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

Protocol Title: Human-centered Design and Communities of Practice to Improve Delivery of Home-based Tuberculosis Contact Investigation in Uganda

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(*If applicable*) **Clinicaltrials.gov Registration #:** Click or tap here to enter text. NCT05640648

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.

   In a previous randomized control trial, we identified gaps in the tuberculosis (TB) contact investigation cascade in terms of implementation. We are now proposing to work on quality improvement to the routine contact investigation procedures. We will do this using Human-centered design (HCD) and Communities of Practice (CoP), two novel and under-studied strategies for facilitating effective and sustainable implementation. The first phase of this study is formative, as we will explore stakeholder preferences for how contact investigation can be best delivered by applying the HCD and CoP methodologies. The deliverable for this phase will be a well-defined implementation strategy for household contact investigation that will be evaluated in a prospective, randomized, controlled trial for phase two.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.
   The expected duration of the project is 5 years.

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.

The Global STOP TB Partnership has set the ambitious goal of eliminating tuberculosis (TB) by 2050.[1] Since 1990, when TB was recognized as a global crisis and the DOTS Strategy was initiated, TB control programs have prioritized "passive" case finding, in which TB patients self-refer to health centres. Unfortunately, it has recently become evident that passive case finding is inadequate to achieve the 16% annual decline in incidence needed for TB elimination.[2] Moreover, passive case finding leaves symptomatic cases in the community where they continue to transmit TB, and neglects vulnerable populations including children, people living with HIV, and the poor. These groups bear a disproportionate burden of TB morbidity and face difficulties in traveling to clinics for evaluation.[3] Uganda is one of WHO's designated "high HIV-TB-burden countries," with an annual TB incidence of 234/100,000, an HIV prevalence of 5%, and approximately half of all notified cases of TB occurring among persons living with HIV (PLHIV).[4-6] Furthermore, almost half of all identified TB cases in Uganda's recent TB prevalence survey had never sought TB evaluation.[5] Therefore a major priority of the 2017 Revised Uganda National TB and Leprosy Programme Strategy is to develop novel strategies for identifying undiagnosed individuals with TB and rapidly linking them to care.[7]

To address these problems, there is a need to extend TB case-detection and treatment services into the community through "active" case-finding strategies. One such approach is household contact investigation, which involves 1) locating household contacts of index TB patients at the time of diagnosis and treatment initiation, 2) visiting the households to screen contacts for TB symptoms, and 3) referring contacts who screen positive to clinics for TB evaluation and testing. Contact investigation has a high yield for identifying active TB cases; systematic reviews show that, in low-income countries, 3.3-4.5% of household members of TB patients will have active TB.[8] In addition to the benefits to the individuals diagnosed, active case-finding strategies may also reduce the overall burden of TB in the population through earlier diagnosis and treatment and consequent reduced transmission. A recent cluster-randomized trial from southern Africa found that community-wide household contact investigation may reduce TB prevalence by 18% and TB transmission by 55%.[9]

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In 2011, WHO recommended that TB contact investigation be routinely implemented in high-burden countries.[10] Similarly, Uganda's 2010 National TB guidelines endorse household TB contact investigation, and task village health teams attached to every primary health unit with this responsibility, although until recently this was not being done routinely.[11] However, several pilot studies have measured the yield of contact investigation in Uganda[12-14], and over the last four years, Uganda has introduced household contact investigation throughout Kampala District. Our Makerere-based research group, the Uganda TB Implementation Research Consortium (U-TIRC), has been leading an operational evaluation of barriers to and facilitators of household contact investigation in this context. This work led to a randomized, controlled trial of novel behaviourally-informed interventions to improve implementation of contact investigation, including home-based evaluation for TB and HIV, and SMS-facilitated linkage of newly diagnosed individuals to care and treatment. The detailed results of these evaluations are described in the literature review below, but the overall finding of these studies is that major gaps exist in delivering home-based TB evaluation services to household contacts. Additional implementation research is thus needed to better engage household contacts and community health workers in these activities. Therefore, the overall objective of the new research program proposed here is to pilot novel strategies for quality improvement in the routine public health system, in collaboration with the Kampala Capital City Authority and the Uganda National TB and Leprosy Programme. The two strategies that we propose to use are *human-centered design* and *communities of practice*.

Human-centered design (**HCD**) is "a creative approach to problem-solving which seeks to understand problems from the perspective of the people [one is] designing for, in hope of arriving at unexpected answers they will embrace."[15] Widely used to re-engineer consumer products and experiences outside health, HCD provides a conceptual framework for creating more effective interventions through a set of methods and a philosophy centered around "empathy [for end users], context, ideation and iteration."[16] The goal is to be able to tailor solutions that are feasible, affordable, and, most of all, desirable to users.[17, 18] To our knowledge, HCD has not been previously used to find remedies for barriers to delivery of TB services. Thus, if effective in this setting, there is an opportunity for wider application and rigorous evaluation of HCD for other similar delivery problems in TB and beyond.[19]

Communities of Practice (**CoP**) are groups of professionals organized for peer support and systematic learning. CoP offer an adaptive, user-driven framework to promote collaborative problem-solving and continuous process improvement in health care.[20, 21] CoPs work through a variation on experiential learning, but are able to accelerate the acquisition of expertise by creating a fertile environment for sharing and making tacit knowledge explicit.[22, 23] To date, this approach has not been widely used to improve TB care outside the use of certain specialized settings, such as training of practitioners to manage drug-resistant tuberculosis.[24]

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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.

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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.

Our *research question* is to determine if a human-centered design approach to quality improvement delivered through health worker communities of practice is feasible and acceptable, and if it is likely to be efficient and effective for improving delivery of routine home-based TB contact investigation. Our *hypothesis* is that a quality improvement process employing human-centered design and delivered through health worker communities of practice will prove feasible and acceptable to health workers and is likely to be efficacious and effective for improving delivery of routine household TB contact investigation.

Our *specific objectives* are:

Phase 1:

(1) to determine under what circumstances human-centered design and communities of practice are feasible and acceptable for delivering routine household TB contact investigation, and

(2) to measure how the efficiency and effectiveness of the delivery of routine household TB contact investigation change over time following introduction of a quality improvement strategy employing human-centered design and communities of practice.

Phase 2:

(3) implement and evaluate a novel implementation strategy consisting of implementation facilitation and continuous quality improvement

To address our primary objective, we propose a *mixed-methods study* to determine the feasibility and acceptability of human-centered design and communities of practice as a way of delivering quality improvement interventions for household TB contact investigation. To address our secondary objective, we propose a concurrent, *prospective longitudinal study* to collect preliminary estimates of the change in efficiency and effectiveness of household contact investigation with quality improvement activities using *interrupted time-series analyses*. For our third objective, we will carry out a prospective, stepped-wedge, cluster-randomized trial in 12 sites in Central Uganda.

