Interrupting HIV and TB stigma in the household during TB contact investigation in Uganda: A Randomized Controlled Trial

HIV-TB Stigma Trial Protocol

Table of Contents

Background

An estimated 39 million people worldwide are living with HIV, and an estimated 20% do not know their status because they are unaware that they are at risk, unable to access counseling and testing, or unwilling to accept testing because of stigma and fear. Layered on to the stigma of HIV is the risk of tuberculosis (TB), the leading cause of death among persons living with HIV (PLWH). Approximately 40% of those with TB worldwide are unaware of their TB status. Like HIV-related stigma, TB-related stigma is common and reduces willingness to test and engage in care. Moreover, layered HIV-TB stigma introduces interlinked social and psychological barriers to testing for HIV and TB among the close contacts of TB patients. There is a critical need for targeted interventions to address layered stigma, reduce fear of testing, and increase uptake of testing among individuals at high risk of HIV and/or TB.

Home testing is a promising approach to increase testing and linkage to care for HIV and TB because it can reach individuals outside the health system, eliminate the costs of attending clinics for testing, and offer testing in a familiar environment. Nevertheless, many individuals offered home HIV testing in sub-Saharan Africa decline to test. We have previously shown that social interactions at the time HIV testing is offered during TB home visits strongly influence perceived stigma and test uptake. When potential testers discern that others have declined, they say that they fear that testing will be socially discrediting. In adjusted analyses, individuals were four times as likely to decline testing when the first member of their home declined testing as when that individual accepted.

Nearly a century of research demonstrates that observations of the decision-making behaviors of peers profoundly influence perceptions, judgments, and subsequent behaviors. Moreover, status and social ties among group members modify their influences on one another. The scientific premise of this proposal is that we can apply established principles from behavioral science to facilitate interactions within the household that reduce stigma and promote uptake of HIV testing. We hypothesize that offering and delivering HIV testing with an intervention to reduce household stigma will have strong effects on the proportion of patients completing HIV testing and linking to care.

Project Overview

This project aims to evaluate the effects of a complex intervention on household HIV stigma and uptake of testing among household members undergoing TB contact investigation. We will recruit a prospective cohort of multiple-contact households undergoing routine contact investigation for TB. Community health workers (CHW) will use acceptance-optimized sequencing of invitations and a prosocial invitation script to offer salivary testing for HIV to household members (Figure 1). We will measure HIV and TB stigma using standardized, locally validated instruments before invitation and after completion of post-test counseling. We will measure the proportion consenting to HIV testing, the yield of HIV diagnoses, and the proportion of new PLWH linked to HIV care at 1 month. We will also reassess household HIV and TB stigma at 3 months in a subset of participating households. Participants may also be contacted at a later point for interviews, focus-group discussions or surveys to better understand the implementation, mechanisms, and impact of the intervention.

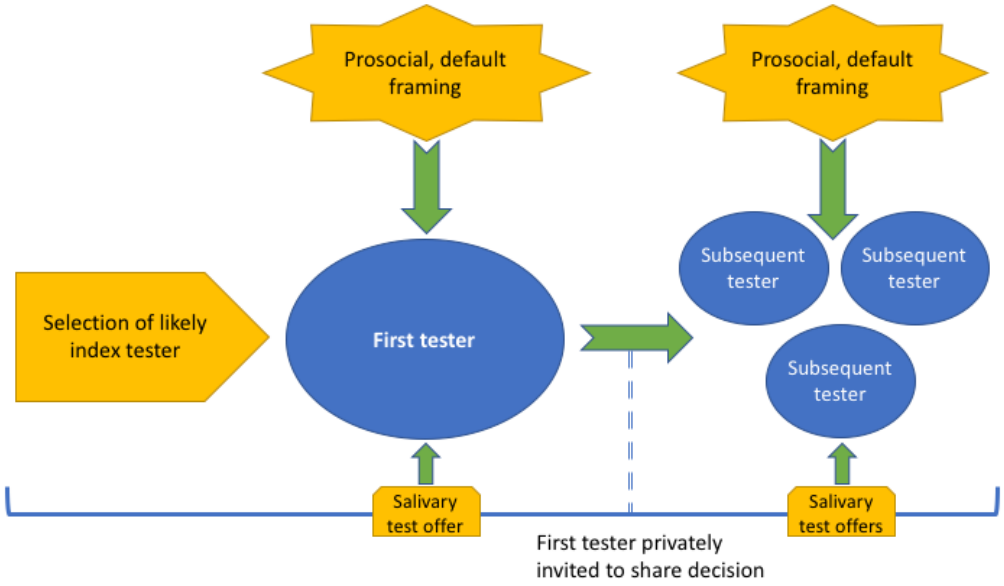


Figure 1: Multidimensional intervention to increase HIV testing acceptability.

Project Timeline

Due to disruption from COVID-19, we plan to begin the trial in October 2021.

Project Personnel

Table 1: Project Personnel

US Principal Investigator	J. Lucian Davis
Ugandan Principal Investigator	Achilles Katamba
Co-Investigator	Mari Armstrong-Hough
US Study Coordinator	Amanda J Meyer
Ugandan Study Coordinator	Joseph Ggita

Methods/Designs

Study Design

We will carry out a prospective, household cluster-randomized, controlled implementation trial evaluating a complex, multi-component, social and behavioral intervention. The intervention is designed to normalize the use of HIV testing in the household and increase detection of HIV.

Target Setting and Population

This study will be conducted in Kampala, Uganda, and will involve TB index patients and their household contacts. Households will be recruited and enrolled through index patients initiating treatment for pulmonary tuberculosis (PTB) at Kampala Capital City Authority health facilities. We will enroll index patients and their households from three public-sector, primary care facilities: Kiswa, Kawaala, and Kisenyi Health Centers.

This study will enroll ***households*** (index patients + their household contacts). Only household contacts are eligible for participation; close contacts are *not* eligible. For the purposes of this study, ***household contacts*** are defined as those individuals "sleeping under the same roof" as the index patient for one or more nights within the past three months. ***Close contacts***, who will not be enrolled in this study, are those who do not live in the household but have spent 12 or more hours in an enclosed space with the index patient in the past three months.

Index Patient and Household Eligibility

Index patient and household eligibility will be determined based on the following criteria:

- Index patient is eligible for contact investigation
    - TB patient of any age identified in the facility's NTLP TB Treatment Register as initiating treatment or returning for 2-week follow-up
- Index patient or legal guardian agrees to study procedures in addition to routine contact investigation
- Index patient has at least 2 self-reported household contacts age 15 or above
- Household is within the boundaries of the Kampala Capital City Authority, Uganda
- Does not have MDR TB

Contact Participant Eligibility

Household contact eligibility will be determined based on the following criteria:

- Household contact age ≥15 years
- Agrees to study procedures in addition to routine contact investigation

Participant Recruitment

Index Patient and Household Recruitment

Upon encountering a patient initiating treatment for TB or returning for 2-week follow-up, study CHWs will assess index patients for household-level eligibility for the study. All index patients whose households meet these criteria will be asked to provide verbal consent after reviewing an information sheet. If the index patient is a minor (age < 18 years), the guardian of the index patient will be asked to provide verbal consent.

