HRP-503B – BIOMEDICAL RESEARCH PROTOCOL
(2017-1)

Protocol Title: Interrupting HIV and TB stigma in the household during TB contact investigation in Uganda

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INSTRUCTIONS
This template is intended to help investigators prepare a protocol that includes all of the necessary information needed by the IRB to determine whether a study meets approval criteria. **Read the following instructions before proceeding:** 1. Use this protocol template for a PI initiated study that includes direct interactions with research subjects. Additional templates for other types of research protocols are available in the system Library. 2. If a section or question does not apply to your research study, type "Not Applicable" underneath. 3. Once completed, upload your protocol in the "Basic Information" screen in IRES IRB system.

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SECTION I: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

An estimated 39 million people worldwide are living with HIV, but nearly half 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); about 40% of those with TB worldwide are also unaware of their TB status, and for similar reasons. This layered 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, including those living with an index TB patient.

Home testing is a promising approach to increase testing and linkage to care for HIV because it can reach individuals outside the health system, eliminate the costs of traveling for testing, offer testing in a familiar environment, and increase engagement with care among those found to be living with HIV. Nevertheless, many individuals offered home HIV testing in sub-Saharan Africa decline to test. Our group has previously shown that social interactions at the time HIV testing is offered strongly influence perceived stigma and test uptake. When potential testers discern that others have declined, they say they fear that testing will be socially discrediting. In adjusted analyses, individuals were 4 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 peers' choices 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 social and behavioral science to facilitate interactions within the household that reduce perceived stigma and promote uptake of HIV testing. Specifically, we will design an intervention that 1) optimizes the order of test invitations to establish testing as the normative choice; 2) frames testing as a prosocial behavior that promotes household well-being; and 3) maximizes acceptability by offering oral testing. We hypothesize that offering and delivering HIV testing in ways that reduce perceived stigma will ultimately have strong effects on the proportion of patients completing HIV testing and linking to care.

Together with our partners in Uganda, we propose to develop and pilot a complex intervention to increase uptake of home HIV testing and linkage to HIV care among household members offered home-based HIV testing. We aim:

Aim 1: **To develop a complex intervention to increase uptake of testing for HIV among household members by reducing perceptions of stigma associated with HIV and testing for HIV.** Lay health workers (LHWs) will deliver a novel invitation strategy for HIV testing in 20 purposively sampled households that includes 1) acceptance-optimized sequencing, 2) prosocial messaging, and 3) salivary HIV testing. We will administer HIV and TB stigma scales before and after the invitation. We will interview all household members following the visit and engage LHWs in focus group discussions to explore feasibility and acceptability of the invitation strategy. We will iteratively refine the intervention to optimize acceptability and reductions in perceived stigma, for evaluation in Aim 2.

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Aim 2: **To evaluate the intervention on household HIV stigma and uptake of testing among household members undergoing TB contact investigation in a household-randomized pilot trial.** We will recruit a prospective cohort of multiple-contact households undergoing routine contact investigation for TB. Households will be randomized to one of two study arms. Households in the control arm will receive routine household contact investigation services, including free, optional oral HIV testing. Households in the intervention arm will receive routine household contact investigation services and free, optional oral HIV testing with the social-behavioral framing intervention. LHWs in the intervention arm will use acceptance-optimized sequencing of invitations and a prosocial invitation script to offer salivary testing for HIV to household members. We will measure our co-primary outcomes of HIV and TB stigma using standardized instruments before invitation and after completion of post-test counseling. We will measure the proportion consenting to HIV testing, yield of HIV diagnoses, and the proportion of new PLWH linked to HIV care at 1 month and 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 and impact of the intervention.

The expected impact of these studies is to generate preliminary data on a novel approach to offering home testing that reduces perceived stigma within households and its effects on testing and linkage to and retention in care, built on the scientific premise of longstanding research on group processes and social decision-making. These data will inform a future randomized study evaluating the clinical impact of these new stigma-reducing approaches to offering and delivering HIV counseling and testing. Our proposal aligns with NIH priorities for interventions that increase access to HIV care and reduce the effects of stigma on PLWH, PLWH with TB, and adolescents and children.

2. Probable Duration of Project: State the expected duration of the project, including all follow-up and data analysis activities.

The activities described here will take place from April 1, 2019 until approximately March 30, 2021.

3. Background: Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

UNAIDS has called for 90% of persons living with HIV (PLWH) to know their HIV status by 2020[1,2]; the World Health Organization (WHO) has called for elimination of active TB as a public health threat by 2035. Nonetheless, major gaps exist: one-third of PLWH do not know their status; similarly, almost 40% of TB patients go undiagnosed each year. To reach these ambitious targets, HIV testing services must reach another 7.5 million people by 2020, and TB testing services another 4 million people.[3] New data from the Population-based HIV Impact Project show that achieving high status awareness is a greater challenge than achieving high antiretroviral therapy uptake or viral load suppression in 7 Southern African countries, including Uganda.[4]

Home testing and counseling services for HIV can increase status awareness and linkage to care. Home-based testing services are an important tool for reaching the UNAIDS/WHO targets by reaching and engaging populations who are unable or disinclined to visit facilities. Home testing programs can increase the proportion of individuals in the community who are aware of their HIV status[5-8] and support linkage to HIV care.[9,10] The improvements can be dramatic among key high-risk populations: a home-based HIV counseling and testing intervention in Zambia increased status awareness among 15-19-year-olds from 28% to 89%.[11] However, uptake of home-based testing is mixed in sub-Saharan Africa.[12,13] Furthermore,

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status awareness must be maintained through regular testing, but most home testing strategies involve a single test opportunity. Moreover, a systematic review found that the effectiveness of linkage strategies varies.[14]

Household contact investigation for TB provides a platform for engaging high-risk households for home HIV testing.[15,16] Household TB contact investigation is a longitudinal service offered over 2 years to the close contacts of TB patients. This offers an opportunity for LHWs to reach high-risk individuals with low rates of status awareness; prior studies show that offering HIV testing to adult and adolescent household contacts of TB patients is a feasible approach with substantial yield, in spite of suboptimal rates of consent to testing.[17,18] In our preliminary studies, nearly 60% of individuals reached in multiple-contact households were aged 15-25, and more than half were unaware of their HIV status.[19,20] Moreover, contact investigation represents an opportunity to deliver interventions to reduce stigma at the household level and engage household members over time, ensuring that status awareness is sustained and that those in need are linked to care.