Setting

The proposed quality improvement activities will take place within the Uganda Ministry of Health primary health clinics (designated as Level IV clinics by the Uganda MOH, the highest level of free-standing clinic not affiliated with a hospital). We have selected three representative sites for our formative activities (Kawaala, Kiswa, and Mukono) based on several criteria. Eligible sites had to (1) be public, primary care clinics that offer TB evaluation services with GeneXpert rapid molecular testing for TB as the primary test; (2) currently diagnose at least 20 TB patients per month; (3) currently offer household TB contact investigation led by a team of community health workers and facility-based health workers; and (4) have sufficient capacity for diagnostic evaluation and treatment to accommodate additional possible and confirmed TB patients among the household contacts of index TB patients referred for these services.

For Phase Two, in which we will be evaluating the human center designed implementation strategy through a step wedge trial, we will conduct the trial at 12 sites, selected from a list of 15. We are including 3 additional sites as alternates during the pre-trial preparations, because of an anticipated 20% dropout rate among enrolled sites that might occur because of changing circumstances or leadership at the sites in the pre-trial period. These sites were selected due to the availability of a GeneXpert machine for TB testing, volume of clients in a given month (at least 12 newly diagnosed TB patients) and other institutional factors such as reliable electricity, water etc. For study feasibility, only health centres within 150km of Kampala, Uganda were eligible.

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Study activities

Community health workers experienced in delivering household TB contact investigation in Kampala as part of its previous programmatic introduction by National Tuberculosis and Leprosy Programme (NTLP) and our previous operational evaluation will be re-trained by a representative of the NTLP in household contact investigation procedures with assistance from our research team. This training will include a refresher course in electronic data capture of routine TB contact investigation data from the official TB registers and/or from participants themselves. The expected duration of the training will be two days.

Community of practice intervention development activities

For our mixed-methods analyses focused on feasibility, we will audio-record the regular quality improvement sessions convened by the community health workers at the two clinics. For follow-up data collection about acceptability, we will develop interview and focus group discussion guides with approximately six-to-eight relevant questions based on our analyses of the recorded quality improvement sessions. We will engage approximately eight community health workers plus the available clinic-based health care workers doing TB work (currently five staff members per clinic for a projected total of 10 health care workers), providing for an estimated total sample size of approximately 18 community- or clinic-based health workers. Empirical studies of qualitative methodology show that "saturation," the point at which no new themes or information appear and conclusions can be reached, typically requires only 10 to 15 subjects.

Human-centered design intervention development activities

IDEO.org's multidisciplinary teams of designers, engineers, human factors specialists, and business strategists (henceforth these will be referred to as "the design team," or simply as the designers) use a mix of exercises and innovative strategies to identify the needs, wants, and desires of the target communities and to navigate the contextual social, business, environmental, and technological nuances of the issues they are addressing and problems they are solving. The design team aims to identify delivery strategies that are desirable to the end-user.

Human-centered design entails a multi-phased process. The objective of Stage I (the so-called "Inspiration Stage") is to develop an understanding of the community context, gain insights into the population and processes of interest, identify unmet needs and opportunities for design, and gather feedback on early intervention concepts that emerge during Stage I interviews.

In Stage II (the "Ideation Stage"), data from Stage I are analysed and synthesized to summarize preliminary findings. These findings help identify the user needs that will become the focus for design and intervention development. The study team generates potential ideas and concepts to take forward in future interviews and interactions with participants. Using an iterative approach, new ideas and concepts are shared with end-users, to obtain and incorporate feedback in several cycles of idea generation. The design team also works closely with Ministry of Health, local stakeholders and researchers to ensure that emerging solutions are desirable for end-users.

In Stage III (the "Prototyping Stage"), the designers will test the new strategy among small groups of individuals and solicit feedback on the new strategy, involving key informants as they did in Stage I. The objectives at this stage are to ensure the proposed quality improvement intervention is acceptable and feasible for the TB programme and other key implementers. This stage will involve minor redesigns based on feedback received from the proposed strategy. At the end of this stage, an intervention designed to improve TB contact investigation will be finalized.

The human-centered design process may require participation from the participants themselves (i.e. index patients and household contacts). In addition, the design team will seek input from community members where

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TB prevalence is high and from those routinely involved in quality improvement activities within the health system, especially if their input or perspectives are required to improve an aspect of contact investigation. We will structure such activities as mixed-methods data collection procedures, and obtain verbal consent from community members, index patients and their contacts, since participation of clients in quality improvement procedures is not standard practice in Uganda. We will develop interview and focus group discussion (FGD) guides with approximately six-to-eight relevant questions per session based on the specific quality-improvement objectives. These guides may include some activities that help participants open up about their experiences and opinions (see supporting document Interview and FGD sample activities). Participants will not be required to provide personal identifying information, although age and gender of participants will be recorded. Participants will be modestly compensated in the amount of 10,000 Uganda Shillings (approximately USD $3) for their time and transport costs in participating these sessions, which will last no more than 60-90 minutes. This is a well-accepted amount of compensation for the time required to participate in community-based studies; this amount is commonly approved by local IRBs and not considered coercive.

During the human-centered design process, we will also initiate Community of Practice (CoP) activities to facilitate quality improvement of household TB contact investigation. CoP activities include regular meetings of community and facility-based health workers; structured review of routine data on the contact investigation delivery cascade; discussion of the effects of previous delivery innovations; formulation and documentation of quality improvement goals and innovations to achieve them; and coordination by a thought leader. We will collect qualitative and quantitative process data to refine the CoP components and adapt them to the needs and preferences of community health workers and other stakeholders, including TB unit and health centre staff. At the conclusion of the pilot, we will carry out interviews and focus group discussions with participating community health workers to invite feedback for improvement and scale-up of CoP activities.

Stepped Wedge Implementation Trial

We previously completed mixed-methods studies during the formative and design research phase of the project, and now are initiating the implementation and evaluation phases of the study.

To achieve the objectives outlined above for the implementation and evaluation phase, we will carry out a stepped-wedge, cluster-randomized implementation trial at TB treatment units within clinics and hospitals in Central Uganda, with nested mixed-methods, health economic, and modelling studies. The design of this implementation trial will allow us to determine the effectiveness of the proposed implementation strategy and also characterize its fidelity and context, costs, and epidemiological impact relative to standard implementation practices for TB contact investigation. The primary outcomes of the study will be the proportion and counts of eligible contacts who complete TB evaluation; secondary outcomes will include the proportion and counts of identified contacts diagnosed with and initiated on treatment for active TB.

Randomization

Following a baseline two-month period of data collection, the intervention strategy will be introduced at two new sites every 2 months until all 12 sites (6 pairs) have transitioned from the usual care to the intervention (Figure 1).

