Enhanced patient counselling and enhanced SMS reminder messages to improve access to community-based eye care services in Meru, Kenya: An embedded, pragmatic, automated, individual-level, two arm, superiority RCT within an adaptive platform trial

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Abstract

Background

The Vision Impact Project (VIP) is a major community-based eye screening programme running in Kenya with the aim of promoting eye health for all. Previous studies embedded within the programme in Meru County have found that a third of people who are screened require care for an eye problem, however only half of these people manage to access outreach treatment clinics. Access varies between sociodemographic groups, and only 32% of young adults (18-44 years old) were able to access care. In previous mixed-methods work our team conducted interviews and surveys with non-attenders from this 'left-behind' group to explore what could be done to improve access.

Methods

Younger adults told us that better counselling at the point of referral would be very likely to improve attendance rates. Based on their feedback, we have developed a script that will be read to participants in the intervention arm at the point of referral, and then sent as a reminder SMS the following day. We will assess whether attendance rates are higher among those randomised to receive this enhanced counselling compared to those who receive standard care.

The primary outcome will be the proportion of people from the left-behind group who attend triage clinic. Our secondary analysis will examine overall mean attendance across all groups. We will calculate Bayesian posterior probabilities of attendance in each arm every 7 days and continually recruit participants until one of the following stopping rules have been met: there is a >95% probability that one arm is best; there is a >95% probability that the difference between the best arm and the arms remaining in the trial is <1%.

Discussion

This Bayesian RCT will be embedded into the clinical workflow software that is used to manage referrals and clinic attendance. It will test whether a simple, low-cost, service user-derived intervention is able to improve access to services among a population group that is currently being left behind.

Keywords

Eye care, health services research, Bayesian trial, embedded trial, equity

Reporting guidelines

This protocol has been prepared in line with the SPIRIT checklist[1] and incorporates relevant elements from the CONSORT[2] extensions for equity-oriented[3] and pragmatic[4] trials.

Trial registration

This trial will be registered with International Standard Registered Clinical/soCial sTudy Number (ISRCTN) once ethical approval has been granted.

Funding

This work was supported by the National Institute for Health Research (NIHR) (using the UK's Official Development Assistance (ODA) Funding) and Wellcome [215633/Z/19/Z] under the NIHR-Wellcome Partnership for Global Health Research. The views expressed are those of the authors and not necessarily those of Wellcome, the NIHR or the Department of Health and Social Care.

Trial sponsor

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The study sponsor and funders will not have any role in- or ultimate authority over the study design; collection, management, analysis, and interpretation of data; writing of the report; or the decision to submit the report for publication.

Introduction

Background and rationale

Many health programmes experience large mismatches between those identified with a clinical need and those who access services. A recent international systematic review of 'no-show' appointments across all medical specialities in primary and secondary care estimated that 23% of clinic appointments are not attended, with the highest rate observed on the African continent (43%).[5] Complex supply and demand factors govern access to health services,[6] and systematically marginalised populations are often the least likely to receive care.[7,8] Improving access to care lies at the heart of Universal Health Coverage (UHC) and is a core element in the Sustainable Development Agenda.[9]

Eye services offer an instructive case study. Approximately 1.1 billion people (over 10% of the global population) live with vision impairment that could be easily corrected.[10] Two very cost-effective interventions - spectacles and cataract surgery – could eliminate over 90% of all vision impairment worldwide. Although provision of these services has risen in recent decades, effective coverage rates exhibit marked socioeconomic gradients at the international and intra-national levels, for example, the global effective refractive coverage is reported at 36%, with high-income countries reporting 90% and low-income only 6%.[10]

In major eye screening programmes, once people have been identified with an eye need and referred on, only around 30-50% of these people access care, and research from Nigeria and Sri Lanka suggests that unmarried (primarily widowed) women and people living in rural areas are the least likely to access care.[11]

Our research collaborative (LSHTM, Peek Vision, COESCA, Kenyan MoH, University of Botswana, NNJS, Dr Shroff's Charity Eye Hospital) is working with four major eye screening programmes to identify the population groups least able to access care in each setting (Table 2).

Table 2. Eye screening programmes

Country	Programme description	Dates	Population
Botswana	The 'Pono Yame' national school-based programme. Screeners travel to every school in the country and refer positive cases to local triage and treatment camps	2022-2024	One national programme: 500,000 children aged 5-18y
India	House-to-house community-based screening in three sites in central Uttar Pradesh.	2023-2025	Three sites: each with 50,000 to 70,000 adults and children.
Kenya	Community-based screening programmes in Meru and Kwale with	2022-2025	Two sites with: each with approximately 1

	school-based and primary care facility-based screening.		million adults and children
Nepal	Regional primary care-based passive screening programme in Rajbiraj, Eastern Nepal.	2022-2023	One regional site with approximately 70,000 adults and children

This current trial focuses on the Meru screening programme in Kenya, but is nested within the broader 'IM-SEEN' continuous quality improvement collaboration,[12] comprised of LSHTM, Peek Vision, COESCA, Kenyan MoH, University of Botswana, NNJS and Dr Shroff's Charity Eye Hospital using Wellcome Trust and NIHR funds, and working with national eye care administrators in each setting.

This particular protocol outlines an intervention to be implemented in Kenya's Vision Impact Project in Meru County. Previous studies conducted by our team found that only 50% of people found to have an eye care need during screening were able to access local treatment outreach clinics, once referred. An equity analysis found that age was associated with access: only 30% of younger adults (aged 18-44 years) accessed care once referred.

In interviews with younger adults who were not able to access care we identified a number of barriers and potential solutions to improve access to care for this group. We then conducted a survey with 401 additional young adults who were not able to access care and asked them to rank the potential solutions/service modifications by likely impact. One of the top-rated ideas was to provide additional information about treatment outreach clinics at the point of referral and in follow-on SMS reminder messages. Specifically, younger adults who were not able to access care told us that enhanced counselling should include information on;

- The outreach treatment clinic opening times,
- the services that are available at these clinics (vs those that require onward referral to hospital-based services),
- any costs involved at the outreach clinic,
- and the importance of attending

This trial is intended to test whether provision of this additional information is associated in a higher probability of accessing care. The trial is being conducted under an overarching adaptive platform trial protocol that is being used to test multiple low-risk service modifications to improve access to care, with a focus on 'left-behind' groups.