Stigma inhibits testing for HIV, care-seeking behaviors, and engagement in HIV care. Systematic reviews and meta-analyses demonstrate that stigma and perceived stigma are consistently associated with lower uptake of HIV testing[21-23], doubled odds of late presentation for HIV/AIDS care[24], lower likelihood of initiating ART after diagnosis[21,25], lower levels of adherence[21,26], and lower engagement in care.[26] However, the mechanisms that link HIV stigma and these outcomes are less well understood.[26]

Layered stigma is associated with worse outcomes than HIV stigma alone. Stigma is best understood as a dynamic social process rather than an individual attribute.[27,28] When stigma is layered, social devaluation from two socially discrediting conditions can operate synergistically. Households undergoing TB contact investigation face or anticipate facing at least two stigmatized conditions, HIV and TB. TB-HIV stigma has consequences for TB care-seeking, TB-HIV outcomes, and HIV management.[29]

Uganda provides a representative setting for expanding and improving home HIV testing by reducing household stigma for HIV & TB. Uganda is a high HIV-TB-burden country, with estimated HIV prevalence of 7.1% and TB prevalence of 253 per 100,000. More than 25% of PLWH are unaware of their HIV status.[30] Uptake of door-to-door home HIV testing ranges from 69%–95%[7,8,13], but uptake of HIV testing among household contacts of TB patients is only 53%.[20] The PLWH Stigma Index found that >60% of Ugandan PLWH experienced malicious gossip in their family or community in the past year and nearly 10% had been excluded from family activities.[31] TB stigma may be even more common in Uganda; nearly 50% of survey respondents hold stigmatizing attitudes toward TB, compared to 26% with stigmatizing attitudes toward HIV.[32]

There is a need to build awareness of and capacity for integrating stigma hypotheses and measures into research on HIV-TB in Uganda. We propose two specific capacity-building initiatives that will draw on experiences building capacity for mixed-methods and implementation research through our Fogarty D43 Pulmonary Complications of AIDS Research Training program. First, we will sponsor a doctoral student from Makerere University to work on this project. Second, each year, we will sponsor a symposium highlighting current research and future priorities in HIV and TB stigma at the Makerere Joint Annual Science and Health Conference at Makerere University, and include patients, families, researchers, and program officials.

Home HIV testing decisions in high-prevalence settings are commonly reached by households, not individuals. A meta-ethnographic review of 20 studies from East and Southern Africa found that decisions in response to offers of home-based HIV testing and counseling took place at the household or family level, not the individual level.[33] Moreover, “courtesy stigma” (carryover stigma experienced by family members of the afflicted individual) can affect everyone in the household.[34-36] Thus, individuals may decline testing not only because they fear the social consequences they will face individually, but because

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they fear that their family will also face negative social outcomes. Interventions to reduce stigma and improve testing uptake must account for the social nature of participants' decision-making processes: observing others' HIV testing decisions may either normalize or marginalize testing for HIV.

There is a need for novel interventions to reduce HIV stigma that are targeted to households. Although stigma is often measured at the individual level, the production of stigma is a social process that occurs in groups.[37-39] Stigma processes within households may be particularly important for the outcomes of younger members: In a Kenyan study, 46% of children living with HIV were lost to follow-up due to enacted stigma[40] or fear of stigmatization within the family or wider community.[41] Yet a critical review found that among 100 studies assessing community-level factors such as stigma in low- and middle-income countries (LMIC), only 5 evaluated interventions that aimed to act on group environments.[21] There is a need for novel interventions that address stigma as a social process occurring within social groups rather than merely an individual experience.

A household stigma reduction intervention might not only improve the effectiveness of home testing services for promoting status awareness, but also have far-reaching effects on linkage to and engagement in care. Households are particularly powerful sites for intervention because they are primary social groups, composed of individuals with close, durable social ties to one another.[42] Because ties among primary groups tend to persist even when stressed, these groups are critical, and often irreplaceable, sources of social support for PLWH, which is associated with a range of improved physical and mental outcomes.[43-45] *An intervention to reduce stigma at the household level may not only increase willingness to consent to test, but also ease subsequent steps in the continuum of HIV care and improve quality of life among PLWH.*

Stigma reduction interventions are promising, but have thus far shown modest effectiveness. Strategies to reduce stigma and improve HIV test uptake typically focus on creating awareness (peer education, social marketing, school curricula), providing support (empathy instruction, counseling, support groups), influencing norms (community organizing, stigma discussions), or developing policies.[39,46] A meta-analysis of 42 studies to evaluate effectiveness of stigma reduction programs found small but significant effects on knowledge and attitudes towards PLWH; effectiveness was higher among programs that incorporated multiple sessions.[47] However, most studies suffered methodological flaws, lacking appropriate randomization, allocation concealment, or follow-up assessment; there is a need for greater rigor and better-quality data.[47]

Prosocial and behaviorally informed messaging can increase motivation to participate in health-related activities, including those that primarily benefit others. Experimental evidence shows that historical non-vaccinators are motivated by prosocial messages more than by appeals to their own health.[48,49] A randomized controlled trial found strong evidence that behaviorally informed messaging increased the return rate of HIV self-sampling kits.[50] We hypothesize that prosocial framing of HIV testing as a communal (rather than merely individual) good will increase uptake of testing during household contact investigation for TB.