After study enrollment, a CHW will work with the index patient and, if available, treatment supporter to schedule the home visit. Households will be randomly assigned to one of the two CHW teams to receive the intervention or standard-of-care strategy.

Contact Participant Recruitment

After the enrollment of the household through the index patient, household contact investigation will take place. All household contacts who meet these criteria will be asked to provide verbal consent after reviewing an information sheet. If the contact is a minor (aged 15-17), he or she will be asked to provide verbal assent with his/her parent/guardian providing consent. ***Enrolling in the study does not require eligibility for or consent to HIV testing***. Those who choose to participate in the study and are eligible for HIV testing will be subsequently offered testing and may consent or decline. Those who choose to participate in the study and report conditions that render them ineligible for HIV testing, such as already known to be a PLWH, testing negative within the last three months, or currently in TB treatment, will not be offered HIV testing but will be eligible to participate in other study procedures.

Subset of participants for reassessment of stigma at 3 months

A two-stage stratified random sample will be selected for reassessment of stigma 3 months after the home visit. First, a random subset of 50 households will be selected. Then, a random contact will be selected from within each household.

Sample Size Estimations

Approximately 152 households containing approximately 304 household contacts will be enrolled, half from each study arm. For purposes of the randomization sequence, we will inflate this number by 15% to 175 households to account for non-completion of household visits (*i.e.* drop-out). We analyzed power for a 2-arm household-randomized, controlled trial using mixed model tests for two proportions in a two-level hierarchical design (household, contact). The assumptions and parameters within these calculations are based on formative research. They include:

1. The test statistic is the effect regression coefficient from a mixed-effects logistic regression model.
2. Alpha = 0.05
3. Power = 90%
4. The proportion consenting to testing in the control group will be 85%.
5. The proportion consenting to testing in the intervention group will be 98% (a difference of +13% vs. the control group).
6. An average of two household contacts will be eligible for HIV testing per household.
7. The intraclass correlation (ICC) will be 0.59.

Sensitivity of the Sample Size Calculations

The total number of households needed is sensitive to the mean cluster (household) size. Under the preceding assumptions, the necessary number of households may range from 152 if the mean number of eligible contacts per households is 2 to 138 if the mean number of contacts per household is 3. The total number of households needed is also sensitive to the ICC. Sample size estimates assuming a range of possible ICC values, ranging from the value observed during the preliminary research (0.59) to higher values (0.65, 0.70), are presented in the **Appendix** (Section 2: Complete Power Analysis Report). Finally, the total number of households needed is sensitive to the baseline (control group) proportion of tests accepted. Sample size estimates assuming three possible baseline testing rates (75%, 80%, and 85%) in control group households are described in detail in the appendix. We will plan an interim power analysis to readjust sample size targets as necessary for actual mean cluster size and ICC after enrolling the first 100 households.

Intervention Strategy

RCT Design

This randomized, controlled trial will evaluate a novel strategy for delivering HIV testing to household members during TB contact investigation in order to reduce stigma and increase uptake of HIV testing. The trial will use a two-arm, household-randomized, controlled design.

Norming: Socio-behavioral Intervention

The intervention to be evaluated in this study is a multidimensional, socio-behavioral "Norming" intervention. The components of this intervention are designed to harness household dynamics and prosocial inclinations to encourage individuals to accept the HIV testing invitation. Each component is briefly described below:

In households assigned to the Intervention only, the following procedures will take place:

Selection of first tester

CHWs will be encouraged to offer HIV testing to the individual nominated by the index patient as most likely to test. If this person is not present, CHWs will decide which household contact should be invited for testing first based on prior research. The order of subsequent testers will be at the discretion of the CHW in all cases.

Prosocial script

CHWs will use a prosocial script encouraging HIV testing. The script is labeled as "prosocial" – meaning "for the group" – because it features language that frames HIV status awareness for each member of the household as beneficial for the entire household and HIV testing as an activity that benefits all and not just the individual. This prosocial script will be as follows: "Knowing your status sets a good example for your household."

Opt-out test framing

CHWs will follow an "opt-out" framing strategy for offering HIV testing, as opposed to standard "opt-in" framing. The opt-out script will be as follows: "This test kit is approved by the Ministry of Health and used in KCCA health facilities. I am going to offer you a free HIV test now, is that okay?" The Luganda translation is as follows: "Enkola ey'okukebera eno yakkirizibwa ekitongole ky'ebyobulamu ekya Ministry of Health era ekozesebwa mu malwaaliro g'ekitongole kya KCCA. Ngenda kukuwa okukeberebwa kuno okwobwereere essaawa eno, tukkiriziganyizza?"

Sharing first tester decision to test

If the initial household contact who is offered HIV testing agrees to test for HIV, the CHW will privately ask if he or she is willing to share his/her decision to test with other members of the household. We will not ask individuals to share HIV test results with members of their household. The CHW will ask if the client is willing to share their decision to test only after they have received the HIV test results. This invitation will be as follows: "Would you like to share your decision to test with the others? Sharing is completely optional. However, learning that someone else in their household decided to test sometimes gives people the strength to test themselves. Sharing your decision might help another person find the strength to test." The Luganda translation is as follows: "Wandyagadde okugabana n'abalala ab'ewaka okusalawokwo okwokwekebeza? Okugabana n'abalala kyakyeyagalire. Wabula, omuntu omulala bwamanya nti waliwo omuntu mu bewaka asazeewo okukkiriza okukeberebwa ebiseera ebimu kiwa abantu amaanyi nabo okukkiriza okukeberebwa. Okugabana okusalawokwo n'abalala kiyinza okuyamba omuntu omulala okufuna amaanyi okukeberebwa."

We will record whether contacts share their testing decisions. CHWs will also collect data on baseline characteristics, including age, gender, relationship to the index patient, HIV status, date of prior HIV testing results, testing preferences, perceptions of social influence within their homes, and perceptions of HIV- and TB-related stigma in their household.

Control Strategy (Standard of Care)

The control arm will lack the socio-behavioral intervention components. The order of testing invitation will be decided by the CHW without access to information about the index patient's nominee. CHWs will be trained at baseline to provide standard, opt-in framing of test offers, without any mention of asking contacts to share their testing decision with other household contacts. Oral HIV kits will also be used in control households. We will explore the standard strategies used in key informant interviews.

Randomization and Allocation Strategy

Variable block randomization will be done at the level of the household and will be performed at the time of household enrollment. Block sizes will have a minimum of 4 households, a maximum of 8 households. We will utilize *Study Randomizer*, an online randomization tool with concealed allocation, to generate the allocation sequence. When a CHW determines that an index patient is eligible for the study, and after the index patient or guardian has provided verbal informed consent, the CHW will place a phone call to the study coordinator. The study coordinator will then enroll the household using the Study Randomizer tool and share the study allocation with the CHW. The CHW will then record the appropriate allocation in the survey software, along with the randomization ID, and contact the appropriate CHW team

for the household visit. The index patient will be given the name of the community health worker who will visit the household, and immediately connected with that person by telephone to arrange the home visit.