The wider literature suggests that SMS reminders can play a small but important role in improving access to care.[13–15] There is much less research on verbal counselling and the provision of information at the point of referral. A systematic review published in JAMA in 1992 found that 'orienting patients' was associated with lower rates of non-attendance.[16] Qualitative research with hypertensive patients in western Kenya found that inadequate counselling was a major barrier to attending clinic appointments. Specifically, lack of understanding on the importance of referrals, and misconceptions

about the clinics emerged as key themes.[17] The same research team went on to develop a multi-component referral adherence intervention that included enhanced information provision a core element.[18] A similar ongoing study in rural Malawi is using enhanced counselling and SMS reminder messages to improve referral uptake for hearing services.[19]

Aims

In this study we aim to test whether provision of additional information around clinic opening times, services, costs, and the important of attending via in-person counselling at the point of referral and via reminder SMS messages increases the probability of accessing treatment outreach clinics compared to standard care. Our focus is on people aged 18-44 as this group has been found to experience the worst access to care in previous work.

Trial design

This is a Bayesian, pragmatic, superiority, two-arm, individual-level, randomised controlled trial, embedded within Kenya's Vision Impact Project screening programme. We will use routinely collected referral and attendance outcome data derived from the patient management and flow software.

Study setting

This trial will be embedded within the Vision Impact Project (VIP) that is operating in Meru, Kenya. The programme has screened over one million people in the past year using a simple smartphone-based visual acuity screening app. Hundreds of thousands of people have been identified with an eye need and referred for free further assessment at local treatment outreach clinics. However, only half of those referred have been able to access this free care.

Our trial will be integrated into the screening and patient management software developed by Peek Vision. Peek Vision is a leading provider of eye screening software worldwide. The 'Peek Capture' app is used to screen participants for vision impairment, to capture observations by screeners and health practitioners, and to gather demographic data, as well as linking participants to a referral system that tracks each of their progression through the local eye health system. The same app is used to collect data on visual acuity, socioeconomic status, referral status, and attendance status (our primary outcome). Previous work has shown that only 46% of people are able to access treatment outreach clinics in Meru, and people aged 18-44 are the least likely to be able to access care.

Eligibility criteria

As a pragmatic trial, the eligibility criteria are determined by the local VIP programme. We will include all adults (>18 years) who participate. We will exclude those who do not meet local clinical service eligibility criteria.

Interventions and administration

The intervention is a script and reminder SMS message that have been developed in line with suggestions from people aged 18-44 who were found to have an eye need during screening; referred

to their local treatment outreach clinic; but were not able to access care. During interviews with 49 people from this group, 27 different potential service modifications were suggested. We then asked 401 additional people from this group to ascribe a simple score to each suggestion, ranging from 'likely to make a large difference' to 'likely to make a small/no difference' on a three-point Likert scale. The top-ranked suggestions were discussed at a workshop with representation from the VIP programme, the programme funder, the programme implementing partner, the county health management team, and the community advisory board. This group unanimously agreed that it would be feasible to implement and test a counselling intervention that bundled together four suggestions: providing additional information about the treatment outreach clinic opening times, the services that are available at these clinics (vs those that require onward referral to hospital-based services), the importance of attending, and stating that the assessment is free. A draft script that included these elements was reviewed and revised by all of the above stakeholders and two lay representatives from the left behind group. The text was translated into Swahili and back-translated into English to check that meaning had not been lost.

Control arm: usual care referral counselling

*"I have examined your eyes, and you have a problem, I have referred you in the system and you will receive an SMS with where and when you are supposed to attend treatment. You will come for treatment on **Date** at ** xx hospital**, the examination will be free and you will be informed of anything else on the material day.*

Intervention arm: enhanced referral counselling script

"I have found a problem with your eyes. I am referring you to the outreach treatment clinic that will be held at [location] on [date] between [time] and [time]. At the clinic, eye care professionals will perform a specialist assessment and provide any eye drops or medicines that you might need. If you need glasses, the specialists will tell you what kind you need, and what your prescription is. The assessment is completely free. Note that a small proportion of people will be found to have complex eye problems that require onward referral for hospital assessment and special lenses that cost more than standard glasses. However, the vast majority of people have their needs fully met at the outreach triage clinic and do not need hospital referral.

With treatment, you will be able to see more clearly. This will help with your work, seeing faces, and using your phone. It is important that you attend the clinic to protect your vision. The clinic will only be running from [day] to [day], so if you don't manage to attend, you may not be able to get free care again in the future."

The relevant script will be read out to the participant by the screener at the point of referral. The wording of the usual care counselling script is based on the screening programme training materials and observations of what screeners currently tell participants. No elements have been removed i.e. this script accurately reflects usual care. Screeners do not usually read this information out to participants; however, we are introducing standardised wording to reduce the risk of contamination

i.e. screeners delivering the same enhanced counselling elements to participants in both the intervention and control arms.

All people who are referred are sent automated SMS reminder messages on the day of referral and the day before the appointment, and on the appointment day. These messages are generated and sent by the Peek Vision app. The content of the intervention SMS was developed by the research team in collaboration with lay representatives from the left-behind group. The messages are sent in either English or Kiswahili, depending on the participant's chosen language.

Control SMS Script

Dear <<name>>, you were examined and found to have an eye problem. Kindly report on <<location>> on <<date>> for assessment. For more information contact Meru Referral Hospital.