People are inclined to do as they observe. Experimental evidence has long shown that individuals' observation of how group members ahead of them behave can profoundly shape their perceptions, judgements, and subsequent behaviors.[51-53] Moreover, social influence theories from the sociology of networks suggest that that individuals' social status and social network position determine the scope of their influence on other group members.[54,55] Thus, individual testing decisions are likely to be influenced by observations of how others before them behave, especially if those others are of higher status or socially central to the household.

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We focus on interrupting stigma as a social process within a primary social group—the household—rather than temporarily circumventing it. Many interventions to improve uptake of HIV counseling and testing attempt to circumvent stigma by increasing individual privacy, such as by providing oral self-testing kits. However, these approaches do not reduce stigma; rather, they temporarily shield testers from the consequences of stigma, thereby leaving the possibility of stigma subsequently influencing linkage to and retention in care. Indeed, such interventions may increase the perception—including the misperception—that testing is socially discrediting. Those who test positive must be empowered to seek and engage in HIV care; those who test negative must be empowered to maintain status awareness by testing regularly.

We aim to reduce stigma within the household, a group characterized by close, persistent social ties. While households are powerful social resources for accessing social support and overcoming barriers associated with community-level stigma, they have been largely ignored as a site of intervention for reducing stigma. In contrast, many interventions aim to operate on stigma more broadly at the community-level, such as through community discussions or social marketing. These approaches can reduce stigma, but are difficult to target to primary social groups. Even individuals who anticipate relatively little stigma in the wider community may fear stigma within an important primary group such as their household, especially if they perceive that influential primary group members hold negative assessments of PLWH or people who test regularly. Reducing perceived, anticipated, and enacted stigma within the household may have both larger and longer-lasting effects on status awareness, care-seeking behaviors, and engagement in care.

Finally, we adapt well-established principles from the social and behavioral sciences to reduce social uncertainty for potential testers, normalize testing, and reduce perceived stigma within households. We apply insights gained from experimental evidence on the role of conformity in group perception and behavior, prosocial motivation, and default choices to reduce HIV-TB stigma and increase uptake of HIV testing. We reason that reducing perceptions that other household members hold negative views of testing or PLWH will increase test uptake and strengthen social support available to PLWH within the household, beginning a virtuous circle of decreasing enacted stigma.[54]

4. Research Plan: Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths. Describe the setting in which the research will take place.

Wide variation in uptake of home-based HIV testing and counseling suggests that small differences in how testing is offered may have large effects on test uptake by altering perceptions about stigma within the household. The objective of this project is to optimize a complex, behaviorally-grounded intervention to reduce perceived HIV stigma within households and thereby increase uptake of HIV testing and counseling among household members undergoing contact investigation for TB.

We will explore several hypotheses, including: 1) acceptance-optimized sequencing of HIV test offers is acceptable to clients and health workers; 2) inviting the first tester to share with other household members their affirmative decision to test, without any obligation to share the results, is at least as acceptable to clients as concealing choice; 3) learning that the first household member chose to test will decrease perceived stigma; 4) provider-initiated invitation scripts employing prosocial messaging(55) can decrease stigma associated with testing; and 5) oral HIV testing will decrease HIV stigma by de-medicalizing HIV testing in the household setting. In this aim, we will carry out participatory research with household members who are offered home HIV testing while undergoing contact investigation for TB and LHWs delivering contact investigation. The expected outcome is a

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novel approach to offering HIV testing centered around stigma reduction, as well as data on its acceptability to household members and health workers.

Population. We will include *household contacts* identified by index patients initiating treatment for TB at Kampala Capital City Authority health facilities. We will include households eligible for contact investigation under Uganda National TB Guidelines, including those with index patients who are microbiologically confirmed or clinically diagnosed including index patients who are children <5. We will exclude households for which the index patient reports <2 contacts over age 14, those who live outside of greater Kampala and those diagnosed with MDR-TB for both Aims of the study.

Procedures for Aim 1

LHW focus group discussions. A social scientist and trained assistant will facilitate focus group discussions (**FGD**s) with LHWs responsible for carrying out household contact investigation for TB, including home-based HIV counseling and testing for household contacts 15 years and older.

Script development. We will develop the prototype script following the focus group discussions with non-participating LHWs, and initially refine the script through training and retraining of the study LHWs.

Oral testing offer. LHWs will provide routine household contact investigation services, including TB education, screening, sputum collection, HIV testing, and clinic referral, according to routine public heath protocols. In purposively selected households and following the prototype invitation script, LHWs will offer oral HIV testing first to the household member statistically most likely to accept (*e.g,* oldest female), then to other eligible adults and adolescents using the FDA-approved OraQuick ADVANCE rapid HIV-1/2 antibody test.

Iterative, experience-based interviews. A social scientist will privately interview members of 20 purposively sampled households, including households in which all eligible members accepted HCT during TB contact investigation, and households in which some or all did not accept HCT. We will prompt each household member to recount their decision process, describe their primary social ties and sources of social support, complete short stigma scales, and suggest changes to the prototype script and other aspects of how testing is offered. We will collate these data and adapt intervention components after every 5 households.

