON

CONSENT FORM V1 30/10/2020

PATIENT CONSENT FORM FOR TAKING PART IN SURVEYS

CONSENT FORM FOR PARTICIPANTS IN RESEARCH STUDIES

Determining trustworthiness and safety of Remote Consulting in primary Healthcare for chronic illness

King's College Research Ethics Committee Ref: XXX

National Institute for Medical Research, Tanzania Ref: XXX

National Health Research Ethics Committee of Nigeria Ref: XXX

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

Please tick

I confirm that I understand that by ticking each box I am providing voluntary consent to this element the study. I understand that it will be assumed that unticked boxes mean that I DO NOT consent to that part of the study. I understand that by not giving consent for any one element I may be deemed ineligib for the study. ☐

1. **I confirm that I have read and understood the information sheet dated [V1 30/10/2020] for the above study. I have had the opportunity to consider the information and asked questions which have been answered satisfactorily.** ☐

2. **I consent voluntarily to be a participant in this study and understand that I can refuse to answer questions and I can withdraw from the study at any time, without having to give a reason, up until 4 weeks after my final interview** ☐

3. **I consent to the processing of my personal information for the purposes of the study as explained to me in the information sheet. I understand that such information will be handled in accordance with the terms of the General Data Protection Regulation (GDPR) and the UK Data Protection Act 2018 and relevant regulations in Nigeria and Tanzania.** ☐

4. **I understand that my information may be shared with the collaborating universities on this research trial.** ☐

5. **I understand that my information may be subject to review by responsible individuals from University of Ibadan, SFUCHAS and Kings College London for monitoring and audit purposes.** ☐

6. **I understand that confidentiality and anonymity will be maintained and it will not be possible to identify me in any research outputs.** ☐

7. **I agree to be contacted in the future by University of Ibadan, SFUCHAS and Kings College London researchers who would like to invite me to participate in follow up interview for this project.** ☐

8. **I agree that the research team may access my medical records for the purposes of this research project.** ☐

9. **I agree that the research team may use my data for future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. (In such cases, as with this project, data would not be identifiable in any report).** ☐

10. **I agree that my doctor may be contacted if any unexpected results are found in relation to my health.** ☐

_____	_____	_____
Name of Participant	**Date**	**Signature**

_____	_____	_____
Name of Researcher	**Date**	**Signature**

Appendix 4. Participant Distress Protocol

There is a risk that participation in the interview might trigger emotional discomfort, raise safety concerns. Where such distress and emotional discomfort or clinical concerns occur, the researcher will trigger and implement the distress protocol to minimise risk of potential harm to participants. The participant will be asked if they would like to take a break from the interview. The researcher will attempt to establish what caused the distress. The researcher will then offer the participant the options of resuming the interview, continuing the interview at a later time, or terminating the interview. After the interview, participants will also be given information about available formal support should they need ongoing support.

In the event that participants disclose any idea of self-harm or other risk to themselves or others, this will be treated as urgent. Consent will be sought from the participant and the matter will be discussed with a senior member of the treating medical team immediately. A list of reported symptoms or concerns which will trigger the distress protocol is detailed in a table below. All triggers of the distress protocol and the actions that are taken in response will be recorded on a file note placed in the site file with anonymised details of the case.

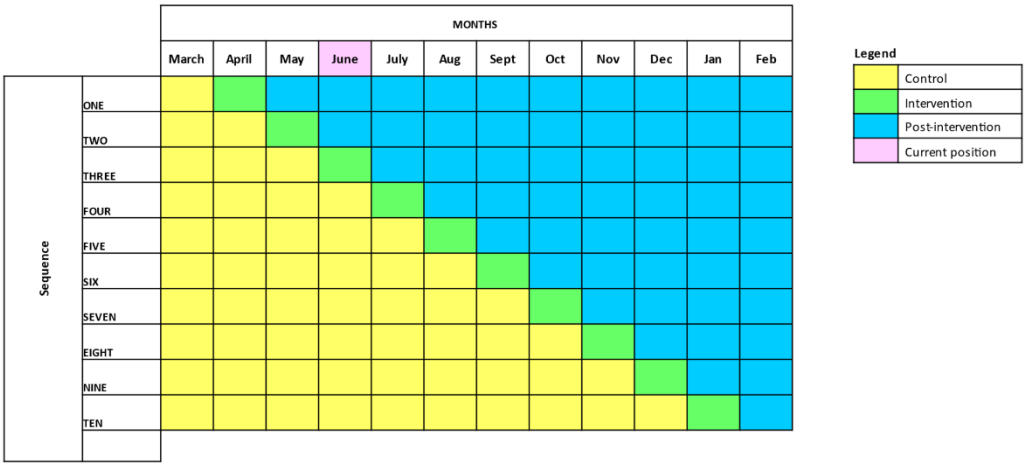
Categories	**Triggers**	**Actions taken**
Concerns identified when screening or interviewing patient/carer		
Researcher concern	Any concern about unaddressed need affecting the participant's wellbeing.	Ask participants permission to discuss with their primary healthcare team. Discuss with senior clinician at study site.
	Researcher experiences strong negative emotions during or after conducting interview or survey	Take time to reflect following interview or survey. Debrief and speak to PI and discuss within the research team.
Patient concerns	Any concern raised by the participant regarding their health that they wish to discuss with their medical team.	'Postpone' discussion of these issues until end of interview or survey. Suggest participant contacts their medical team; offer to help them do so.
	Participant discloses ideation of self-harm or risk to themselves or others.	**Urgent discussion with senior clinician treating them.**
	Participant expresses distress during interview or survey.	Ask whether participant would like to pause or stop interview or survey. Offer discussion with their clinical team. Remind them of contact telephone number.