Intervention SMS script

We found that you had an eye problem. Please attend the outreach clinic at <<location>> on <<date>> between 9am-5pm. The specialist assessment is free
If you are found to have a complex problem, you may be referred to a hospital for further care or specialist glasses, and this may include a fee
However, the vast majority of people who attend the outreach get their eye problem fixed without the need for any further referral
It's important that you attend to protect your vision, and you might not have a future opportunity to access free care. See you on <<date>>

Figure 1 shows the point at which the interventions are delivered.

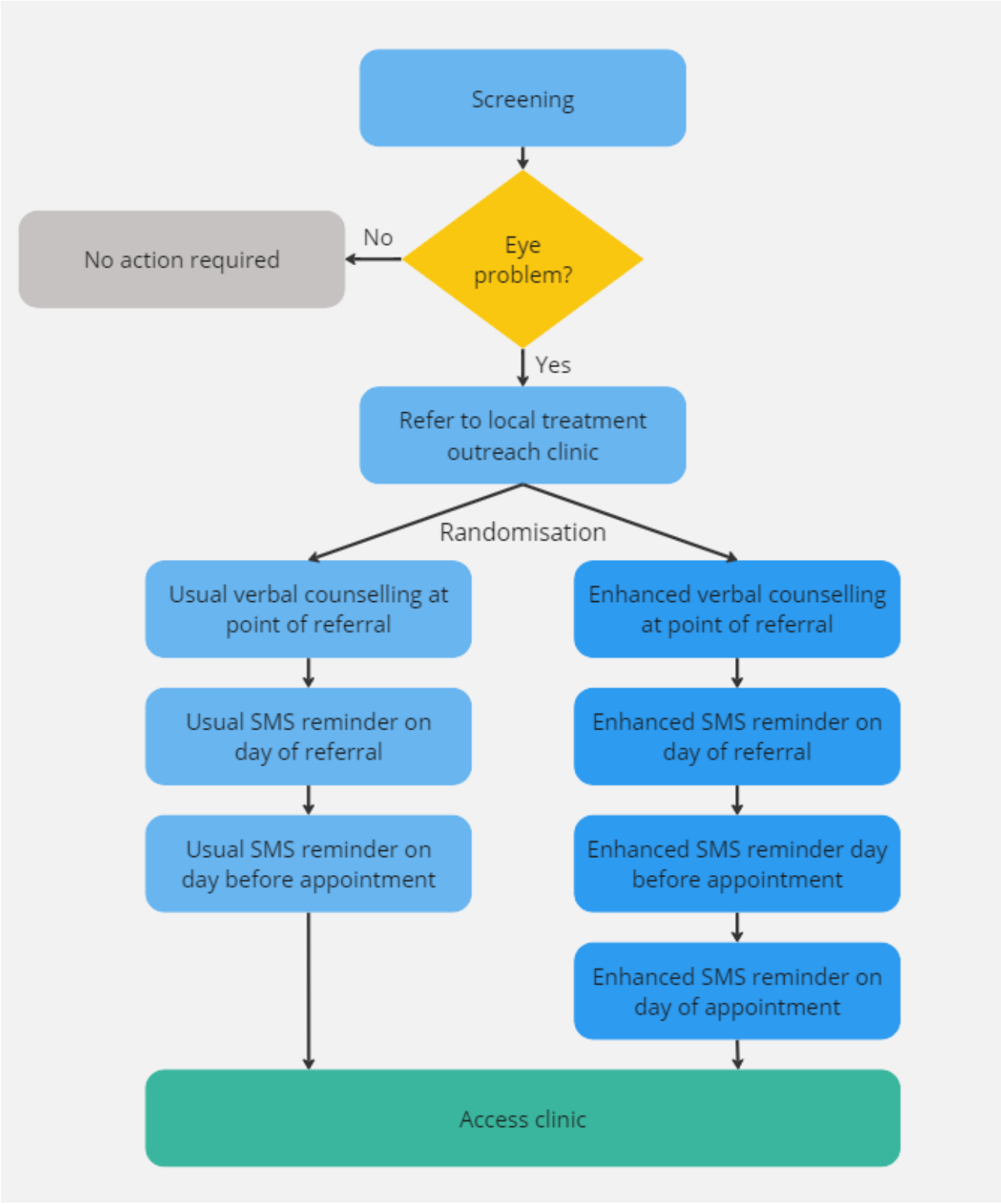

Figure 1: Delivery of interventions

Theory of change

Ultimately, we want people with eye problems to receive the care that they need. We are assuming that those who are able to access clinics receive appropriate, timely, and high-quality care. We are

assuming that improved vision as a result of this treatment leads to improved function and social and economic participation. We are assuming that this overall impact will be driven by improving access to treatment clinics. An important factor that drives this outcome is the decision made by referred participants to attend.

In previous qualitative work, people who were not able to access care told us that the provision of adequate information was important in shaping their initial decision around seeking care. In this study, screeners will verbally provide this additional information at the point of referral. This information will also be provided in three follow-up SMS messages. Figure 2 illustrates the causal chain, using an adaptation of the *Behaviour Centred Design* framework.[20]