Households randomized to intervention group (Intervention A) will be offered the social-behavioral intervention described above. Households randomized to the standard-of-care group (Intervention B) will be offered oral testing without any social-behavioral intervention. CHWs will operate in teams that are always assigned to the same arm of the study. There will be three teams of CHWs in total: one intervention group, one standard-of-care group, and one clinic-based group that will always carry out initial enrollment of index patients and record any clinic follow-up by individuals in either arm of the study.

Blinding

Blinding of the assigned intervention to community health workers is not feasible as they must be trained to deliver either the standard of care or the intervention strategy. Community health workers will also assess the outcome of test acceptance. Participants will not be informed about whether they are assigned to the intervention or the control strategy. Investigators and research staff will be blinded to study outcomes until data cleaning is completed at the end of the trial and the database is locked.

Study Measures and Outcomes

Demographic and Clinical Data

We will record data on baseline characteristics, including age, gender, relationship to the index patient, HIV status, date of prior HIV testing results. We will also secondarily assess the ability of index patients to predict testing preferences and social influence within their homes. Measurements will include (A) anticipated testing preferences of contacts as reported by index patients, and (B) social influence dynamics as reported by the index patients and contacts.

Primary Study Outcomes

Our primary outcome is uptake of HIV testing, defined as the proportion of eligible individuals in the household who undergo testing after a test offer. We will also report the proportion of eligible individuals offered testing, and the proportion of eligible individuals who consent to testing who are actually tested. We will also examine linkage to HIV care, defined as self-reported attendance at an HIV clinic within 1 month among participants receiving a positive test result. Our secondary outcome is the within-visit change in perceived HIV-TB stigma during the first household contact tracing visit (and after three months), using the adapted Van Rie scale.

TB and HIV Stigma Scale

Regardless of intervention or control arm, CHWs will deliver a short, 13-item TB and HIV stigma scale to all household contacts at the beginning (prior to TB evaluation) and end of the household visit (after all TB and HIV procedures). The scale was adapted from the Van Rie TB HIV stigma scale specifically for this context and is found in **Appendix 1c**. The scales will be administered first at the beginning of the home visit, then again after post-test counseling.

Social Influence and Testing Preferences Sub-Study

Outcomes will include congruence of (A) index patient's perceptions about contacts' testing preferences with contacts' actual testing decisions and (B) index patient's perceptions about household influence with contacts' actual influence nominations. See **Appendix 1d** for data collection instrument.

Analysis Plan

We will describe the proportion consenting to HIV testing, the yield of HIV diagnoses, proportion of new PLWH linked to HIV care at 3 months, reliability of index patient nominations for most-likely tester, reliability of index patient

nominations for most influential household member, decisions of subsequent testers, and perceived HIV-TB stigma scores. We will calculate and compare uptake across each of the trial arms using an intention-to-treat analysis as our primary analysis. For secondary analyses, we will perform a per protocol analysis for participants for whom there is a randomization mismatch between data recorded electronic CRF and Study Randomizer records. Finally, we will construct models adjusted for imbalances in baseline confounders as needed.

To test the hypothesis that a norming intervention can increase test uptake, we will compare testing uptake among the intervention households and control households using cluster-adjusted chi-squared tests of proportion and by fitting mixed effects logistic regression models with two levels (household, contact.) To test the hypothesis that acceptance-optimized sequencing of oral HIV test invitations and prosocial messaging can decrease HIV stigma within households, we will evaluate change in HIV-TB stigma using cluster-adjusted dependent t-tests and fitting multilevel models with clustered standard errors. We will use the same tests to evaluate changes in HIV-TB stigma measured 3-months after the household visit for a two-stage stratified random sample of participants.

We will also conduct a causal mediation analysis to determine the degree to which the effects of the intervention on stigma explain the improvement in test uptake using observed-variable structural equation modeling. All hypothesis tests will be carried out at alpha of 0.05, corrected for multiple tests as appropriate. We will report household ICC for stigma as well as test uptake and will consider a household ICC of >0.2 a sufficient level of clustering necessitating adjustment.

We will measure the proportion of testing preference predictions made by the index patient about their contacts that were accurate. We will also measure the proportion of social influence nominations by the index patient that align with nominations by the household contacts. Furthermore, we may use regression analyses to identify index patient or household characteristics associated with accuracy of index patient testing/social influence perceptions.

Covariates to be included in each model (if applicable) are presented in Table 2.

Table 2: Individual- and Household-Level Covariates

Level	Covariate
Index Case	Age Gender Education HIV Status
Contact	Age Gender Education Relationship to Index Patient HIV testing history (month/year of last test) Self-reported Symptoms of TB
Households	Number of Rooms Number of Windows Number of Individuals Income (if applicable)

Study Procedures

The study involves 5 key steps: (1) CHW Training; (2) Index Patient Invitation and Recruitment; (3) Household Procedures; (4) Administration of HIV-TB stigma scale before and after household procedures using CommCare; and (5) CHW documentation of study outcomes including consenting to testing, HIV diagnoses, and whether or linked to care at 1-month using CommCare.

Details on each procedure can be found below.

(1) CHW Training

We will carry out a participatory training with the study CHWs. First, CHWs will meet as a group to discuss study aims, the trial design, and the importance of study controls. Next, CHWs will be assigned to different roles, including clinic-based CHWs, intervention CHWs and Standard of Care CHWs. Each group will separately review and role play their assigned procedures. Clinic-based CHWs will be trained to provide TB education and counseling, index patient enrollment, and randomization procedures. Intervention CHWs will be trained to deliver the social-behavioral intervention described above to offer a salivary test. Standard-of-Care CHWs will be trained to deliver a standard offer of opt-in HIV testing using a salivary test.

(2) Index Patient Recruitment and Randomization

Eligible index patients will be approached and invited to participate. After verbal consent, index patient participants will be digitally randomized to receive a home visit from either a team delivering the standard-of-care strategy or a team delivering the intervention (see *Randomization and Allocation Strategy*.) The enrolling CHW will also collect baseline data from the index patient, including demographic information about the individual and household and sub-study questions regarding perceptions of contacts' testing preferences and influence within the household. Index patients will be asked to nominate the household member they believe if most likely to accept an HIV test and the household member they believe most influences health decisions in their home (**Appendix 1d**).

(3) Household Procedures

After being notified by the clinic-based CHW, the assigned CHW team will accompany the index patient to the household to conduct routine household contact investigation and study procedures.

Data Collection Procedures for Intervention Households Only

Administration of Questions to Index Patient

On arrival, one CHW will take the index patient aside and confirm presence of previously nominated household contacts, listing them by first name using the prompt in CommCare. Presence or absence will be recorded.

Administration of Influence Questions to Contacts

During the contact testing periods, the CHW will ask the sub-study questions regarding social influence dynamics to each contact (**Appendix 1d**).