TB Stigma: We will conduct a cross-sectional study nested within the Aim 1 procedures to describe the prevalence and characteristics of TB stigma in a population of households living with a TB patient. This will be achieved by distributing validated parallel Van Rie stigma scales (*Van Rie TB-HIV-related stigma scales, attached*.) to approximately 120 household contacts in approximately 40 consecutive households. The parallel Van Rie stigma scale is a scale that measures both TB and HIV/AIDS related stigma. The scale is structured to capture stigma related to these key domains: fear of transmission and disease, values and attitudes associated with shame, blame and judgments, and disclosure of disease status. These scales have been validated in a variety of settings and have excellent internal consistence, good construct validity, and moderate test-retest reliability.

To further explore the relationship between perceptions of TB and attitudes toward TB evaluation, we will interview 5 low and 5 high TB-stigma scoring individuals from the parallel Van Rie stigma scales. During the study visits described above, the stigma scales will be scored immediately, eligible respondents identified, and eligible respondents invited to a 45-minute interview. If the invitation is accepted, the interview will be preferentially conducted during the same household visit, although if time or space concerns make this infeasible or unacceptabale, the interview may be rescheduled to a different time and location as specified or agreed to by the participant. In addition to stigma scale score, participants will be purposively selected to ensure variation by age and gender among interviewees.

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These interviews will be conducted by a trained social scientist fluent in both English and Luganda in order to conduct interviews in the language of preference for the participants.

The comparison between TB stigma scores and TB evaluation outcomes will be analyzed using a bivariate analysis. TB evaluation outcomes include whether the participant successfully completed sputum collection and/or if they completed a clinic follow-up if indicated by the health care worker.

COVID Health Worker Cohort: We will also establish a prospective cohort of COVID-engaged health workers to longitudinally evaluate the psychosocial and physiological impact of COVID-19 response on health workers involved in TB units. Our aim is to learn more about health worker stress, burnout and the impact these things may have on HIV-TB services and the health system as a whole.

We propose to reach out via telephone to survey and/or interview health care workers at any TB clinics around Uganda who are now also working on the frontline of the COVID-19 response to gather additional insights on the impact of the COVID-19 pandemic on TB and HIV services as well as gain insights on the impact of COVID-19 on health care worker stress and burnout over time. Clinics we plan to reach out to include those where we (U-TIRC) have previously worked on prior research projects or where partner organizations, such as Walimu, have strong connections with clinic staff to widen the scope of this study given the importance and urgency of gaining insights about the pandemic. We will interview health care workers repeatedly over the course of the pandemic including obtaining brief interviews approximately 3-6 months after the pandemic is deemed to be under control. These interviews will cover health workers' experiences responding to COVID-19 and delivering routine services such as TB care, TB contact tracing, and HIV testing in the context of COVID-19. We will characterize the psychosocial dimensions of health worker response to COVID-19. We will invite them to voluntarily participate in a short, structured baseline telephone interview. We will then invite those who consent to participate in further short interviews at regular intervals as the COVID-19 outbreak matures. We might also have other interactions with these health workers in regard to TB and COVID-19 experiences, all of which will take place via telephone, or if recommendations by the Ministry of Health change, in person while maintaining appropriate social distancing and/or personal protective equipment. Any qualitative data collected through these efforts will be audio recorded, transcribed and de-identified, and then destroyed. Only research study staff will have access to these files which are to be stored on secure cloud-based servers (Box.com) even after de-identification. At each qualitative data collection point, participants will be reminded that they may leave the study at any time, indicate a preference not to answer any question, and that the qualitative interview will be recorded.

Measures. We will assess perceptions of stigma within the household using a pair of validated, comprehensive, parallel scales designed to assess perceived/attributed stigma for HIV and TB that we have adapted to the household level.(61) (*Van Rie TB-HIV-related stigma scales, attached*.) We will measure composite household stigma by pooling the measures of perceived and enacted stigma from all members of the household. We will collect individual 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 test, and self-reported symptoms of TB (including cough, subjective fever, or weight loss). We will collect measures of household stability, including household tenure in years.

Sample size. We will deliver the script and interview contacts from 20 households (approximately 40-60 individuals). In most studies, 10-15 subjects per group are required to reach saturation, the point at which interviews do not yield new themes.(62,63) We will carry out ≥2 FGDs with 15 experienced LHWs. For TB stigma related questions, we will distribute the stigma scale up to 40 households

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(approximately 100-120 individuals). We will attempt to build a cohort of between 60 and 100 health care workers from around Uganda engaged in HIV and TB care during and after the COVID pandemic. Due to the changing nature of the pandemic and the changing staffing requirements for clinics, this number may change.

Analysis. After professionally transcribing and importing interviews into a qualitative data analysis application, we will carry out a grounded-theory analysis. Two coders will independently read transcripts to identify themes, produce a codebook, and apply codes. We will assess the acceptability of acceptance-optimized sequencing of HIV test offers to clients and LHWs by inductive analysis of responses to the prototype sequence, and acceptability of inviting the first tester to share their choice to test (but not results) by inductive analysis of themes relevant to sharing of test decision. For both acceptability outcomes, we will calculate the proportions who affirmatively describe each element of the intervention as acceptable in principle and estimate the extent to which this is correlated within households. We will qualitatively assess change in perceived stigma associated with learning that the first household member chose to test as well as change in perceived stigma associated with provider-initiated invitation scripts that apply prosocial messaging by analyzing the decision narratives. Because the aim of the interviews is to iteratively refine the intervention, the prototype will evolve over the course of data collection, and we will not conduct formal statistical tests.