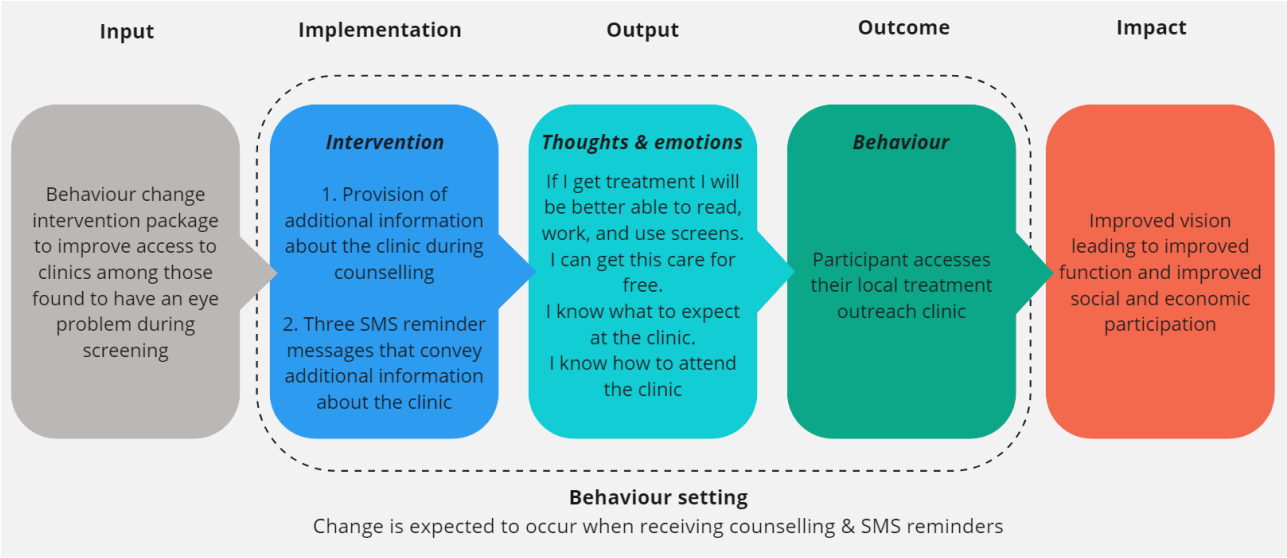

Figure 2: Causal pathway in our theory of change

We fully acknowledge that a wide range of other factors influence access to care, especially those relating to the supply-side. Furthermore, we recognise that the intervention we are testing resonate with the classical 'information deficit model'. In its pure form, this model has received justifiable criticism for oversimplifying behaviour change - often in the context of paternalistic and culturally insensitive information provision.[21] In contract, our intervention is grounded in the lived experiences of those who have been unable to access care for want of basic information, and the wording has been developed with representatives from the target population. By offering information at four points in time, including on the day of the appointment, we hope to overcome the so-called 'setting transfer problem' that occurs when a participant has to remember their intention to do something in a future time and space.[20,22]

Discontinuing or modifying interventions

Arms will be discontinued (or modified to remove the risk) if there is evidence that they are harming exposed individuals.

Adherence

There are no *a priori* strategies to improve adherence.

Concomitant interventions

As our trials will be embedded within routine service delivery, we cannot exclude the possibility that other initiatives will be introduced by local teams before, during, or after individual trials. We will report all programmatic changes that take place during individual trials that could bias our findings.

Outcomes

This RCT is part of a platform trial which focuses on testing interventions that improve equitable access to eye services among those identified with a need during screening. We will use attendance as a proxy for access. Our analysis focuses on the population groups found to have the lowest attendance at baseline.

Primary outcome: The proportion of people attending triage clinic on their appointed date from the left-behind group (adults aged 18-44 years old), measured using attendance data collected by staff when people check-in.

The left-behind group has been identified at baseline as part of the 'identify' stage of the IM-SEEN process. A focus on left-behind groups is important to programme managers who are trying to close gaps, extend health service coverage, and ensure that their services do not exacerbate existing inequalities.

When referred participants check-in at ophthalmic clinics, attendance status is recorded by administrative staff using the Peek app, which automatically updates a central database that holds records of each participant's eye care need, sociodemographic characteristics, arm allocation, and attendance status at the ophthalmic clinic on the appointed date. Our Bayesian algorithm will review the attendance data for every referred participant every 72 hours and calculate the probability of attendance within each arm. In our modelling we have estimated that 100 people will be referred every 72 hours.

Secondary outcome: The proportion of people attending triage clinic on their appointed date across the entire population, measured using attendance data collected by staff when people check-in.

If an intervention is found to increase attendance among the left-behind group, we also want to check whether there has been an impact on the overall mean attendance rate. This is to hedge against adopting an intervention that improves access for the left-behind group but leads to a large overall fall in attendance across the entire programme. We will use absolute percentage differences in attendance for comparisons between the left-behind and general populations exposed to the intervention.

Participant timeline

This trial is embedded within routine screening programmes. From the individual participant perspective, they will flow through the screening programmes as normal; participants will present

and have their eyes checked by a first-line screener in their own home or community meeting place, depending on the setting. The screener will ask a series of sociodemographic questions and perform a 'tumbling E' visual acuity assessment, all using the Peek smartphone app. Those who screen positive will be referred to a local triage centre where their eyes will be re-checked by a more highly skilled practitioner and treatment will be delivered. Those requiring more advanced care will be referred on to the appropriate service provider.

Sample size

As we are using stopping rules, will not pre-specify a minimum sample size or estimate effect sizes for the intervention arms. Instead, participants will be continually recruited until sufficient data accrue to trigger one or more of the other stopping rules. Triallists have argued that this approach is more "efficient, informative and ethical" than traditional fixed-design trials as this approach optimises the use of resources and can minimise the number of participants allocated to ineffective or less effective arms.[23] Every 72 hours the algorithm will review the attendance data and calculate the probability of attendance within each arm.

Operating characteristics for individual trials of interventions administered to individual participants

In line with our master APT protocol and extensive scenario modelling, we will use the following stopping rules for this trial:

1. There is a >95% probability that one arm is best, i.e. the difference between the two arms is >0%.
2. There is a >95% probability that the difference between the best arm and the arms remaining in the trial is <1%.

We will check if any of the stopping rules have been met every 7 days, starting from the date of the first referred person's clinic appointment. People are usually given an appointment one week after their screening date, and approximately 80-100 people are referred each working day (Monday – Friday). As such, approximately 400-500 people are referred each week. In our previous cross-sectional analysis we found that one third of all referred people are aged 18-44 years old, so we expect approximately 100-150 people from our target population to be referred each week. We will perform an interim analysis after 35 days of starting the trial, i.e. after we expect to have outcome data from >500 people from our target population.