		Month															
Block	**Site**	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1	1 2			1st													

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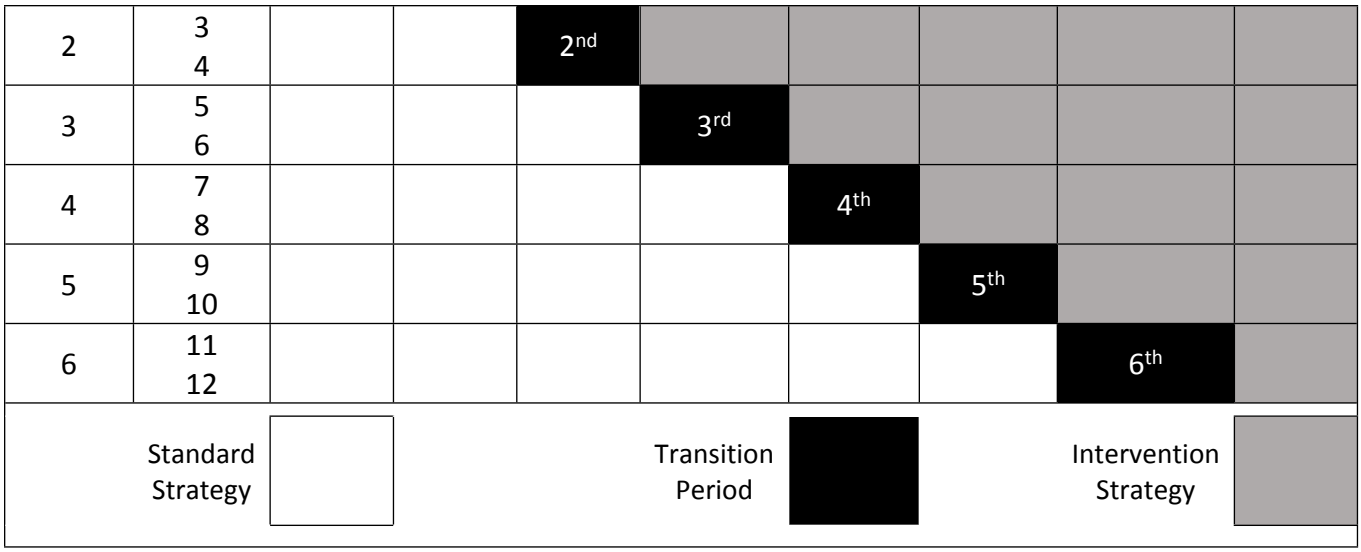

Figure 1: Stepped-Wedge Implementation Trial Design

With guidance by the study statistician, the 12 health facilities will be randomly assigned to one of the six allocation blocks (figure below) using a simple two-stage process, restricted by clinic volume. This sequence of allocation will be determined through a simple random drawing during a public randomization ceremony held in Kampala, Uganda. For example, a senior clinician representative of each health center (*e.g.,* the TB focal person), the Health Facility Administrator-in-Charge, and the District Health Officer will be invited to attend a public randomization ceremony chaired by the Uganda NTLP Director. First, health facilities will be randomly assigned with restriction into six blocks of two by having one clinician from each health facility draw 1 of 6 balls (labelled A, B, C, D, E, F) from each of two opaque bags (one including high volume sites, another low volume sites), without replacement. Blocks will then be randomly assigned to an intervention initiation sequence by asking a senior NTLP representative to draw 6 numbered balls (1-6) from an opaque bag. The first number drawn will represent the initiation time assigned to Block A, the second to Block B, and so on, until all six blocks have been assigned a place in the sequence. The sequence will progress at equally spaced, 2-month intervals during the trial period, starting at the beginning of month 3.

Blinding

Blinding of the assigned intervention is not feasible with the stepped-wedge cluster randomized implementation trial design, because interventions are implemented at the health facility level and all health facilities receive both the usual care and the intervention strategies. Community Health Workers will collect all data, and adjudicate all outcomes, except TB diagnoses and treatments initiated. Where possible, the investigators and study staff, with the exception of the statistician and data manager, will be blinded to any aggregated analysis of TB outcomes by study period.

Interventions

The table below provides an overview of the standard NTLP-recommended TB contact investigation procedures (column 1) at each of the three principal time venues and visits, and two different strategies for implementing these procedures, the Usual Care strategy (column 2) and our Intervention Strategy procedures (columns 3 and 4). The intervention strategy includes two major components, the *implementation facilitation package* and the *continuous quality improvement package*. All of the implementation facilitation tools are added to the usual care strategy to provide community health workers with additional options for implementing the contact investigation procedures, while the continuous quality improvement package provides tools for community health workers to improve the implementation and maintenance of the tools.

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Visit/Venue	Usual Care Strategy	Intervention Strategy (Usual Care+)	
Standard NTLP contact investigation procedures	Standard CHW Implementation	Implementation Facilitation plus	Continuous Quality Improvement
1. TB Unit Index Case Visit a. Invite cases to participate in contact investigation b. Enumerate Household/close contacts	CHW- driven education CHW-driven enumeration	1. TB Education Pamphlet 2. Contact Identification Tool	
2. Home or Community Contact Visit(s) a. Invite contacts to TB screening b. Contact intake & symptom screening c. Collect TB specimens or refer to TB unit - Expectorate sputum collection if symptoms & ≥5 years - Refer if symptoms & <5years - Refer if symptoms & not producing sputum d. CHWs transport specimens to lab - GeneXpert MTB Ultra Testing e. Results Reporting f. Clinical evaluation +/- chest radiography	CHW-instructed expectoration CHW collects sputum CHW transports sputum to TB lab Contact transports self to clinic	3. Sputum Collection Video 4. Community Health Riders - CHR collects sputum CHR transports sputum to TB lab CHR transports contact to TB unit	1. Community of Practice Meetings 2. Audit & Feedback Reports 3. Group Chat Application
3. TB Unit Contact Visit - Offer TB treatment if active TB diagnosed - Offer TB preventative Therapy if active TB excluded			

TB education pamphlet
The TB education pamphlet seeks to provide the index TB patient with basic education on TB including but not limited to how it is spread, how to prevent TB and information on how to contact their health care worker. All items in the TB education pamphlet are derived from the NTLP resources, suggestions from TB health care workers and WHO guidelines on the rights of TB patients.

Contact Identification tool
Index patients often have difficulty enumerating their close contacts accurately. In order to standardize the process of contact enumeration, a contact identification tool was developed that allows for standardized conversations about areas where the index patient may spend a lot of time (such as home, work, religious gatherings etc.) using prompts such as "Where do you sleep?", "Do you attend a church, mosque or other religious gathering?" and "Do you have a job outside of your home?". After the index patient identifies locations where they spend their time, the CHW can then individually prompt the index patient to think about contacts at each location type and gather basic information about contacts from that location such as name, phone number and relationship to the index patient. This tool has been integrated into the CommCare (Dimagi, Cambridge, MA) digital survey application and is therefore an electronic tool that is secured with HIPAA level protections and encrypted.