Parallel follow-up survey and short-form interview, and validation studies: We will also conduct two sub-studies nested within Aim 1 participants. These studies will help to adapt and validate a variation of the Van Rie HIV- and TB-related stigma scales to 1) improve their legibility to TB patients and their close contacts, 2) more effectively target these scales to distinguish between the presence of perceived stigma from the household versus perceived stigma from the community at large. We will make adjustments to the scales and then conduct short follow up surveys and/or interviews with Aim 1 participants to compare HIV and TB stigma scale answers with those provided at baseline. We will re-contact these participants via telephone, through a secondary household visit or through an invitiation to an acceptable site such as the health facility or the U-TIRC study offices.

Procedures for Aim 2:

Routine data collection. We will collect routine household contact investigation and home HIV testing uptake data from the contact registers of the 4 participating TB units.

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 split into Clinic Based CHWs, Intervention CHWs and CHWs doing Routine Contact Investigation. Each group will separately review and role play their assigned procedures. Clinic Based CHWs will be trained to provide TB education and counselling, index patient enrolment, and randomization procedures. Intervention CHWs will be trained to deliver the social-behavioural intervention finalized in Aim 1. Standard of Care CHWs will be trained to deliver a standard offer of opt-in HIV testing. Both Standard of Care CHWs and Intervention CHWs will be trained in the use and delivery of oral HIV testing kits including the delivery of HIV education and counselling.

Household-Randomized controlled trial. LHWs attached to 2 TB units in Kampala Uganda will identify, invite, consent, and enroll approximately 152consecutive, eligible index patients for household contact investigation for TB. We anticipate these households containing approximately 304 household contacts with approximately 1:1 randomization (half in each study arm). Upon index patient consent, we will collect demographic information from each index patient at enrollment, including age, gender, occupation (if applicable), income (if applicable), education in years, and household composition,

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including number, age, gender, relationship to, and perceived influence of self-reported household contacts. After study enrolment and collection of index patient demographic data, 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. The study CHW will note the self- reported number of household contacts aged 15 or older and requisition the appropriate number of HIV test kits based on the number of reported contacts, adding two extra kits for extra margin.

LHWs will carry out home visits in pairs or with 3 LHWs dependent on the needs of that household. A LHW employed by the clinics will provide routine contact investigation services and a trained study LHW will collect research data and deliver the intervention for those randomized to the intervention arm of the study. While the LHW carries out standard contact investigation screening, the study LHW will administer a short HIV-TB stigma scale individually to all consenting adult members of the household in both arms. The research LHW will follow the assigned script based on randomization allocation to identify household members who are eligible and invite them to test for HIV, recording time-stamped offers, test decisions, and test results. The research LHW will collect household- and individual-level demographic, socioeconomic data, stigma scales, measures of household stability, including household tenure in years as well as relationship to and perceived influence of household members and clinical data using a structured survey.

Procedures for all households: Upon arrival, the CHWs will enroll all eligible, consenting household contacts in the study. But before doing this, at the start, CHWs will introduce themselves and ask for introduction of contacts. At this time the master list of all the contacts will be created.

- 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 Routine Contact Investigation households, depending on the household assignment.

- For the intervention arm, one CHW will take the index case to a private area to ask the influence questions using the paper form (master list) as a key. After completing this exercise, the CHW will then embark conducting household contact screening interviews followed by HIV testing and any other study related activities. All data will be collected via CommCare.

- Meanwhile, the other CHW will be conducting routine TB contact investigation activities and any other clinical procedures in household TB contact investigation. Details of these procedures are found below:

a) Index case influence questions

After enrollment, CHWs will introduce themselves and ask for the introduction of contacts and it is at this time when a contacts master list will be created. Index patients will then be asked the influence questions. The questions will be asked in two steps, once to capture the number and once to capture the name. The other CHW will go head to conduct routine TB contact investigation activities.

b) Household contact screening interview

After household contact enrolment, 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).

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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. We will ask the index patient 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.

c) 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 detail the process of HIV testing in Luganda and/or English, per client preference. A pictorial guide may 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 counselling.

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.

Randomization: For aim 2 of the study, 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 2, a maximum of 6. We will utilize study randomizer, an online randomization tool with concealed randomization. When a CHW has deemed an index patient and their household to be eligible for the study, and after the index patient or their 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 let the CHW know the study allocation. The CHW will then fill in the appropriate allocation, along with the randomization ID, and contact the appropriate CHW team for the household visit.

Households randomized to intervention group will be offered oral testing with the social-behavioral intervention. Households randomized to the standard of care group 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 be in charge of initial enrollment of index patients and recording any clinic follow up by individuals in either arm of the study.

Integrated intervention. In Intervention Households only, the CHW will present the opportunity to test using the script and procedures described in the next section (“Specification of intervention components”). 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.

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 to 30 minutes) in order to blind other household members from the testing decision of that household contact. Contact decisions to test or not to test as well as test results will be recorded in CommCare.

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Administering the oral test The CHW will open the OraQuick test packet in front of the consenting household contact and hand them 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 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 centre for confirmatory capillary blood testing.

Referral protocol Regardless of study arm, 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.

Specification of intervention components In households assigned to the Intervention only, the following procedures will take place:

a) Selection of first tester: Based on prior research, CHWs will be encouraged to offer HIV testing to the oldest female who is present at the time of HIV testing procedures. However, at the time of index patient enrolment, CHWs will ask the index patient whom they regard as the most influential person at home and that could also be the first tester. Ultimately, CHWs will decide which household contact is invited for testing first which will be documented in CommCare to help keep track of who was invited as the first tester.

b) Prosocial script: CHWs will use a prosocial script encouraging HIV testing. The script features language that makes HIV testing a responsibility of the entire household and not just the individual. This prosocial script will be as follows: “Knowing your status sets a good example for your household.”

c) Opt-out test framing: CHWs will follow an “opt-out” framing strategy for offering HIV testing, as opposed to “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?”

d) Sharing the 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 only ask if they are willing to share their decision to test 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

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household decided to test sometimes gives people the strength to test themselves. Sharing your decision might help another person find the strength to test." Testers' decisions to share or not share whether or not they tested will be recorded.