We conducted simulations to estimate the impact of the early stopping rules on error rates and sample sizes. For both rules, 95% threshold values were used as default. We assumed a fixed 1:1 ratio for two-arm trials where the control arm had 50% outcome rate and the intervention arm has an effect difference of d, ranging from 0% to 5%. A total of 1,000 simulations were conducted for each value of d, and we assumed that interim analysis would take place for every 100 outcomes observed.

Table 3. Expected error rates and sample size, by true effect difference between arms (d)

True effect difference between arms (d)	Type I error (α)	Type II error (β)	Median sample size [IQR]
0%	32.1%		19,950 [3075,43525]
1%		8.4%	8,150 [2500,22650]
2%		3.1%	3,800 [1500,8100]
3%		1.8%	2,100 [1000,4100]
4%		0.4%	1,600 [900,2700]
5%		0.6%	1,200 [700,2000]
10%		0%	500 [400,800]
15%		0%	300 [300,400]
20%		0%	200 [200,300]
25%		0%	200 [200,200]

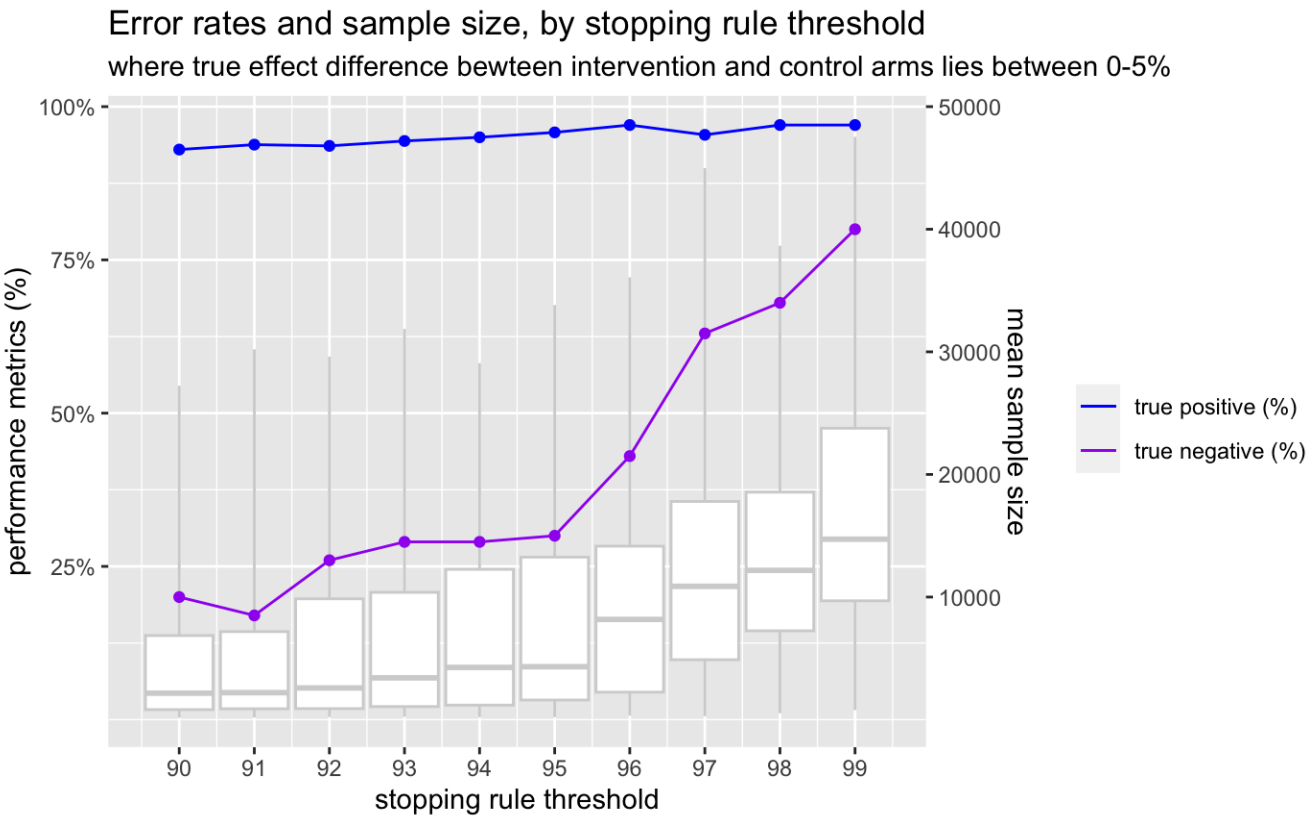

Figure 4. Expected error rates and sample size, by changing stopping rule threshold

In this trial, we prioritize high statistical power (1- β). Minimizing β will protect against the risk of incorrectly identifying an inferior arm as a winning arm. Simulation results show that the expected power in our trial will be at least 98% when an intervention arm is more effective than the control arm by a difference of 3% or greater. When the winning arm is only marginally more effective by a

difference of 1%, our trial will still ensure a statistical power of 92%, which is greater than the power of 80% used in most conventional trials. It is noted that the high statistical power in our trial comes at the cost of increased chance of committing type I error. Furthermore, it will take longer to run the trial to find smaller differences. When there is no difference between arms, we expect 32% chance of making false positive conclusions (Table 3). But we will treat the risk of committing type I error as not a major concern because we expect no or minimal harm in selecting either of the two arms with equal effectiveness.

Recruitment

As the trial is pragmatic, the responsibility for recruiting screening participants lies exclusively with local programme managers. Programme implementers will enrol participants by seeking consent from all those who require referral for further assessment and care.

Allocation

Sequence generation

We will use computer-generated random numbers to generate the allocation sequence and assign all consented, referred participants to intervention arms, with equal numbers of participants in each arm. We will use random size blocks of sizes varying between 4 and 12.

Allocation concealment mechanism

For interventions delivered to individuals, the allocation sequence will be generated within the Peek system in real-time, as participants are referred. As human trial managers are not involved in allocation there is no need for concealment.