Sputum Collection Video
Originally developed by InTuneForLife, a non-profit organization, this sputum collection video has been used throughout Africa to standardize sputum collection and encourage contacts to produce adequate and quality samples. This video is integrated into the CommCare application and can be shown to contacts directly in the household.

Community Health Riders
As many contacts and index patients find it difficult to be at home for in person visits or have timely transportation to/from the health centre, we designed a system of Community Health Riders (CHRs). CHRs are *boda* drivers (motorcycle taxis that are among the most common form of transport in Uganda) that can go to the contacts' location to collect any necessary samples (as determined by a CHW), return them to the TB lab as well as provide transport to and from the health centre for index patients, their contacts and even CHWs as necessary. The CHRs will not have access to personal health information (PHI) but will be equipped with smart phones that contain the sputum collection video (see above) to encourage contact expectoration among the contacts they visit. CHRs will be trained (see below) in the proper handling and transport of medical specimens including but not limited to the donning and doffing of appropriate health safety equipment and road safety measures.

Training of research assistants
Community health workers at participating sites will receive a refresher training in contact investigation following the protocols recommended by the Uganda NTLP (usual care), as well as orientation to collecting all contact investigation data on electronic tablets using case record forms and a secure data capture platform (CommCare) that has been used to collect standard contact investigation data in Kampala for over five years, with periodic refinements.

Trainers from Walimu, a non-profit organization specializing in building capacity in Ugandan health systems, will organize and deliver an ~5-day training of all community health workers, TB focal persons, and other TB unit personnel in TB contact investigation. The Walimu trainers will adapt education and training materials from the Uganda Ministry of Health Contact Investigation Operational Guide, supplemented by other relevant Ministry of

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Health guidelines. Participating CHWs will also receive training on tablet-based data collection and use of the CommCare survey application.

Training on Intervention Strategy (Implementation Facilitation + Continuous Quality Improvement)
Trainers from Walimu will organize and deliver a ~3-5-day training on the optimized intervention strategy for delivery of TB contact investigation to all community health workers at two new sites, every two months, according to the waitlist scheme established during randomization. Additionally, all CHRs will be trained in proper sputum handling techniques, road safety measures and any other health and safety guidelines as advised by the Uganda Ministry of Health to ensure proper health safety protocols are followed. After the in-person training, there will be a ~2-day follow-up supervisory visit after one week of experience with the new components. Participating CHWs will also receive orientation to changes in the CommCare survey application related to the intervention strategy.

Data Capture

For the objectives of assessing the preliminary efficiency and effectiveness of novel quality improvement strategies, we will collect the necessary data using electronic data capture with commercial software, CommCare (Dimagi, Inc. Cambridge, MA), that has been designed for data collection by community health workers on mobile devices in low-income countries. CommCare utilizes encryption and has high levels of data protection (HIPAA standards) to ensure patient confidentiality and data safety. Data will be entered on wirelessly connected (3G or 4G) Android tablets. Data entry can occur offline and will automatically upload to the secure server whenever connectivity is detected. All data will be of a routine nature as defined by locally approved guidelines on household TB contact investigation, obtainable from clinic registers and from the participants themselves.

Sample Size
Community health workers in twelve clinics will identify at least 588 symptomatic contacts (*i.e.* possible TB patients) among 1764 household and close contacts in approximately 2304 eligible index patient clusters over a 16-month period, or up to 7 contacts needing evaluation for TB per referring clinic during each two-month block. With this sample size, assuming a clinic intra-cluster correlation coefficient (ICC) of 0.043 and within-index- patient-cluster ICC of 0.7, and accounting for covariates, we will have 83% power to detect a 15% or greater increase in the proportion completing evaluation from 20% to 35%, at alpha of 0.05, following crossover to the intervention. These estimates account for the proposed stepped-wedge design with 6 steps and a one-step transition period (*i.e.,* an "incomplete" design) at each site. Sample size estimates were reached using PASS 15 and Stata 14, with an extension to account for multiple levels of clustering as per Hemming et al. because index patients and contacts are participants in routine services, and the design of a stepped wedge trial has a fixed duration, we will not limit enrollment if it exceeds these numbers, which may be up to four-fold higher in some or all sites, or more if the intervention strategy is highly effective. For example, if up to 1932 symptomatic contacts, or 23 contacts needing evaluation for TB per referring clinic are identified during each two-month block, we would have 91% power to detect a 10% or greater proportion increase in the proportion completing evaluation from 20% to 30%, at alpha of 0.05, assuming the above noted ICCs.

Evaluation of the fidelity of the intervention strategy
We will propose parallel convergent mixed-methods studies involving quantitative assessments of the fidelity of the implementation strategy and its behavioral mechanisms, using validated psychosocial scales, and we will assess other aspects of fidelity, adaptation, and context through qualitative studies involving interviews and focus group discussions with cases, contacts, community health workers, and community health riders.

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However, prior to that, we describe our plans in this protocol to validate quantitative study instruments.

Quantitative studies
In preparation for nested studies of behavioral mediators of the effects of the continuous quality improvement intervention, we propose a non-human subjects study in which we will recruit up to 200 community health workers at Kampala and (if needed) Mukono sites used in our prior consortium research to validate a general self-efficacy scale and a psychological safety scale using the Uganda-Validated 13-item Center for Epidemiologic Studies Depression scale. We will not collect any personal health identifiers.

Brief Background to Scale Validation Study
Community health workers are commonly used to screen people for tuberculosis (TB) in high- burden settings; however, they have minimal prior clinical experience, which impacts their ability to efficiently screen patients for TB. As outlined in the description of the continuous quality improvement component of the intervention strategy, organizing Community health workers into a formal group, or Community of Practice (CoP), that has regular meetings to discuss their challenges and brainstorm solutions could be an effective way to improve their performance. Understanding the mechanisms through which CoPs do, or do not, lead to improvements in TB care is critical to identify how and under what conditions they should be implemented. For example, we hypothesize that self-efficacy is a mediator through which CoPs improve the delivery of TB care based on preliminary research from a pilot study. We also hypothesize that psychological safety modifies the effect of CoPs on the delivery of TB services. To test these hypotheses, we aim to first conduct cross-cultural validation studies of two widely used scales: the General Self-Efficacy Scale and the Psychological Safety Scale.

Measures
The General Self-Efficacy Scale includes 10 items that measure an individual's self-perceived ability to perform a novel or difficult task. Cross-cultural studies have determined high reliability, stability and construct validity of the General Self Efficacy scale in 25 diverse countries. The Psychological Safety Scale includes 7-items that measure individual's beliefs and comfort level to speak up in teams. Although this scale has not yet been deployed in Uganda, it has been used to assess hospital-based quality improvement teams in Ghana.