Procedures for all households

Upon arrival at the household, the CHWs will enroll all eligible, consenting household contacts in the study. They will introduce the reason for their visit and the services they will offer (TBCI, oral HIV testing) using the introductory script for either Intervention or Standard of Care households, depending on the household assignment. Working in teams of two, CHWs will then conduct household contact screening interviews followed by HIV testing and any other routine clinical procedures for household TB contact investigation.

All data will be collected via CommCare. Details of these procedures are found below:

Household contact screening interview

After household contact enrollment, each contact will undergo a short interview. This interview will capture age, gender, occupation (if applicable), income (if applicable), education in years, relationship to index patient, history of testing for HIV, month and year of last HIV test, and self-reported symptoms of TB (including cough, subjective fever, or weight loss). The short (13-item) version of the Van Rie TB- and HIV-related stigma scales will be administered immediately prior to TB screening, as well as at the conclusion of the visit. The first individual interviewed will be asked to share the number of rooms in the dwelling, the number of windows in the dwelling, and the number of individuals (including children) who dwell there.

All screening interview components will be conducted by a CHW. Screening interview components are identical for all study groups.

HIV testing procedures

Working in teams of two, CHWs will provide household contact investigation services, including offering oral HIV testing.

One CHW will lead and accompany each HIV test while a colleague leads other household members through TB screening.

To begin, the CHW responsible for offering HIV testing will individually invite the client to a place apart from the others. S/he will ask the client if they want to be tested for HIV. S/he will detail the process of HIV testing in Luganda and/or English, per client preference. A pictorial guide can be used to help walk the client through each step of the process using a Luganda- or English-language guide. The CHW will then provide pre-test counseling.

Consenting household contacts who choose to test for HIV will swab their own gums. CHWs will be fully trained to provide HIV counselling and support throughout all testing procedures.

Non-consenting household contacts will be thanked and immediately return to the household.

Social-behavioral intervention script

In Intervention Households only, the CHW will invite the participant to test as the default option using the script described previously. This script communicates that the individual is completely free to opt out of testing, but that testing is the norm. We will use “Opt-Out” testing language along with language letting them know that they can decline. This language will be used instead of beginning by asking if the contact wants to be tested for HIV.

If the household contact decides to opt out of HIV testing, the CHW will carry out a survey. These questions will take approximately the same amount of time as HIV testing and counselling procedures (~20 minutes). This is an effort to blind other household members from the testing decision of the household contact.

Contact decisions to test or not to test as well as test results will be recorded in CommCare.

Administering the oral test

The CHW will open the OraQuick test packet in front of the consenting household contact and hand the contact the test swab. The CHW will remain with the client to directly supervise the test. Consenting clients will be directed to use the test swab to gently swipe once around their upper gums and once around their lower gums. Either side of the swab can be used. The swab will then be placed in the testing liquid for no more than 40 minutes. After 20 minutes has passed, the CHW will assist the participant in reading their HIV testing results. Procedures regarding HIV test results are outlined below. While awaiting test results, the CHW will provide basic education to the contact on HIV and/or TB and answer health related questions that the contact may have.

HIV test results

If the test is negative (one line next to the C and there is no line in any form next to the T), the CHW will provide HIV counselling and support. If the HIV test is positive OR unconfirmed (one line next to BOTH the C and T regardless of how faint OR no line shown in window at all), the CHW will provide HIV counselling and support as well as a referral to the health center for confirmatory capillary blood testing.

Referral and Linkage to Care Protocol

Regardless of HIV test type, if the HIV test is positive or unconfirmed, the CHW will refer the client to the health center for evaluation and care using a referral slip. First, the CHW will explain the result in direct, simple language. For a positive result, they will explain: "The test shows you have HIV. You need to go to the ART clinic. I will support you." The CHW will give the patient a referral slip and phone number to call upon reaching the clinic. Finally, the CHW will engage the client in planning to link to care by suggesting a specific day and time to present at the health facility and by guiding the client to plan for the facility visit, using prompts such as "How will you get to the clinic? Can someone go with you?" While the CHW may facilitate disclosure if requested, the CHW will never share individual results with others.

(4) TB and HIV stigma scales

Study CHWs will individually administer the short-form HIV-TB stigma scales to all study participants regardless of group using the CommCare application. These scales have a total of 13 items.

(5) Documentation and Data management

All enrollment procedures, household contact interviews and HIV testing details will be collected using CommCare. All forms will be available within a customized CommCare application that prevents common errors (such as not filling out a question.). Quality control procedures will include review of all study data collection forms for completeness and accuracy, including quality assurance testing of all validation and skip logic within the application, prior to study initiation. The US study coordinator will initiate reports on missing data and provide feedback to all study team members on the quality of quantitative data. Any errors that are found within the application will be changed within the CommCare application by editing the case data NOT form data. All changes will be recorded using a data management cloud-based tracking sheet that contains information on the change, who made the change and a link directly to the location of the change on CommCare. Any duplicate cases (i.e. two cases for one index patient or contact) will be archived and similarly recorded.

Ethical Considerations

Potential Risks to Participants

There are minimal risks to participants in this study. The primary risks to both index TB patients and their household contacts are the psychological and social risks of disclosure of private information such as place of residence, or of disclosure of an individual's TB diagnosis and/or HIV status. As is done in routine practice, community health workers will make every effort to preserve the privacy and confidentiality of individual participants during household contact investigation. While individuals who have decided to test may be invited to voluntarily share their decision to test with their peers, individual testing and counseling will be carried out privately. Results will be delivered in private and contacts will not be asked to disclose their status following the test. Disclosure of participant HIV or TB status is expected to be rare, if it occurs. No other adverse effects are expected.

Protections Against Risk

To minimize risks to patient autonomy, the community health workers will be carefully trained in how to protect the privacy of study participants and will complete training in Human Subjects' Protection and Good Clinical Practice. Care

will be taken to protect the confidentiality of subjects' HIV and TB status, along with any other potentially stigmatizing information, during enrollment and collection of data. All patient-identifiable data will be stored in locked or password-protected areas accessible only to study personnel. No patient-identifiable data will be collected beyond what is routinely collected by health centers during the course of routine contact investigation.

Study procedures are under regular oversight by the institutional review boards at the participating sites, including the Makerere University School of Public Health Higher Degrees Research Ethics Committee and Yale University Human Subjects Committee, as well as by the Uganda National Council for Sciences and Technology, a government body. In addition, we will liaise with the Ugandan IRBs.

Potential Benefits to Participants

Study subjects will benefit from participation in this study through the potential identification, diagnosis, and treatment of other patients with active TB disease or living with HIV. Diagnosing and treating co-occurring infectious TB cases where they are present will reduce household members' and index patients' risk of reinfection with TB at a later time, and lead to improved health and well-being of the index patient's family. In addition, participation in this study could lead to reduced stigma related to HIV and TB in the patient's household. Potential benefits to society include identification of strategies to reduce HIV- and TB-related stigma. If successful, the intervention could potentially be scaled up to reduce HIV-TB stigma and improve uptake of HIV testing during household contact investigation in similar settings.