Implementation

When the random allocation algorithm within the Peek app assigns a patient to the intervention arm, the Peek app will display a notice to the screener that reads 'Please read script A or B in the patient's preferred language. The screener will then read the corresponding counselling script from a piece of card (A will be the usual care script, B will be the intervention script). The app will also autogenerate and send the enhanced reminder SMS on the same day, the day before the appointment, and on the appointment day to all those assigned to the intervention arm. The control arm will receive the usual SMS reminder on the same day, the day before the appointment, and on the appointment day.

Masking

Who and how

Once assigned by the algorithm, each participant's online record will automatically update to display which arm they have been allocated to. Participants will not be masked to assignment. Screeners will see allocation status as they are required to deliver the intervention. Outcome assessment will be performed by a different group - those responsible for checking-in participants at triage clinic. No steps will be taken to mask these staff to participant allocation status. Ongoing interim data analysis will be performed by the Bayesian algorithm every 72 hours.

Unmasking

Human investigators and programme managers will not be able to access data on allocation of participants to specific arms unless they are involved in delivering an intervention.

The Data Safety and Monitoring Committee (DSMB) will have access to all data at any point and for any reason, including to unmask assignment if required. The trial steering committee members will only be able to access these data as per the adverse event protocol outlined below.

Data Collection

Data collection methods

As stated above, outcome assessment (attendance at clinic) will be recorded when participants check-in at clinic on their appointed date. Each participant's attendance status will be recorded on their central record.

Retention

There are no plans to promote participant retention and complete follow-up.

Data management

All data entry will be performed by programme staff as part of routine screening and clinical care. See the data management plan for further information about coding, security, and storage.

Statistical methods

All analysis will be conducted using R. Baseline characteristics of all participants will be described as mean (SD) or median (IQR) for categorical variables, or as frequencies and proportions for continuous variables.

During this adaptive trial, clinic attendance in each arm will be assessed using Bayesian methods. At each prespecified interim analysis point, a binomial distribution of outcome will be described for each arm using the total number of participants allocated to the arm and the number that attended at clinic. The binomial distribution will be combined with a prior distribution to update the posterior distribution of each arm. A regularizing prior of beta(100,100) will be applied to reduce overfitting until a reliable amount of data is accrued. A Monte-Carlo simulation will be used to update posterior distributions at each interim analysis point. Posterior probabilities will be calculated and compared to the stopping rules as to whether the trial should continue into the next day or end early. If there is sufficient evidence to meet one of the stopping rules, the trial will terminate and proceed to the final analysis stage.

Upon completion of the trial, a complete case analysis will be performed on all eligible participants in the trial on an intention-to-treat basis. The primary endpoint of the trial is clinic attendance the left-behind subgroups after randomization. Within a selected subgroup, the primary analysis will use beta-binomial models to estimate the posterior distribution of attendance in each arm. Posterior probabilities will be calculated to compare the proportion of attendance between arms and to identify an arm that results in the highest likelihood of attendance. For the secondary endpoint, beta-binomial models will also be used but expanded to all participants in the trial. A more detailed

description of the statistical methods will be reported as open access as a separate statistical analysis plan.

Equity analyses

The primary aim of the platform trial is improving equity. We focus on attendance rates in the left-behind group, and also look at how attendance rates in this group compare to those among the entire population.

Non-adherence and missing data

Missing data is not a problem because the outcome is attendance. Non-adherence will depend on the intervention. We will use intention-to-treat analysis.

Data Monitoring

From UK, Dr Luke Allen, Dr David Macleod (data analyst), Min Kim and Dr Nigel Bolster (PEEK engineer) will have access to all data. In Kenya, Sarah Karanja and Dr Michael Gichangi (Co-Principal investigators) will also have access to these data. Data analysis will be conducted by David and Min Kim and shared with all investigators.

An independent Data and Safety Monitoring Board (DSMB) has been appointed with the primary aim of assuring safety of participants in the trial(s). The DSMBs will advise the steering committee and sponsor on continuation or stopping of the trial(s) based on safety and efficacy considerations. The DSMB has three members, all independent of the running of the trial, and all with relevant clinical and epidemiological experience. The DSMB will operate independently of the study sponsor and the steering committee. The DSMB will confirm its own specific meeting arrangements and draw up their own charter, working from the template produced by the Damocles Study Group.[24] It is proposed that the DSMB will meet prior to the beginning of the trial, one third of the way through, and at the end of the trial, to assess the safety of the trial procedures. The DSMB will agree the way it will monitor the data, what it requires from the investigators in this respect and will communicate this to the PIs. All data can be interrogated remotely in real-time. The DSMB may visit the study coordination centre to assess data management, record keeping and other important activities. The DSMB will determine the manner in which it will monitor the data, what it requires from the investigators in this respect and will communicate this to the PIs.

The board comprises a clinical trial specialist who does research in Diabetic Retinopathy, Ophthalmology, Public Health and Health Systems (Dr. Nyawira Mwangi), an ophthalmologist (Dr. Stephen Gichuchi), and a biostatistician (Mr. Moses Mwangi). DSMB will periodically review safety and efficacy data.

Consent

Informed consent will be sought by screeners during screening - at the point that participants are identified as having an eye care need and referred on for further care. At the time of consenting, participants will be given information about the research project, including the objectives and

measures taken to respect the confidentiality of the data collected. Consent will be recorded digitally using an electronic tick box (as appropriate for low-risk trials). The consenting process and the provision of participant information will be delivered through EpiCollect, a mobile phone data gathering tool with an associated web application, providing two-way communication between multiple data gatherers and a project database. This platform will be used solely for the digital consenting process and will be used alongside the Peek Capture App that is used during screening. Participants will be able to take a written copy of the participant information leaflet and consent document. They will be given the contact details of the research managers and will be free to leave the trial at any time. There will be no remuneration for participants.

Patient and public involvement

Lay people and a community advisory board has reviewed and contributed to the development of this protocol and all preceding work around identifying the left-behind group and identifying potential service improvements. Representatives from the left-behind group contributed to the development of the enhanced counselling wording. Lay representatives will assist with interpretation and dissemination of the trial findings.