Appendix 5. Changes to REaCH trial timelines (reported to King's Ethics Committee on 20 August 2021)

As reported at the PMG dated 11.05.22, both trials were running behind our originally planned schedule. Following conformation of the UKRI/ODI funding restoration, Professor Jackie Sturt, Principal Investigator, approached the funder to request a four-month time-only extension. They confirmed on 17.06.21 that they were unable to offer us an extension beyond the current financial year (related to the ODA funding issue) but they would be able to award the study a further five weeks. The trial must now complete by 31.03.22. The final report must be submitted by 30.06.22.

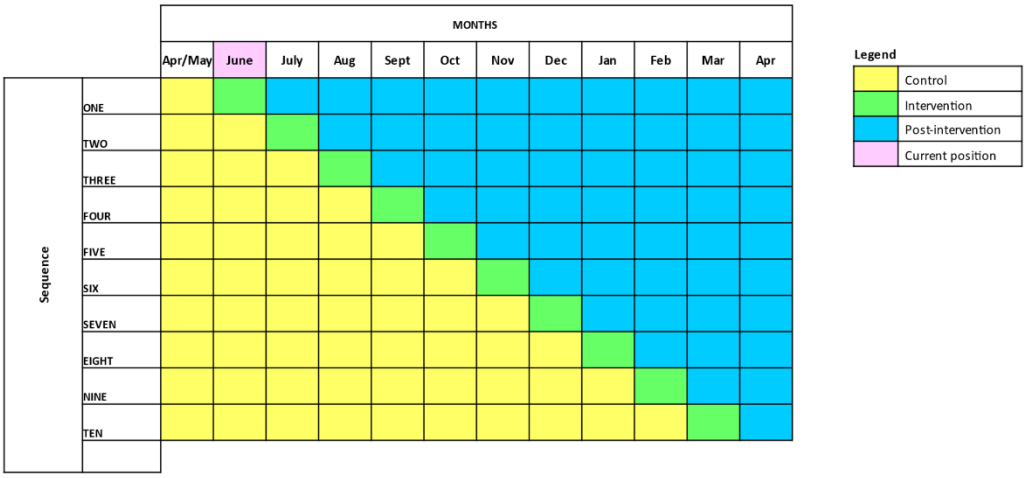
The Nigeria trial is on track to complete final data collection by mid February 2021 and so is able to continue as per current plan.

Nigeria as of June 2021



The Tanzania trial had a delayed start and without changes was currently due to complete in April 2022. We therefore needed to propose some amendments to the trial design.

Tanzania as of June 2021

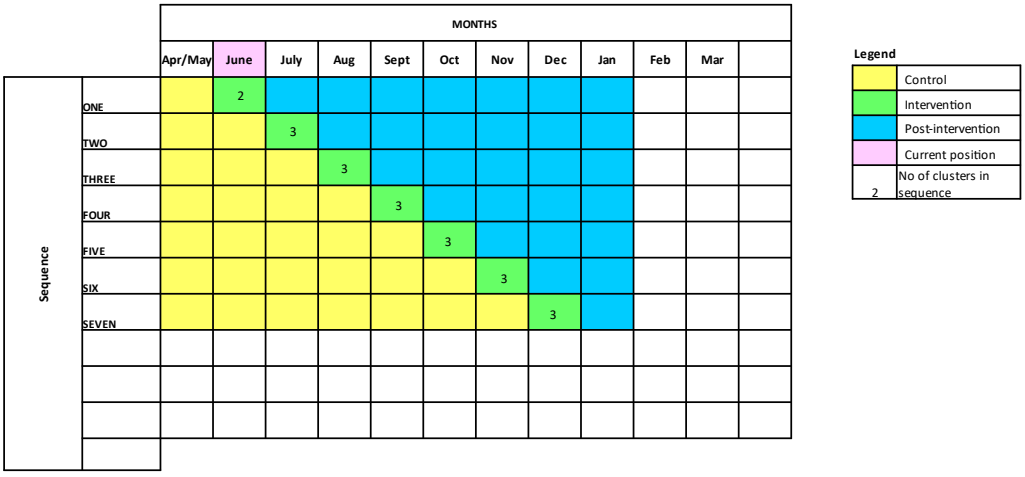


REaCH study proposal to complete both trials by 31.03.22

We proposed to continue the Nigeria trial as per protocol.

We propose to revert the Tanzania trial to the earlier discussion we had when first threatened with loss of funding. This proposal was to reduce the trial length by reducing the sequences and increasing the number of clusters trained in each sequence. We propose six sequences of three or four clusters per sequence.

Tanzania New timeline



Impact on the power of the trial

The trial has a mixture of superiority and non-inferiority inferential goals. As such we originally considered the "minimum detectable effect size" the trial would provide with a power of 80%, type I error rate of 5%, intraclass correlation coefficient (ICC) of 0.05, and cluster autocorrelation coefficient of 0.8. The table below presents the revised power calculation for the Tanzania trial.

				Original design		**Proposed re-design**	
Outcome	**Baseline assumed**	**Denominator population**	**Treatment effect**	**Lower minimum detectable effect**	**Upper minimum detectable effect**	**Lower minimum detectable effect**	**Upper minimum detectable effect**
Face to face consultation /prescription rate	0.25 consults/ prescriptions per person-month	All active patients (n=100)	Incidence rate ratio	0.84	1.20	0.81	1.23
Remote consultation rate	0.02 consults per person-month	All active patients (n=100)	Incidence rate ratio	0.73	1.38	0.69	1.45
Patient trust	3.5 (sd=0.5)	Sampled patients (n=20)	Absolute effect	-0.07	0.07	-0.08	0.08