Appendix

1a. Helpful Links:

OraQuick Video on HIV oral testing: http://www.oraquick.com/Taking-the-Test/How-To-Video

WHO guidelines on HIV testing: https://www.who.int/hiv/pub/guidelines/hiv-testing-services/en/

1b. Complete Power Analysis Report

Report Definitions

N is the total number of eligible contacts in the study.
K1 and **K2** are the number of households in groups 1 and 2, respectively.
M is the average number of eligible contacts per household.
P1 is the proportion for group 1 (treatment group) assuming the alternative hypothesis.
P2 is the proportion for group 2 (control group). This is the proportion consenting to testing in households that receive standard HIV test offers.
Prop Diff = P1 - P2 is the difference in the group proportions assumed by the alternative hypothesis.
Odds Ratio = Odds1/Odds2 is the odds ratio assuming the alternative hypothesis.
ICC is the intracluster correlation.
Alpha is the probability of rejecting a true null hypothesis.

Summary

The following power analysis considers a range of possible values for P1, average number of eligible contacts, and ICC for each of three scenarios: baseline test uptake (P2) of 75%, 80%, and 85% in control group households. In preliminary data, 98% of intervention recipients took the HIV test and ICC was 0.59. In mHealth trial offers if standard home HIV testing, 61% of recipients took the HIV test.

Power calculations assuming a baseline uptake of 75%

P2=0.75
Mixed Models Tests for Two Proportions in a 2-Level Hierarchical Design (Level-2 Randomization)

Numeric Results for Comparing Two Proportions

H0: P1 = P2. H1: P1 ≠ P2

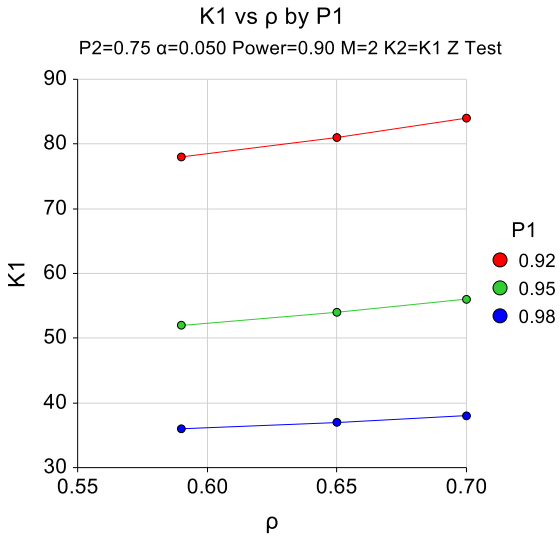
Power	Total Subjects N	Group 1 Clusters K1	Group 2 Clusters K2	Cluster Size M	Group 1 Prop P1	Group 2 Prop P2	Prop Diff P1-P2	Odds Ratio OR	ICC ρ	Alpha
0.90037	1064	266	266	2	0.8500	0.7500	0.1000	1.889	0.5900	0.050
0.90033	1104	276	276	2	0.8500	0.7500	0.1000	1.889	0.6500	0.050
0.90097	1140	285	285	2	0.8500	0.7500	0.1000	1.889	0.7000	0.050
0.90021	1458	243	243	3	0.8500	0.7500	0.1000	1.889	0.5900	0.050
0.90090	1542	257	257	3	0.8500	0.7500	0.1000	1.889	0.6500	0.050
0.90072	1608	268	268	3	0.8500	0.7500	0.1000	1.889	0.7000	0.050
0.90017	708	177	177	2	0.8700	0.7500	0.1200	2.231	0.5900	0.050
0.90067	736	184	184	2	0.8700	0.7500	0.1200	2.231	0.6500	0.050
0.90130	760	190	190	2	0.8700	0.7500	0.1200	2.231	0.7000	0.050
0.90054	972	162	162	3	0.8700	0.7500	0.1200	2.231	0.5900	0.050
0.90068	1026	171	171	3	0.8700	0.7500	0.1200	2.231	0.6500	0.050
0.90158	1074	179	179	3	0.8700	0.7500	0.1200	2.231	0.7000	0.050
0.90125	424	106	106	2	0.9000	0.7500	0.1500	3.000	0.5900	0.050
0.90125	440	110	110	2	0.9000	0.7500	0.1500	3.000	0.6500	0.050

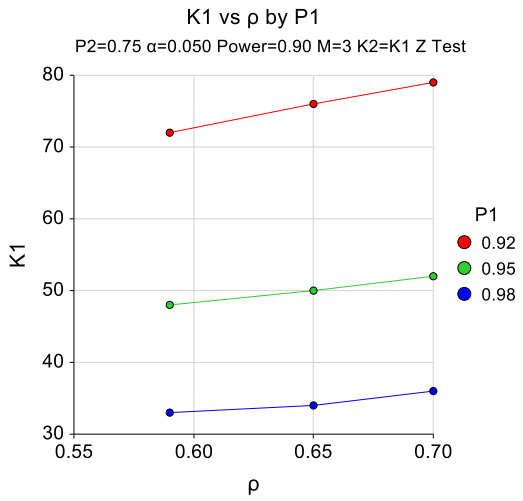
0.90040	452	113	113	2	0.9000	0.7500	0.1500	3.000	0.7000	0.050
0.90157	582	97	97	3	0.9000	0.7500	0.1500	3.000	0.5900	0.050
0.90062	612	102	102	3	0.9000	0.7500	0.1500	3.000	0.6500	0.050
0.90214	642	107	107	3	0.9000	0.7500	0.1500	3.000	0.7000	0.050
0.90007	312	78	78	2	0.9200	0.7500	0.1700	3.833	0.5900	0.050
0.90027	324	81	81	2	0.9200	0.7500	0.1700	3.833	0.6500	0.050
0.90214	336	84	84	2	0.9200	0.7500	0.1700	3.833	0.7000	0.050
0.90289	432	72	72	3	0.9200	0.7500	0.1700	3.833	0.5900	0.050
0.90302	456	76	76	3	0.9200	0.7500	0.1700	3.833	0.6500	0.050
0.90193	474	79	79	3	0.9200	0.7500	0.1700	3.833	0.7000	0.050
0.90234	208	52	52	2	0.9500	0.7500	0.2000	6.333	0.5900	0.050
0.90254	216	54	54	2	0.9500	0.7500	0.2000	6.333	0.6500	0.050
0.90441	224	56	56	2	0.9500	0.7500	0.2000	6.333	0.7000	0.050
0.90515	288	48	48	3	0.9500	0.7500	0.2000	6.333	0.5900	0.050
0.90150	300	50	50	3	0.9500	0.7500	0.2000	6.333	0.6500	0.050
0.90053	312	52	52	3	0.9500	0.7500	0.2000	6.333	0.7000	0.050
0.90652	144	36	36	2	0.9800	0.7500	0.2300	16.333	0.5900	0.050
0.90376	148	37	37	2	0.9800	0.7500	0.2300	16.333	0.6500	0.050
0.90284	152	38	38	2	0.9800	0.7500	0.2300	16.333	0.7000	0.050
0.90733	198	33	33	3	0.9800	0.7500	0.2300	16.333	0.5900	0.050
0.90049	204	34	34	3	0.9800	0.7500	0.2300	16.333	0.6500	0.050
0.90473	216	36	36	3	0.9800	0.7500	0.2300	16.333	0.7000	0.050