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 alongside a visual aid. These scales have a total of 13 items and were validated in the Uganda setting as part of the Aim 1 procedures. The scales will be administered first at the beginning of the home visit, then again at its conclusion. Each time, the CHW will briefly orient the participant to the response categories using a visual aid.

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 etc.). 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. All changes will be recorded using a data management google doc 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.

Follow-up interview. At 3 months, the study LHW or a member of study team will contact a subset of households to schedule a follow-up visit or phone call if a second visit is unable to occur. The study LHW or a member of the study team will re-administer stigma scales to each participating member. Household members who are not present at the second household visit will be contacted by telephone to schedule a follow-up interview.

Sample Size.

During aim 2, we will distribute the stigma scales up to approximately 152 households containing approximately 304 household contacts with approximately 1:1 randomization (half in each study arm). We analyzed power for a 2-arm household-randomized, controlled trial using mixed models tests for two proportions in a two-level hierarchical design (household, contact). The assumptions and parameters within these calculations were based on data from Aim 1 and 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 0.85
5. The proportion consenting to testing in the intervention group will be 0.98 (a difference of +0.13 vs the control group).
6. An average of two household contacts will be eligible for HIV testing per household. The intra-class correlation (ICC) will be 0.59.

The total number of households needed is sensitive to the mean cluster 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

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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 not presented here although considered by the study team. 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 have been considered. We will plan an interim blinded power analysis by an external biostatistician to readjust sample size targets as necessary for actual mean cluster size and ICC after enrolling the first 100 households.

Analysis. In the Aim 2 analysis, our primary outcome is change in perceived HIV-TB stigma after following the first household contact tracing visit; the secondary outcome is uptake of HIV testing; we will descriptively assess linkage to care from both baseline data and intervention households. We will calculate descriptive statistics for participant characteristics, and test associations between characteristics and perceived/attributed household stigma. To test the hypothesis that invitation scripts that apply acceptance-optimized sequencing of oral test offers 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. To test the hypothesis that prosocial messaging and theory-informed sequencing of HIV test offers can increase test uptake, we will compare testing uptake among the intervention households and pre-implementation households using cluster-adjusted chi-squared tests of proportion and by fitting multilevel logistic regression models. 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.

5. Genetic Testing N/A ☒

6. Subject Population: Provide a detailed description of the types of human subjects who will be recruited into this study.

We will include household contacts 15 years of age or older identified by index patients initiating treatment for TB at Kampala Capital City Authority health facilities. We will include households eligible for contact investigation under Uganda National TB Guidelines, including those with index patients who are microbiologically confirmed or clinically diagnosed and index patients who are children <5. We will exclude households for which the index patient reports <2 contacts over age 14, those who live outside of greater Kampala and those diagnosed with MDR-TB for both Aims of the study. 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 days or 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.

For the FGDs, we will include health workers engaged in contact investigation for TB and HIV.

7. Subject classification: Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

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☐Children	☒ Healthy	☐Fetal material, placenta, or dead fetus
☒Non-English Speaking	☐ Prisoners	☒Economically disadvantaged persons
☐Decisionally Impaired	☒ Employees	☒Pregnant women and/or fetuses
☐Yale Students	☒ Females of childbearing potential	

We will carry out focus group discussions and interviews with health workers affiliated with the Kampala Capital City Authority TB units. This is necessary because these health workers have substantial firsthand experience offering HIV testing during household contact investigation for TB and thus are uniquely positioned to offer insight into how to increase the appeal of HIV testing to clients. Recordings of interviews or focus group discussions with health workers will be kept in a password-protected drive and destroyed after transcription. All transcripts will be de-identified, and information will be kept in confidence. We will also request a waiver of written consent to minimize risk of disclosure.

Additionally, TB is a disease with a high incidence among the vulnerable populations listed, and thus it is important to include these patients in order to develop generalizable knowledge and ensure an intervention is designed with input from those who it is targeting.

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?

Yes ☐ No ☒

8. Inclusion/Exclusion Criteria: What are the criteria used to determine subject inclusion or exclusion?

Aim 1 Inclusion/Exclusion Criteria:

Households: We will only include households who meet the Uganda National TB programme guidelines for household contact investigation as outlined below. Additionally, we will only include households with a sufficient number of adults to test study hypotheses about HIV testing.

Inclusion:

- Has an index patient ≥5 years of age with microbiologically confirmed TB
- Has an index patient <5 years of age with confirmed TB

Exclusion:

- Fewer than 2 household contacts over age 14

Contacts: We will include all adult household contacts of TB patients.

Inclusion:

- Household contact to a TB patient
- ≥15 years of age

For the FGDs, we will include health workers employed in Kampala Capital City Authority clinics who are engaged in contact investigation for TB and HIV.

Aim 2 Inclusion/Exclusion Criteria:

Households: We will only include households who meet the Uganda National TB programme guidelines for household contact investigation as outlined below. Additionally, we will only include households with

a sufficient number of adults (at least 2 individuals age 15 or above) to test study hypotheses about HIV testing.

Inclusion:

- Has an index patient with microbiologically confirmed TB
- Has an index patient with confirmed TB via clinical diagnosis

Exclusion:

- Fewer than 2 household contacts over age 14
- Lives outside of greater Kampala area

Contacts: We will include all adult household contacts of TB patients.
Inclusion:

- Household contact to a TB patient
- ≥15 years of age

9. How will **eligibility** be determined, and by whom? Write here

Eligibility of households and individual clients will be determined according to answers to routine screening questions used during household contact investigation by the lay health worker carrying our household contact investigation. If the individual is eligible, the lay health worker will invite them to the study.