Adverse event reporting and harms

An adverse event (AE) is defined as any untoward medical occurrence in a patient or study participant. A serious adverse event (SAE) is defined as any untoward medical occurrence that:

- Results in death
- Is life-threatening
- Requires inpatient hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity
- Consists of a congenital anomaly or birth defect

Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences.

All adverse events will be reported. Depending on the nature of the event the reporting procedures below will be followed. Any questions concerning adverse event reporting will be directed to the study coordination centre in the first instance. The flow chart below has been provided to aid the reporting of adverse events.

Non-serious AEs

All non-serious AEs will be reported to the study coordination centre and recorded in a dedicated AE log within 72 hours. The entry must state the patient ID, date and time of AE, nature, and relation to the intervention, if any. The AE should also be reported to the data and safety monitoring committee within 72 hours. AE logs will be stored on a secure, password-protected file on a LSHTM computer.

Serious AEs

Serious Adverse Events (SAEs) will be reported to the PI and study coordination centre within 24 hours of the local site being made aware of the event (Figure 5). The PI will report the event to the data safety monitoring committee within 48 hours and include it in the study safety report.

An SAE form will be completed and submitted to the PA and study coordination centre with details of the nature of event, date of onset, severity, corrective therapies given, outcome and causality. All SAEs whether expected, suspected or unexpected will be reported to regulatory bodies and the trial DSMB within 48 hours of occurrence. The responsible investigator will assign the causality of the event. All investigators will be informed of all SAEs occurring throughout the study. If awaiting further details, a follow up SAE report should be submitted promptly upon receipt of any outstanding information.

Any events relating to a pre-existing condition or any planned hospitalisations for elective treatment of a pre-existing condition will not need to be reported as SAEs.

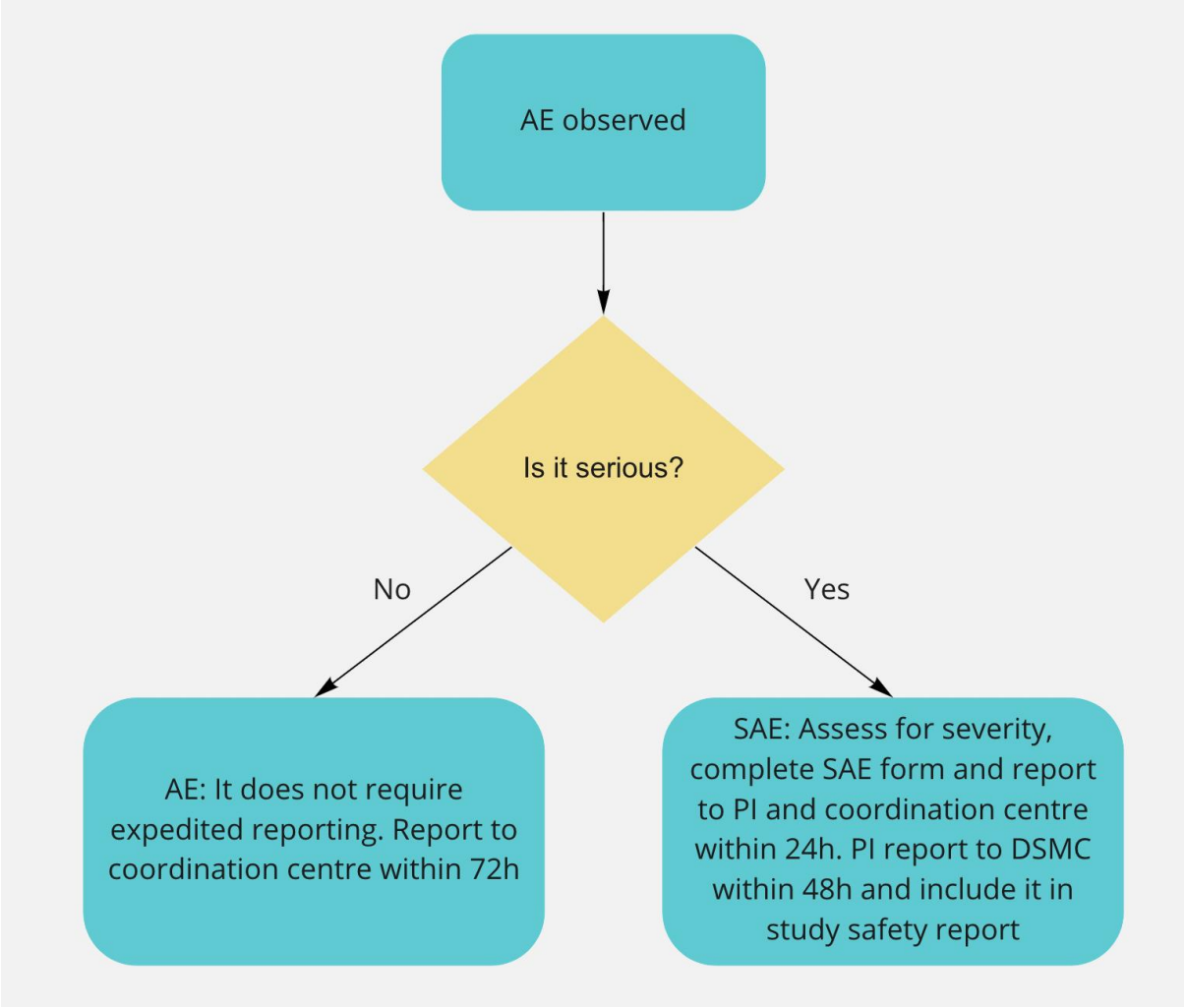

Figure 5: Approach for managing adverse events

Contact details for reporting SAEs

SAE forms will be sent to: gichangi58@yahoo.com and luke.allen@lshtm.ac.uk and the relevant in-country co-PI using the title 'Urgent - SAE'
Tel: Dr Gichangi: +254 701 572 109 (Mon to Fri 09.00 - 17.00, Nairobi)
Tel: Dr Allen +44 (0) 20 7958 8316 (Mon to Fri 09.00 – 17.00, London)