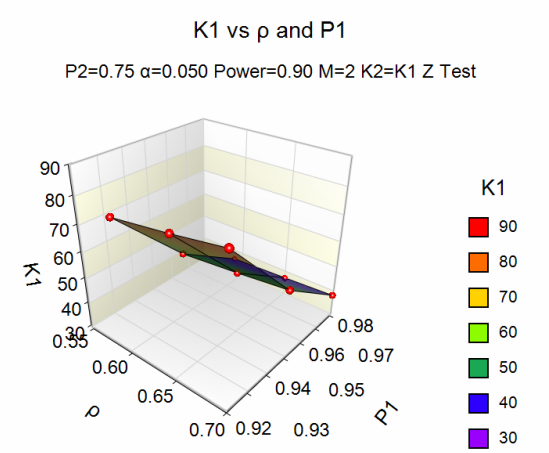
Summary Statement

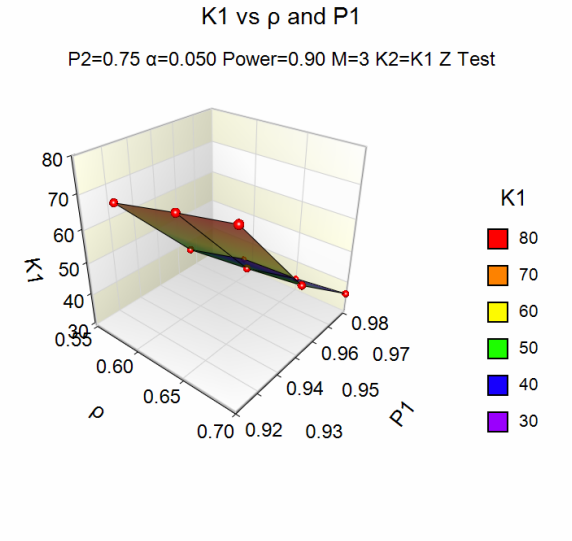
Sample sizes of 156 in group 1 (the treatment group) and 156 in group two, which were obtained by sampling 78 clusters in group one and 78 clusters in group 2 (the control group) with an average of 2 subjects per cluster, achieve 90% power to detect a difference between the group proportions of 0.17. The proportion in group 1 is assumed to be 0.92 under the alternative hypothesis. The proportion in group 2 is 0.75. The test statistic used is the effect regression coefficient from a mixed-effects logistic regression model. The intracluster correlation is 0.5900, and the significance level of the test is 0.05.

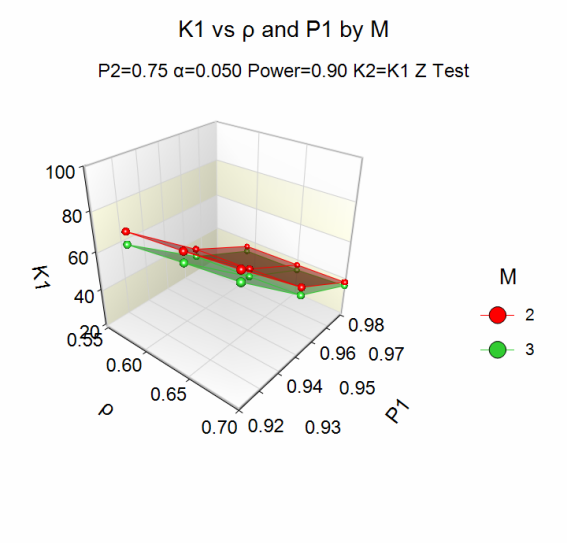
Charts




K1 vs ρ by P1
P2=0.75 α=0.050 Power=0.90 M=3 K2=K1 Z Test
80
70
60
50
40
30
K1
0.55
0.60
0.65
0.70
ρ
P1
0.92
0.95
0.98


K1 vs ρ and P1
P2=0.75 α=0.050 Power=0.90 M=2 K2=K1 Z Test
90
80
70
60
50
40
30
K1
0.55
0.60
0.65
0.70
ρ
0.92
0.93
0.94
0.95
0.96
0.97
0.98
P1
K1
90
80
70
60
50
40
30


K1 vs ρ and P1
P2=0.75 α=0.050 Power=0.90 M=3 K2=K1 Z Test
80
70
60
50
40
30
K1
0.55
0.60
0.65
0.70
ρ
0.92
0.93
0.94
0.95
0.96
0.97
0.98
P1
K1
80
70
60
50
40
30



Power calculations assuming a baseline uptake of 80%

P2=0.80
Mixed Models Tests for Two Proportions in a 2-Level Hierarchical Design (Level-2 Randomization)