Design
We will adapt, pilot, and assess the reliability and validity of the 10-item General Self-Efficacy Scale (Appendix 1) and 7-item Psychological Safety Scale (Appendix 2) among community health workers not involved in the CoP trial. We will use similar methods as other studies that have adapted and validated these scales for use in other contexts. First, we will work with local partners at U-TIRC and Makerere to adapt scale questions. We will consult local experts who have conducted extensive qualitative research with community health workers and /or supervised the pilot CoP to assess linguistic/cultural appropriateness and content validity of the items.

Second, the scale will be translated from English to Luganda and back-translated into English again to verify translation. We will work with local translators who have previously worked with our team. We will resolve any translation discrepancies through discussion with local translators and our research team.

Third, we will pilot the adapted scales on a group of approximately 200 community health workers not involved in the present study. We will recruit community health workers through longstanding partnerships with community health workers and researchers in Kampala using a convenience sampling approach. Specifically, we will invite up to around 12 community health workers currently working on contact investigation at the formative research sites (Kisenyi, Kawaala, Kiswa, Mukono) as the first participants, and encourage additional participants through snowball sampling. Community health workers will be given the option of taking the English

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or Luganda versions of the scales. The surveys will be administered in-person by a trained Ugandan research assistant, with responses captured through electronic data collection.

Fourth, we will assess the reliability and validity of the adapted scales. Reliability is the degree to which the survey items vary relative to their sum scores. Reliability will be assessed using Cronbach's α with α>0.70 indicating adequate reliability. Validity is the extent to which the scale truly measures the intended construct. As self-efficacy is inversely associated with depressive symptoms, we will measure predictive validity by assessing the extent to which depression is inversely associated with self-efficacy in the pilot study. Thus, the pilot survey will also include a measure of depression that has been validated in Uganda: the Center for Epidemiologic Studies Depression scale. The original scale includes 20 items, each rated on 4-point scales, that measure self-reported depressive symptoms in the previous two weeks. This depression scale has been translated into Luganda and empirical studies have concluded that 13 items have high reliability and validity for measuring depressive symptoms among Ugandans. Based on these validation studies, we will employ the 13-item Luganda and English versions of this scale. We will use linear regression to assess the association between the depression score and self-efficacy score. For the General Self-Efficacy and Psychological Safety scales, we will also assess discriminant validity using factor analysis.

Lastly, based on the pilot survey study, we will determine the utility of the adapted scales to assess self-efficacy and psychological safety. Since the General Self-Efficacy Scale has been deemed valid and reliable in 25 countries and the Psychological Safety Scale has been validated in another country in Sub-Saharan Africa, we anticipate adequate reliability and validity for their use in Uganda. However, if our rigorous thresholds for reliability and validity are not met, we will iteratively refine the scales with another round of expert consultation and piloting.

Sample Size Calculation for studies to validate quantitative instruments for future fidelity assessments
A validation study of the General Self-Efficacy Scale in Costa Rica identified the correlation coefficient between self-efficacy and depression to be r=-0.46. Assuming the same correlation coefficient, we would need 35 community health workers to take the pilot study to reach 80% power at the significance threshold of $p<0.05$. To be conservative, we aim to enroll 50 community health workers to take part in the validation study.

Participating community health workers will receive a UGX 20,000 incentive for participation, an amount that will compensate them for their time and any travel expenses without inducement.

Description of Patient Satisfaction surveys.

Human centered design approaches are centered on building empathy and innovating creatively to suit the needs of those they are designing for, making it more appealing and engaging for the end users. There is growing interest in its application to improve healthcare products and services therefore we propose a nested quantitative patient satisfaction survey where we will seek to assess differences in individual patient satisfaction scores among index patients enrolled for TB Contact Investigation using the main study human centered intervention strategy (Tuli Wamu Nawe also referred to as TWN subsequently) and index patients enrolled using the usual care strategy. In addition, we propose to measure descriptively the patient satisfaction of household contacts participating in TB Contact Investigation as delivered using the main study intervention strategy.

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Measures; We hypothesize that Index patients enrolled into TB Contact Investigation using TWN are more satisfied than index patients enrolled into TB contact investigation using the usual care strategies we propose to:
Aim 1: Measure and evaluate the difference in index patient satisfaction scores among index patients enrolled into TB CI using TWN and index patients enrolled into TB CI using the usual care in Uganda. (H_A: Index patients in TWN group will have higher satisfaction scores than index patients in usual care, adjusting for age and sex.)
Aim 2: Measure and describe patient satisfaction among contacts enrolled into TWN.

Design; we shall conduct a crossectional comparative for approximately 6 months during active recruitment for the parent study with approximately 200-400 index patients and close contacts of TB cases receiving contact investigation sevices.

Study procedures:
Inclusion/exclusion criteria (Index cases): We will collect data from consecutive index cases completing 2 months of treatment that have participated in TB contact investigation and are above 18 years with the capacity to provide consent. *Study sites:* Kasambya Health Centre III, Gombe Hospital, Wakiso Health Centre IV, Ndejje Health Centre IV, Bugiri Hospital, Kayunga Hospital, Iganga Hospital, St Francis Naggalama Hospital, Mubende Regional Referral Hospital, Kiboga Hospital, Mityana Hospital, Masaka Regional Referral and six additions sites including Entebbe RRH, Mukono GH(General Hospital), Kasangati HC IV, Kojja HC IV, Jinja RRH and Kawolo GH, Nakaseke GH, Mpigi HC IV and Bweyogerere HC III
Inclusion/exclusion criterial (Contacts): consecutive contacts enrolled into TWN above 18 years that have participated in TB contact investigation led by the Tuli Wamu Nawe team and have a phone number registered in the study database. *Study sites:* Kasambya Health Centre III, Gombe Hospital, Wakiso Health Centre IV, Ndejje Health Centre IV, Bugiri Hospital, Kayunga Hospital, Iganga Hospital, St Francis Naggalama Hospital, Mubende Regional Referral Hospital, Kiboga Hospital, Mityana Hospital, Masaka Regional Referral

Compensation;
Participating index patients will receive a UGX 20,000 (~$5.27 USD) incentive for participation, an amount that will compensate them for their time and any travel expenses without inducement.

Ethical considerations;
We request that a Waiver of Written Informed Consent and Replacement with Verbal Informal Consent Procedures for Cases, Contacts, and Community Health Workers participating in Mixed-Methods Studies of Implementation Fidelity and Context that was granted during a full board review and detailed justification provided below be extended to all cases participating in the additional sites proposed to provide a comparator for patient satisfaction scores.