Responsible Personnel

Chief Investigator (CI)

- The CI has overall responsibility for the conduct of the study and the ongoing safety and evaluation of any IMPs being used in the trial.
- Promptly notifying all investigators, Institutional Review Board (IRB) or Independent Ethics Committee (IEC) and Competent Authorities (CAs) of each concerned member state of any findings that may affect the health of the trial participants.
- Keeping detailed written reports of all AEs/ARs identified in the protocol as critical to the evaluation of safety within the agreed timeframes specified in the protocol.
- Accurate production and submission of the Development Safety Update Reports and progress reports to CAs and IRB/IECs.
- Collate all AR/AEs/SAEs/SARs and report to the Sponsor annually.
- Ensure that the PIs report all SAEs/SUSARs immediately to the Sponsor and to the CAs, IRB/IECs and any other relevant parties within agreed timelines (
- Supplying the Sponsor and IRB/IEC with any supplementary information they request.

Principal Investigators (PI)

- The PIs have responsibility for the research performed at the local site, handling and management of investigational medical products, and informing the CI, Sponsor, Ethics, regulatory bodies and the trial coordinating team, of all adverse events that occur at their site
- Safety responsibilities:
- Ensure trial participant safety and the swift and adequate management of trial participants with any type of AE/AR as per the management protocol described below.
- Reporting all SAEs/SUSARs immediately to the Sponsor and to the CAs, IRB/IECs and any other relevant parties within agreed timelines (i.e. LSHTM, EFMHACA, ORHB, FMOST).
- Assessing each event for causality, severity and expectedness. (Note: a medical decision which must be made by the investigator directly involved with the care of the patient/participant experiencing the AE)
- Ensure adequate archiving of AE records and reports in the local trial office along with the trial master files.
- Collate all AR/AEs/SAEs/SARs biannually and present to the CI.
- Guide and supervise the field research team on accurate recording, reporting of all adverse events.

Field Research Team Members (Coordinators, Nurses, Examiners, Recorders)

- All field research team members are responsible for identifying, recording, and reporting any AE or AR to the PIs regardless of severity or causality.
- Assessing each event for causality, severity and expectedness. (Note: a medical decision which must be made by the investigator directly involved with the care of the patient/participant experiencing the AE).
- Ensure that the participant has received the necessary management. This includes advice/reassuring, referral, offering transport, paying for management, making follow-up visits
- Report to the PIs/Project manager AEs/ARs based on the specified timeline and file all AE/AR recorded forms in the trial master file.

Frequency and plans for auditing trial conduct

The study may be subject audit by the London School of Hygiene & Tropical Medicine under their remit as sponsor, the Study Coordination Centre and other regulatory bodies to ensure adherence to Good Clinical Practice.

Team composition

	Coordinating centre	Trial Steering Committee	Data management team
1.	Luke Allen	James Carpenter (chair)	Nigel Bolster
2.	Malebogo Tlhajoane	Malebogo Tlhajoane	Malebogo Tlhajoane
3.	Sarah Karanja	David Macleod	David Macleod
4.		Luke Allen	Min Kim
5.		Min Kim	Luke Allen
6.		Michael Gichangi	
7.		Nigel Bolster	
8.		Matthew Burton	
9.		Andrew Bastawrous	

Limitations

It is unlikely that the addition of four items of information will have a large effect size. Nevertheless, the provision of this information was rated as 'highly likely' to improve access to clinics by a large majority of those who were surveyed in Meru. This particular intervention is one of many that will be tested in separate trials under the overarching platform trial. Text message reminders have obvious limitations in the context of services for those with poor vision, and many people in Meru do not have their own phone. Every screening participant provides a contact number, and it may be that they can have the message read out to them. Inability to receive or read an SMS message will affect those in the intervention and control arms equally, so this should not introduce bias. With the in-person counselling there is a risk of contamination if screeners end up providing the enhanced counselling information to all participants, irrespective of their allocation. The local trial management team will

conduct observations to get a sense of whether this is happening. Contamination would lead to an underestimate of the intervention effect size.

We have chosen to use a prioritarian approach that focuses on left-behind population groups. This prevents a situation where we accept an intervention that improves the overall mean but is associated with a decline among left-behind groups. This approach does not hedge against the slope of inequality worsening. Unfortunately, using a proportionate approach where we assess whether gains in each group are proportionate to their initial need would risk attributing success to our intervention rather than the more likely detection of regression toward the mean.

Our estimate of the probability/proportion will be biased. Because we choose to stop on average at a "local peak". So for example we're confident A is better than B, but the estimate of the attendance rate in A will be on average an overestimate.

We use attendance as a proxy for access. Whilst this is the closest hard indicator available, the semantic implication of the term places responsibility on people rather than clinical systems or societal structures. We will counterbalance this in the language that we use to talk about barriers and in the framing of interventions. We also note that we focus on a proximal indicator that does not always correlate well with receipt of high-quality care, or good clinical outcomes. We decided to focus on access for three main reasons; first it aligns with the conceptual narrative of Universal Health Coverage and 'leaving no one behind', second attendance data are already routinely collected and available for every single person who is referred, and third, internal Peek data suggests that the 'fall off' gap between those who are referred but do not attend is much larger than other gaps e.g. the proportion of those who attend but do not receive appropriate care, or the proportion of those who receive appropriate care but do not experience improved health outcomes.

Dissemination

The findings will be shared with the programme managers and written up for peer-reviewed publication. No participant names or identifiable information will be used in any of the write-ups. The study findings will be disseminated during quarterly review meetings with implementing partners, community health extension workers and representatives from the county health management committee, and bi-annual partner meetings. We will also publish our findings in peer-reviewed journals, and present abstracts at national, regional and/or international conferences.

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