Numeric Results for Comparing Two Proportions

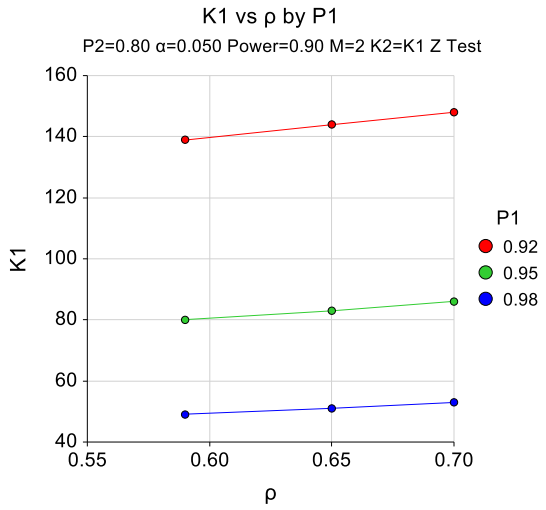
H0: P1 = P2. H1: P1 ≠ P2

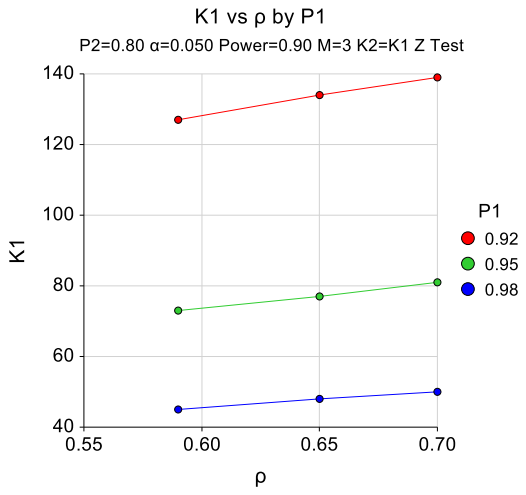
Power	Total Subjects N	Group 1 Clusters K1	Group 2 Clusters K2	Cluster Size M	Group 1 Prop P1	Group 2 Prop P2	Prop Diff P1-P2	Odds Ratio OR	ICC ρ	Alpha
0.90087	848	212	212	2	0.9000	0.8000	0.1000	2.250	0.5900	0.050
0.90087	880	220	220	2	0.9000	0.8000	0.1000	2.250	0.6500	0.050
0.90003	904	226	226	2	0.9000	0.8000	0.1000	2.250	0.7000	0.050
0.90120	1164	194	194	3	0.9000	0.8000	0.1000	2.250	0.5900	0.050
0.90025	1224	204	204	3	0.9000	0.8000	0.1000	2.250	0.6500	0.050
0.90042	1278	213	213	3	0.9000	0.8000	0.1000	2.250	0.7000	0.050
0.90200	556	139	139	2	0.9200	0.8000	0.1200	2.875	0.5900	0.050
0.90152	576	144	144	2	0.9200	0.8000	0.1200	2.875	0.6500	0.050
0.90082	592	148	148	2	0.9200	0.8000	0.1200	2.875	0.7000	0.050
0.90188	762	127	127	3	0.9200	0.8000	0.1200	2.875	0.5900	0.050
0.90190	804	134	134	3	0.9200	0.8000	0.1200	2.875	0.6500	0.050
0.90021	834	139	139	3	0.9200	0.8000	0.1200	2.875	0.7000	0.050
0.90163	320	80	80	2	0.9500	0.8000	0.1500	4.750	0.5900	0.050
0.90156	332	83	83	2	0.9500	0.8000	0.1500	4.750	0.6500	0.050
0.90317	344	86	86	2	0.9500	0.8000	0.1500	4.750	0.7000	0.050
0.90114	438	73	73	3	0.9500	0.8000	0.1500	4.750	0.5900	0.050
0.90107	462	77	77	3	0.9500	0.8000	0.1500	4.750	0.6500	0.050
0.90338	486	81	81	3	0.9500	0.8000	0.1500	4.750	0.7000	0.050
0.90114	196	49	49	2	0.9800	0.8000	0.1800	12.250	0.5900	0.050
0.90200	204	51	51	2	0.9800	0.8000	0.1800	12.250	0.6500	0.050
0.90447	212	53	53	2	0.9800	0.8000	0.1800	12.250	0.7000	0.050
0.90250	270	45	45	3	0.9800	0.8000	0.1800	12.250	0.5900	0.050
0.90563	288	48	48	3	0.9800	0.8000	0.1800	12.250	0.6500	0.050
0.90514	300	50	50	3	0.9800	0.8000	0.1800	12.250	0.7000	0.050

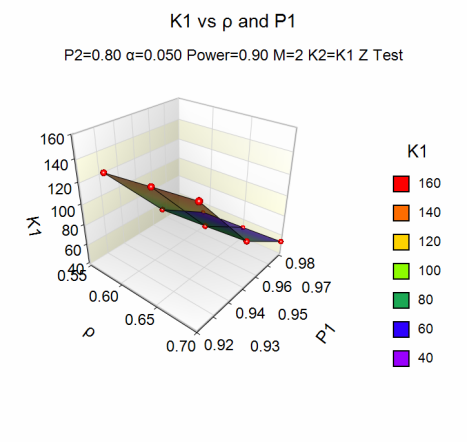
Summary Statement

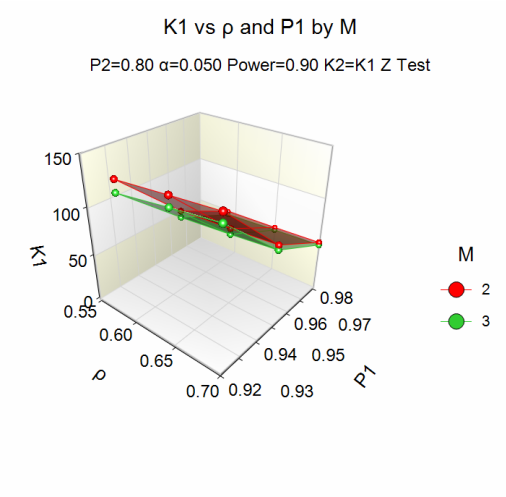
Sample sizes of 278 in group 1 (the treatment group) and 278 in group two, which were obtained by sampling 139 clusters in group one and 139 clusters in group 2 (the control group) with an average of 2 subjects per cluster, achieve 90% power to detect a difference between the group proportions of 0.12. The proportion in group 1 is assumed to be 0.92 under the alternative hypothesis. The proportion in group 2 is 0.8. The test statistic used is the effect regression coefficient from a mixed-effects logistic regression model. The intracluster correlation is 0.59, and the significance level of the test is 0.05.

Charts









Power calculations assuming a baseline uptake of 85%

P2=0.85
Mixed Models Tests for Two Proportions in a 2-Level Hierarchical Design (Level-2 Randomization)

Numeric Results for Comparing Two Proportions

H0: P1 = P2. H1: P1 ≠ P2

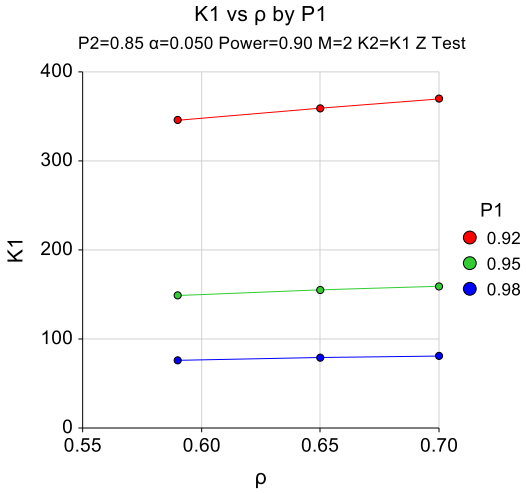
Power	Total Subjects N	Group 1 Clusters K1	Group 2 Clusters K2	Cluster Size M	Group 1 Prop P1	Group 2 Prop P2	Prop Diff P1-P2	Odds Ratio OR	ICC ρ	Alpha
0.90053	1384	346	346	2	0.9200	0.8500	0.0700	2.029	0.5900	0.050
0.90049	1436	359	359	2	0.9200	0.8500	0.0700	2.029	0.6500	0.050
0.90058	1480	370	370	2	0.9200	0.8500	0.0700	2.029	0.7000	0.050
0.90030	1896	316	316	3	0.9200	0.8500	0.0700	2.029	0.5900	0.050
0.90082	2004	334	334	3	0.9200	0.8500	0.0700	2.029	0.6500	0.050
0.90039	2088	348	348	3	0.9200	0.8500	0.0700	2.029	0.7000	0.050
0.90057	596	149	149	2	0.9500	0.8500	0.1000	3.353	0.5900	0.050
0.90127	620	155	155	2	0.9500	0.8500	0.1000	3.353	0.6500	0.050
0.90002	636	159	159	2	0.9500	0.8500	0.1000	3.353	0.7000	0.050
0.90017	816	136	136	3	0.9500	0.8500	0.1000	3.353	0.5900	0.050
0.90119	864	144	144	3	0.9500	0.8500	0.1000	3.353	0.6500	0.050