(Aim 2) Description of measures to assess fidelity of the Community of Practice meetings

Community Health Workers, Community Health riders and facility health workers involved in TB care will hold regular intra and inter clinic meetings after introduction of the implementation strategy in order

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to create a community of practice within themselves. Specific reference is made to the second major component of the intervention strategy. These meetings will be recorded to provide insights to implementation success. All meetings will be recorded using a recorder availed to clinic staff participating in the study by study staff. The clinic staff will store the recorder in a TWN lockbox in each clinic, clinic staff will also enable virtual recording for any virtual meeting that will be held as a back up to the primary recording devices. CHWs will be asked to record all meetings for documentation so that it becomes routine.

A study research assistant will collect the recordings quarterly and store them on a password protected folder, Box Secure. Recordings will NOT be transcribed or translated. All recordings will be deleted within 5 years, following completion of the COP fidelity checklist. A study research assistant will be trained to use the fidelity checklist. They will listen to a stratified random sample of recordings and check off the elements and qualities that are present in a given CoP meeting. Recordings may be reviewed at increased speed and the fidelity checklist completed.

Description of nested studies of behavioural mediators of the effects of the continuous quality improvement intervention

In order to assess how the Community of Practice may influence community health workers' (CHWs) and community health riders' (CHRs) delivery of contact investigation for TB, we will measure CHWs' and CHRs' perceptions of three constructs throughout the trial: social support, self-efficacy, and psychological safety. These three constructs are low-risk data. Social support is the perception that CHWs and CHRs can rely on their colleagues for help. Self-efficacy is CHWs' and CHRs' confidence to perform tasks and reach goals. Psychological safety is their perceived comfort to share work-related successes and failures with their colleagues. We will assess social support by administering the Multidimensional Scale of Perceived Social Support, 2-Way Social Support Scale, and/or the MOS Social Support Survey. We will assess self-efficacy using the General Self-Efficacy Scale. We will assess psychological safety using the Psychological Safety Scale. All five measures are rated on 4-point scales, including response options of never, rarely, sometimes, and always. All five measures have been used in Uganda previously.

A trained Ugandan social scientist will administer the scales to CHWs and CHRs over the telephone after receiving verbal informed consent. Telephone-based survey administration and verbal informed consent is required due to logistical constraints of traveling to multiple rural clinic sites. The social scientist will collect responses via Qualtrics, a cloud-based, secure, Yale-based survey collection platform. The social scientist will administer the scales at four points during the trial: 1) two months before crossing over into the intervention phase, 2) at cross-over, 3) two months after cross-over, and 4) four months after cross-over. In order to link CHWs' and CHRs' social support, self-efficacy, and psychological safety with their performance delivering TB contact investigation, we will also collect CHW and CHR CommCare Study ID and clinic. We will also measure CHW and CHR demographic characteristics, including age, gender, occupation, years of experience at the clinic, years of experience in the health field, and educational attainment.

Costing

Health system cost data will be collected from all 12 sites. Cost data will be collected through detailed budgetary analysis, interviews of key staff members, review of logbooks and/or timesheets to record proportions of staff time devoted to various activities, and direct observation (*e.g.*, time-motion studies). Time and motion data will

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be collected from participants in approximately 50 index patient households as follow up for contact investigation in the control and intervention period.

Cost data will include collection of macro and micro costs from all 12 health facilities and analysed from a modified societal perspective. These costs will be summarized and conceptualized into 3 broad categories: cost of design, initiation and maintenance and clearly delineated as research related or programmatic costs. We propose to use paper-based time and motion survey forms and macro cost questionnaire to collectsome of the following cost data including but not limited to:

Costs estimates from health system perspective

- Overhead study and clinic costs such as water, electricity and security.
- Capital investments such as trainings, equipment, and intervention design
- Recurrent costs such as community health rider hire and consumables such as laboratory supplies and CHW operational costs.
- Human resource costs including salaries of CHWs and supervision staff support.
- Implementation costs
- Building costs such as rent furniture for clinics
- Travel time
- Additional time required for the intervention as compared to the standard of care.

Cost estimates from the patient perspective.

- Time and motion studies of contacts to get screened and evaluated for TB
- Opportunity costs (e.g. lost wages) associated with TB screening and evaluation of contacts in routine care vs a more flexible intervention care.

1) Time and motion data collection

- Research study staff will train health workers to collect start and end times of each activity they perform and who is engaged in carrying it out. (e.g. index enrolment, travel time by community health workers, travel and sputum collection time by community health riders). The survey forms will be scanned and uploaded to a secure password protected box folder and data quality checks run by our research staff.

2) Cost data collection.

- Research Study staff also will gather additional data on overhead costs, capital investments and implementation costs from key administrators at the clinics as well and from key study personnel using survey tools and interview guides, where applicable.
- Finally, we will estimate patient related costs of standard in home visit screening care compared to more flexible screening options such as time and motion data for TB evaluation and screening and opportunity costs related to lost wages and travel.

COVID-19 Considerations

No Yale employees will be part of the routine in-person stepped-wedge trial data collection. All Yale team members are currently vaccinated and if at a later time, in-person activities are required, appropriate health precautions will be taken including but not limited to N95 mask usage and social distancing. All field team members including CHWs, community health riders, study staff, and trainers are eligible for vaccination in Uganda

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at this time with many already receiving vaccination. As TB is also a respiratory illness, medical grade N95 masks are routinely used during contact tracing procedures to prevent the spread of TB. These masks also prevent the spread of COVID-19. All field team members, including study staff and routine health workers will undergo a refresher training in how to appropriately use masks. As Uganda has not had a large outbreak of COVID-19, the local IRB has determined that research activities may proceed as usual.

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.

Our study population for Objective 1 will consist of four different participant types: health workers, index TB patients, household contacts of TB patients, and individuals living in communities where TB is prevalent. For Objective 2, we will be evaluating the performance of these health workers in providing household TB contact investigation to index TB patients and their household contacts according to Uganda National TB and Leprosy Programme (**NTLP**) guidelines and WHO TB contact investigation guidelines. We will measure the success of using a CoP and HCD-informed implementation strategy by the performance of health workers in delivering these strategies.

For objective 2, our target settings include urban and peri-urban communities surrounding clinics and hospitals with TB treatment units. Our target population includes the household and non- household close contacts of index TB cases who have been newly diagnosed in these clinics. The unit of randomization will be the clinic (N=12). The unit of analysis will be the close contacts interviewed and screened for active TB during the 16-month trial period (estimated n=588, more details in sample size section above).

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.

☒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	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?
Yes ☐ No ☒

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 that a quality improvement intervention appropriately targets the individuals who it aims to help.

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

Health workers, Formative Design Activities: We will recruit community health workers (n=~8) and TB unit health care workers (n=~10) assigned to offer TB contact investigation services at three study sites to participate in these quality improvement activities.