For interviews with health care workers, individuals will be identified by the study team based on the employment records at the health centres of interest in Kampala, Uganda.

10. **Risks:** Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

There are minimal risks to participants in this study. The primary risks to both index TB patients and to 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. The primary research risks for health-care workers arising from the qualitative studies are the potentially punitive actions by the employer in response to the information they provide for research.

11. **Minimizing Risks:** Describe the manner in which the above-mentioned risks will be minimized.

As is done in routine practice, lay 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.

Recordings of interviews or focus group discussions with health workers or household contacts will be kept in a password-protected drive and destroyed after transcription. All transcripts will be de-identified, and information will be kept in confidence.

To minimize risk of loss of privacy or confidentiality, we will carry out a verbal informed consent process using the attached research study information sheets.

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12. **Data and Safety Monitoring Plan:** Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.)
    a. What is the investigator's assessment of the overall risk level for subjects participating in this study? Minimal
    b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? N/A
    c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here http://your.yale.edu/policies-procedures/forms/420-fr-01-data-and-safety-monitoring-plans-templates for
        i. Minimal risk
        ii. Greater than minimal

    d. For multi-site studies for which the Yale PI serves as the lead investigator: N/A

The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency (quarterly). During the review process the principal investigator will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

The principal investigator and the Institutional Review Board (IRB) have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies.

The investigator will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project through 1) weekly study meetings carried out via teleconference during and immediately following the data collection period, or 2) via email as they are reviewed by the principal investigator. The protocol's research monitor(s), Fogarty International Center of NIH (sponsor/funder) and the relevant IRB of Makerere University (local collaborator/host) will be informed of any UPIRSO, including adverse events, or Reportable Event within 5 days of the event becoming known to the principal investigator.

13. **Statistical Considerations:** Describe the statistical analyses that support the study design.

Aim 1 is a formative qualitative study to refine an intervention; it is not designed for statistical tests. Based on the findings of the formative study described here, the study team will specify the final intervention and submit a modification to this protocol for a pilot study evaluating that intervention.

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In the Aim 2 analysis, we will calculate and compare uptake across each of the trial arms using an intention-to-treat analysis. We will also consider a per protocol analysis and model adjusted for imbalances in baseline confounders as secondary analyses. 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 invitation scripts that apply acceptance-optimized sequencing of oral test offers 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 conduct a causal mediation analysis to determine to what degree 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.

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SECTION II: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, check off N/A and delete the rest of the section.

A. RADIOTRACERS ☒N/A
B. DRUGS/BIOLOGICS ☒N/A
B. DEVICES ☒N/A

SECTION III: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. Targeted Enrollment: Give the number of subjects:
   a. Targeted for enrollment at Yale for this protocol: 0
   b. If this is a multi-site study, give the total number of subjects targeted across all sites:
   -40 to 60 individuals drawn from 20 households (Aim 1)
   -Approximately 8 to 15 lay health workers with experience carrying out TB contact investigation
   -Approximately 60-100 health workers participating in HIV and TB care services during the COVID-19 pandemic
   - Approximately 152 index patients and their approximately 304 household contacts (Aim 2)

2. Indicate recruitment methods below. Attach copies of any recruitment materials that will be used.

☐ Flyers	☐ Internet/web postings	☐ Radio
☐ Posters	☐ Mass email solicitation	☐ Telephone
☐ Letter	☐ Departmental/Center website	☐ Television
☐ Medical record review*	☐ Departmental/Center research boards	☐ Newspaper
☐ Departmental/Center newsletters	☐ Web-based clinical trial registries	☐ Clinicaltrails.gov
☐ YCCI Recruitment database	☐ Social Media (Twitter/Facebook):	
☒ Other: Lay health worker invitation		

* Requests for medical records should be made through JDAT as described at
http://medicine.yale.edu/ycci/oncore/availableservices/datarequests/datarequests.aspx

3. Recruitment Procedures:

a. Describe how potential subjects will be identified. Lay health workers will invite eligible index patients to invite them and their households to the study.. For the FGDs, study staff will invite current lay health worker employees to participate by telephone at their workplace, during normal business hours. For health workers involved in the cohort during the COVID-19 pandemic, study staff will invite health care workers involved in HIV and TB care services whom study staff have identified through consortium health care sites, existing study sites, or through partner relationships to participate via telephone.

b. Describe how potential subjects are contacted.
   -Eligible index patients will be verbally invited to participate when they are offered routine household contact investigation
   -Eligible household contacts of consenting index patients will be verbally invited to participate during household contact investigation for TB
   - For the FGDs, lay health workers will receive a telephone invitation to voluntarily participate in a single focus group discussion.

- For the health worker COVID cohort, health workers will receive a telephone invitation to voluntarily participate in several short interviews or surveys about the effect of the pandemic on their own experiences and the delivery of services for HIV and TB

c.

Who is recruiting potential subjects?

-Lay health workers will recruit eligible household contacts they encounter during household contact investigation for TB.

-For the health worker, a researcher from Makerere University's Uganda TB Implementation Research Consortium will recruit potential participants.

4. Assessment of Current Health Provider Relationship for HIPAA Consideration:

Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

☐Yes, all subjects

☐Yes, some of the subjects

☒No

If yes, describe the nature of this relationship. *Write here*

5. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.) This is an international study, not subject to HIPAA.