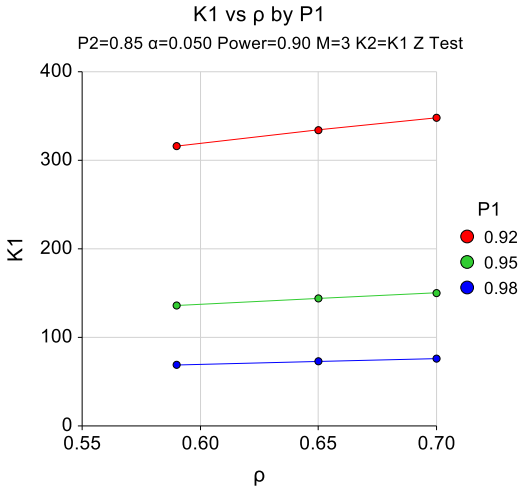
0.90069	900	150	150	3	0.9500	0.8500	0.1000	3.353	0.7000	0.050
0.90296	304	76	76	2	0.9800	0.8500	0.1300	8.647	0.5900	0.050
0.90343	316	79	79	2	0.9800	0.8500	0.1300	8.647	0.6500	0.050
0.90205	324	81	81	2	0.9800	0.8500	0.1300	8.647	0.7000	0.050
0.90103	414	69	69	3	0.9800	0.8500	0.1300	8.647	0.5900	0.050
0.90182	438	73	73	3	0.9800	0.8500	0.1300	8.647	0.6500	0.050
0.90116	456	76	76	3	0.9800	0.8500	0.1300	8.647	0.7000	0.050

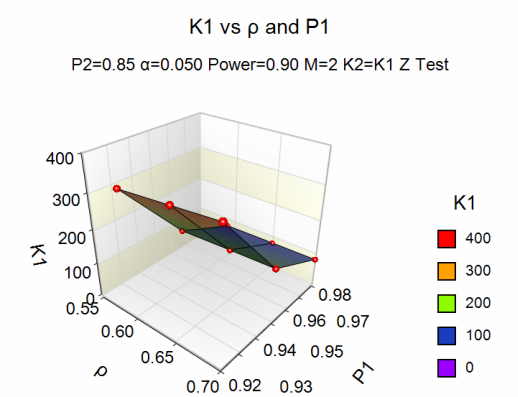
Summary Statement

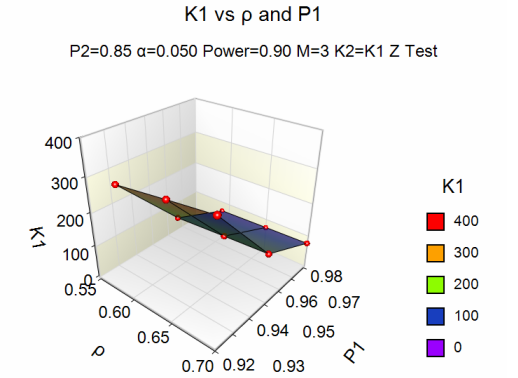
Sample sizes of 692 in group 1 (the treatment group) and 692 in group two, which were obtained by sampling 346 clusters in group one and 346 clusters in group 2 (the control group) with an average of 2 subjects per cluster, achieve 90% power to detect a difference between the group proportions of 0.07. The proportion in group 1 is assumed to be 0.92 under the alternative hypothesis. The proportion in group 2 is 0.85. The test statistic used is the effect regression coefficient from a mixed-effects logistic regression model. The intracluster correlation is 0.59, and the significance level of the test is 0.05.

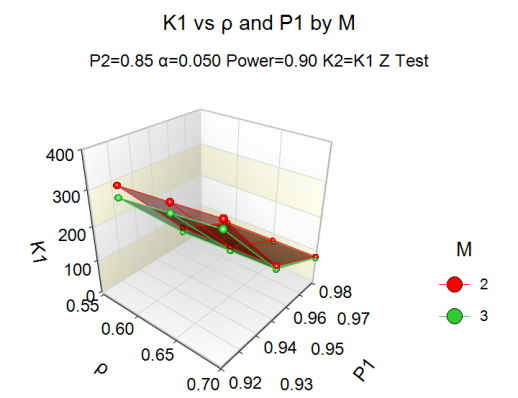
Charts











References

Ahn, C., Heo, M., and Zhang, S. 2015. Sample Size Calculations for Clustered and Longitudinal Outcomes in Clinical Research. CRC Press. New York.

1c. Adapted Van Rie TB/HIV Stigma Scale

Adapted Scale Items
TB Stigma Subscale
1. Some household members think that those with TB are disgusting.
2. Some household members keep a distance from those with TB.
3. Some household members are afraid of those with TB.
4. Some household members try not to touch those with TB.
5. Some household members prefer not to have those with TB living in their household.
6. If a person has TB, some household members will behave differently towards them for the rest of their life even after recovering from TB.
7. Some household members may not want to eat or drink with relatives who have TB.
HIV Stigma Subscale
1. Some household members think that those with HIV are disgusting.
2. Some household members keep distance from those with HIV.
3. Some household members are afraid of those with HIV.
4. Some household members try not to touch those with HIV.
5. Some household members prefer not to have those with HIV living in their household.
6. If a person has HIV, some household members will behave differently towards that person for the rest of his or her life.

1d. Sub-Study: Testing Predictions and Social Influence

i. Questions for Index Patients, to be collected at time of enrollment

Enumerate Household Contacts: Now, I would like to know more about the people you stay with at home. Let's talk about each of them one by one. (collect name and ordinal number, *1 through n*)

For each contact, ask the testing prediction: Do you think [contact name] would accept a free HIV test?

Social Influence questions, in which the index patient will nominate one of their contacts for each answer. Name and number for the nominated contact should be recorded; contacts can be nominated more than once. **The index patient cannot be nominated.**

- ***Domain 1**: Model Behavior*
    1. English version: Who do other household members model their behavior after?
    2. Luganda version: Abawaka wano, ani gwebasinzirako okusalawo eneyiisa yabwe?
- **Domain 2**: *Health Advice*
    1. English version: Who in the household is most knowledgeable about health matters?
    2. Luganda version: Kunsonga zebwobulamu, birowozo byani awaka wano ebisinga omugaso?
- **Doman 3**: *Approval*
    1. English version: When engaging in health behaviors, whose approval is considered most important in the household?
    2. Luganda version: Nga wenyigira mu byobulamu, okugeza nga okufuna obujanajabi, okwekebeza oba okufuna eddagala, awaka wano ani yebuziibwako okukola okusalawo?

ii. Questions for Contacts

Social Influence questions, in which the contact will nominate a household contact for each answer **using the same social influence questions above**. Name and ordinal number for the nominated contact should be recorded; contacts can be nominated more than once. **The index patient cannot be nominated, but contacts may nominate themselves.**