Health workers, Stepped-Wedge Trial: In collaboration with clinic-based representatives of the Uganda National TB and Leprosy Programme NTLP (*e.g.* the site NTLP focal person) and the Uganda Ministry of Health (*e.g.* Administrator-in-Charge), research staff will invite selected CHWs and community health riders and clinic HCWs at each study site to participate in interviews, surveys, and/or focus group discussions, following verbal consent.

Contact investigation is provided to index patients and household contacts according to local protocols approved by the public health systems. As this is a quality improvement project aiming to test an implementation strategy, local protocols will be followed for inclusion of index patients and close contacts during all phases of the study. The inclusion criteria are described below:

Index TB patients:

Inclusion characteristics:

- Consecutive index TB patients enrolled into TB care
- Willing to participate in routine contact investigation proceedings

Exclusion characteristics:

- Reside more than 40 km from the health centre (approximately 1 hour by means of common public transport (boda, taxi etc.))
- Have multi-drug resistant TB
- Lacking capacity to consent to contact investigation procedures
- Those who have no close contacts.
- Decline to refer close contacts for contact investigation procedures
- Previously completed TB contact investigation within the last 2 months

Close Contacts at the Household:

Inclusion characteristics:

- Meet definition of close contacts of index TB patients (at least 12 cumulative hours of contact with the index case in enclosed space during the previous 3 months)

Exclusion characteristics:

- Already taking treatment for active pulmonary TB
- Lacking capacity to consent to contact investigation procedures
- Declining contact investigation procedures

In addition, for the qualitative data collection with index patients and contacts only, we will exclude individuals who do not speak English or Luganda.

For HCD related design activities, we will include those involved in routine quality improvement activities within the health system (i.e. community health workers, TB unit staff, Ministry of Health policy makers, etc.); index patients and their household contacts who have had TB contact investigation services provided in their home; and individuals in the community whose opinions may be solicited to inform design of the quality improvement interventions because of their leadership roles in the community (e.g., church leaders, district officials, etc.). We will purposively select approximately 30 index patients, 30 close contacts, and 30 key informants with experience in TB, during several iterations of the design process.

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Key Informant Interviews with Programmatic Officials: Key informant interviews will be conducted with implementing clinic TB focal persons before and after implementation to assess fidelity, acceptability and any other insights into implementation success.

Case and Contact In-depth Interviews: In-depth interviews will be conducted with a purposive sample of 20 cases and 50 contacts eligible for the stepped-wedge trial during the intervention phase to assess fidelity, acceptability and any other insights into implementation success.

Focus Group Discussions (FGDs) with Community Health Workers and/or Community Health Riders: We will hold FGDs with CHWs and/or Community Health Riders 6 months after introduction of the implementation strategy at that site to assess fidelity, acceptability and any other insights into implementation success.

Provider Interviews and Time-and-Motion Studies: Providers at each study site who are (a) aged ≥18 years; (b) employed by the facility; and (c) involved in the conduct or supervision of health center work related to TB contact investigation will be included.

9. How will eligibility be determined, and by whom? Write here
   Health workers will be identified by study team members as those already engaged in TB care and contact investigation services at the study sites.

Community health workers or study staff will invite community members, index patients and household contacts to participate in qualitative data collection activities at the clinics or within the communities themselves (key informant interviews, and focus-group discussions). If they agree to participate, a research staff member will administer verbal consent at the beginning of the data collection procedures.

Health care workers and providers will be identified at each clinic by study staff members. If they agree to participate, a research staff member will administer verbal consent at the beginning of the data collection procedures.

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

This is a minimal risk study. During the design phase, participants described their experiences and opinions about routine contact investigation proceedings and we did not identify or observe any excess physical risks. During the stepped-wedge trial, standard contact investigation procedures will be delivered and the added additional services provided during the intervention phase of the study do not pose any additional risks beyond those encountered in everyday life. The primary risk to participants is breach of privacy.

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

    All data collected is that which is being routinely collected in health facilities as we are currently focusing on quality improvement of existing programs. In order to minimize the risk of breach of privacy, we will collect all performance data using electronic tablets and a mobile application using CommCare. All data will be stored on an encrypted cloud-based server that is password protected. Only approved study staff will have access to the data. We will de-identify all data, qualitative and quantitative, as soon as possible. As many journals now require a data repository in order to publish, we will create a repository of de-identified data. For qualitative data, we will only create a data repository if we can ensure no means of re-identification as,

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for example, CHWs and community health riders are few in the country and could be connected back to their data if we listed the health centre that an individual participant was associated with.

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 risk study
    b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? Minimal risk
    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

This protocol presents minimal risks to the subjects and therefore 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 during regular study meetings and via email as they are reviewed by the principal investigator. The protocol's research monitors, including the local IRB at Makerere University and the international IRB at Yale will be informed of severe adverse events within 10 days of the event becoming known to the principal investigator (the length of time currently required by the other IRBs).

d. For multi-site studies for which the Yale PI serves as the lead investigator:
    i. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed? We do not anticipate any adverse events as all study related tasks of interest are those being carried out routinely by the health facilities. If unanticipated problems involving risks to subjects arise, such as inadvertent breach of privacy, subjects will be notified by a community health worker. They will be reminded that participation is voluntary and they may continue with routine TB contact investigation services or withdraw.
    ii. What provisions are in place for management of interim results? No reporting of interim results is planned as we are currently working on quality improvement and as such this is minimal risk for participants. Therefore, an interim analysis is not required for safety reasons.
    iii. What will the multi-site process be for protocol modifications? All sites during the design phase were located in the same metropolitan area in Kampala, Uganda and neighboring Mukono, Kampala, and fall under the same PI's and the same IRB's jurisdiction, so the process will be the same at each and all sites. The sites selected for the stepped-wedge trial are all within 150km of Kampala, and similarly fall under the same PI's and IRB's jurisdiction.

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

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We will compare the two strategies overall (1°) and for each stage of the contact investigation cascade (2°), as well as yield of diagnoses/treatments for active and latent TB (2°). We will construct multilevel logistic models (or Poisson models for counts), adjusted for clustering within clinics/communities and within index patient clusters, to estimate proportions (or counts) with exact binomial 95% confidence intervals. We will compare primary outcomes between control and intervention periods using adjusted chi-squared tests of proportion. We will determine and report ICC at both health centre and index patient levels. We will fit a multilevel, generalized linear mixed-effects model with a logit link and random effects for clustering and fixed effects for step (*i.e.*, point in time). For sustainability we will analyze the interaction between intervention and time-elapsed-since-intervention-initiation to determine if the intervention effect strengthens or weakens over time as it becomes routinized, looking at both TB evaluation and diagnosis. We will also explore variation in delivery processes and outcomes for the following:

(1) Health facility clusters,
(2) Community health workers, and
(3) Clinically important sub-groups including women, men, younger children (age<5), older children (age 5-14), adults, and PLHIV, all in pre-specified sub-group analyses.