The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

6. Process of Consent/Assent: Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

All patients and their household contacts will receive a verbal invitation to participate in accordance with National TB guidelines. Additionally, all willing and eligible index patients and their household contacts will be asked to review the research study information sheet /verbal informed consent document outlining all study related activities, then provide verbal consent to participate in the study. Lay health workers trained in administering informed consent procedures, Human Subjects' Protection and Good Clinical Practice will carry out and document all verbal informed consent encounters. For participants under age 18 who do not meet the definition of an emancipated minor, permission to participate will be obtained from a parent or legal guardian. Among index patients, children aged 14-17 must provide assent to participate after their parent provides permission. Among contacts, only household members 15 years of age or older will be eligible for HIV testing; those aged 15-17 must provide assent to participate after their parent provides permission.

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After a participant agrees to participate and/or a parent provides permission, the lay health worker will carry out the routine contact investigation procedures, recording clinical and demographic information about the patient on an electronic tablet. This information will include names and ages of all household members, contact telephone numbers for the index patient and a treatment supporter.

7. Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent: Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

8. Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use.
   Subjects who do not speak English or Luganda will be excluded from this formative study. All LHWs administering study protocol will be fluent in both English and Luganda. All consent forms will be available in both English and Luganda and will be administered in the language of preference.

As a limited alternative to the above requirement, will you use the short form* for consenting process if you unexpectedly encounter a non-English speaking individual interested in study participation and the translation of the long form is not possible prior to intended enrollment? YES ☐ NO ☒

Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

Several translated short form templates are available on the HRPP website (yale.edu/hrpp) and translated HIPAA Research Authorization Forms are available on the HIPAA website (hipaa.yale.edu). If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via modification prior to enrolling the subject. *Please review the guidance and presentation on use of the short form available on the HRPP website.*

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

9. Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study. If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

☐Not Requesting any consent waivers

☒Requesting a waiver of signed consent:

☐ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☒ Entire Study – We will obtain verbal consent from household contacts participating in interviews and intervention optimization and piloting using the attached informed consent information sheets. We will obtain verbal consent from health workers also.

For a waiver of signed consent, address the following:

- Would the signed consent form be the only record linking the subject and the research? YES ☒ NO ☐
- Does a breach of confidentiality constitute the principal risk to subjects? YES ☒ NO ☐

OR

- Does the research pose greater than minimal risk? YES ☐ NO☒
- Does the research include any activities that would require signed consent in a non-research context? YES ☐ NO ☒

SECTION IV: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

1. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research? We will collect individual age, gender, occupation (if applicable), relationship to index patient, history of testing for HIV, month and year of last test, and self-reported symptoms of TB (including cough, subjective fever, or weight loss).

2. How will the research data be collected, recorded and stored? Focus group data along with any interview data will be digitally recorded and transcribed. Audio recordings will be destroyed when transcription is complete. All qualitative data will be de-identified at a point in time when deemed appropriate by the PI. Households interview data will be collected using password protected tablets with a secure data capture application and stored on a secured server.

3. How will the digital data be stored? ☐CD ☐DVD ☐Flash Drive ☐Portable Hard Drive ☒Secured Server ☐Laptop Computer ☒Desktop Computer ☐Other

4. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?

   The lay 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.

   HIV results will be stored using a custom-built, secure clinical data capture application called Commcare (Dimagi, Cambridge, MA). Community health workers have previously used this application for secure data collection during household contact investigation and home HIV testing offers.

   The audio files from qualitative data collection will be stored on a secure, encrypted, password-protected drive in the research offices in Uganda. All names inadvertently used during the discussions will be replaced by number-based aliases (e.g., Participant #1) in the final transcripts. Transcripts will be entered into a password-protected software program and only members of the research team will

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have access to this program. Hard copies of transcripts will be kept in a locked file cabinet. Audio files will be destroyed once transcripts are complete.

A positive HIV test is not reportable to the Ugandan government by law. The 2016 Uganda National HIV Testing Guidelines state throughout (e.g., page 10, Privacy and Confidentiality) that HIV results may only be reported or recorded with individual patient consent. Test results will only be shared with the clinic or added to their patient record if patients give verbal consent to do so.

All portable devices must contain encryption software, per University Policy 5100. If there is a technical reason a device cannot be encrypted please submit an exception request to the Information Security, Policy and Compliance Office by clicking on url http://its.yale.edu/egrc or email it.compliance@yale.edu

5. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.
   Identifiers will be destroyed upon completion of transcription and qualitative analysis.

6. If appropriate, has a Certificate of Confidentiality been obtained? *N/A*

SECTION V: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

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 of 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.

SECTION VI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. Alternatives: What other alternatives are available to the study subjects outside of the research?
   Any individual may choose not to participate at any time. Participation or non-participation will not affect their access to routine contact investigation services.
2. Payments for Participation (Economic Considerations): Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.
   No payments will be made to participants.
   Health care workers will receive 20,000 UGX (approximately $5.50 USD) for participation in interviews
3. Costs for Participation (Economic Considerations): Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.
   There are no costs to participants.

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4. **In Case of Injury:** This section is required for any research involving more than minimal risk, and for minimal risk research that presents the potential for physical harm (e.g., research involving blood draws).

    a. Will medical treatment be available if research-related injury occurs? *N/A*

    b. Where and from whom may treatment be obtained? *N/A*
    c. Are there any limits to the treatment being provided? *N/A*
    d. Who will pay for this treatment? *N/A*
    e. How will the medical treatment be accessed by subjects? *N/A*

IMPORTANT REMINDERS

Will this study have a billable service? Yes ☐ No☒

A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient's insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include x-rays, MRIs, CT scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study's funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.

If answered, "yes", this study will need to be set up in OnCore, Yale's clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities?
Yes ☐ No ☒

IMPORTANT REMINDER ABOUT RESEARCH AT YNHH

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. **By submitting this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.**

APPROVED BY THE YALE UNIVERSITY IRB 6/29/2021