There is a strong biological rationale for each of these analyses, given known differences in TB diagnostic performance by sex and in WHO recommendations for TB evaluation by age and HIV status.

We will prepare flow and cascade diagrams to illustrate key contact investigation process measures, as in our previously published work. We will produce time-series graphs demonstrating change in cumulative likelihood of completion of contact investigation and each of the component process measures over time. We will prepare tables describing associations between provider and clinic characteristics and likelihood of completion, stratified by key individual- and household-level characteristics of community members. Tests of significance will be applied as needed at the adjusted $p<0.05$ level.

Primary Outcomes

1. Referred contacts completing TB evaluation
    a) Count (Number of contacts who complete TB evaluation within 60 days of index patient diagnosis)
    b) Cumulative proportion (Number of contacts who complete TB evaluation within 60 days of index patient diagnosis divided by the number of total contacts referred for TB evaluation, defined as providing sputum, undergoing chest radiography, or undergoing evaluation by a clinician at the TB diagnostic unit)
2. Cumulative TB diagnostic yield among all contacts identified, within 60 days

Secondary Outcomes

1. Proportion completing each step of the contact tracing cascade, with the denominator the number eligible at the end of the previous step.
    (a) Proportion of eligible index cases
        (i) who were invited,
        (ii) who accepted invitation,
        (iii)who identified at least one contact
        (iv)who had at least one contact interviewed
        (v) who initiated TB treatment (within 2 months), and (vi)who completed TB treatment (within 12 months)
    (b) Proportion of all named contacts

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(i) who were reached,
(ii) who screened positive, (iii)who had sputum collected, (iv)who had sputum delivered, (v) who had sputum tested, (vi)who were diagnosed,
(vii) who initiated treatment (within 60 days of diagnosis)
1. for active TB disease
2. for latent TB infection
(viii) who completed treatment (within 12 months)
1. for active TB disease
2. for latent TB infection

2. Timeliness of contact investigation (Median days from case diagnosis)
(a) Time to case invitation
(b) Time to contact screening visit
(c) Time to contact testing, radiographic evaluation, or clinical evaluation
3. Pre-specified sub-group analyses for all primary and secondary outcomes
(a) Subgroup
(i) Adults
(ii) Older Children (age 5-14)
(iii) Young Children (under age 5) (iv) Persons living with HIV
(b) Contact type
(i) Household
(ii) Non-household close contacts
1. Workplace
2. Social
(c) Clinic site /community

Qualitative Analysis Techniques: The research team will develop data coding and scheming sheets. The data code scheme for tracking individual data outputs will be maintained in an Excel spreadsheet. The research team will be responsible for stripping data outputs of any identifying information, and for applying a coding scheme for identifying study participants without personal information. While in the field, team members will capture quotes, stories, and/or observations from their daily download sheets, write key takeaways on post-its, and begin to look for emerging themes and patterns. The research team will identify themes and patterns emerging from the data during the fieldwork and collate these. The research team will also transport a copy of de-identified data outputs to their office in San Francisco and New Haven for further analysis in order to refine themes and identify additional variants, collaborating remotely with members of the ICAP team, in order to identify key insights and opportunity areas for design.

Analysis techniques: We will use inductive analysis techniques for analysing qualitative data, including developing an open coding tree. 20% of the transcripts will be double-coded during second cycle coding and measures of concordance presented. Differences will be resolved by consensus or by consultation with the local PI.

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

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C. 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: Approximately 4700. Since index patients and contacts are participants in routine services, and the design of a stepped wedge trial has a fixed duration, we will not limit enrollment if it exceeds these numbers, which may be up to four-fold higher in some or all sites, or more if the intervention strategy is highly effective.

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: Consecutive enrollment of index TB patients and their households presenting at study sites. Health workers who are working within the TB units at the study sites.		

* 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. All health workers already working in TB units at study sites will be recruited. Community Health Workers will identify consecutive index TB patients presenting at the study sites. This will subsequently lead to household visits or phone based interviews of eligible TB patients where all close contacts will be recruited for TB evaluation services. Community members whose opinions could be valuable to the design process were identified by key informants within the catchment area and by study staff during that phase of the study.

b. Describe how potential subjects are contacted. Health workers will be contacted by study staff. Index TB patients and their household contacts will be contacted through routine interactions with community health workers.
Community members were contacted by study staff or community health workers prior to the design process initiation to invite these key informants to participate. Verbal consent was obtained prior to design activities for these members as well as for index patients and their household contacts.

c. Who is recruiting potential subjects? Study staff will recruit health workers while community health workers will recruit index TB patients and their household contacts. Study staff and community health workers alike will recruit individuals for the design process.

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?

☒No

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.

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.

Health workers

Health workers participating in qualitative data collection will only be asked to comment on issues related to their role and observations in administering contact investigation including the usual care and the human centered design implementation strategy. They will not be asked to answer personal questions. We will not obtain signed consent from these heath workers, based on DHHS regulation 46.117 (c):

Regulation	***Must meet EITHER of the following requirements to qualify for waiver of signed consent:***
46.117 (c)	(1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; *OR* (2) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

We believe that this research poses minimal risk of harm to health workers, and that, as part of routine quality improvement activities, this research would not require consent outside of the research context. In lieu of signed consent, all participants will be informed of their right to decline to participate in general and to decline to answer specific questions, if desired.

Participation in all study-related activities will be voluntary and all providers will be informed that they can choose to stop participation at any point. The audio files from qualitative data collection will be stored on a secure network and password protected. All names inadvertently used during the qualitative interviews 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 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. No other study instruments/databases (pre-/post-training questionnaires, password-protected U-TIRC database) will collect or contain personally identifiable information.

Index TB patients, household contacts and key informant community members: Design process and qualitative components evaluating contact tracing implementation strategy

We will be requesting a waiver of written informed consent in accordance with DHHS regulation 46.117 (c) as the research presents no more than minimal risk of harm to subjects and the only item connecting participants to the research would be the consenting document. Per DHHS guideline 46.117(c), the requirement for written informed consent can be waived if:

Regulation	***Must meet EITHER of the following requirements to qualify for waiver of signed consent:***

46.117 (c)	***(1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; OR*** ***(2) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.***

Index TB patients and their household contacts will be invited to participate in this public health evaluation in accordance with guidelines of the Uganda NTLP. We believe this research meets the first condition outlined above: (1) The consent form would be the only document connecting index patients and their contacts to the results of the focus group discussions or interviews and the primary risk for the entire study is a breach of privacy. Additionally, health-worker interventions to improve the quality of care are a routine part of public health practice and do not pose a risk to the participants.

We will obtain verbal consent for qualitative data collection with index patients, contacts and community members; while the purpose of these fits with routine quality improvement, since these activities do not commonly include community members, and because we are offering compensation for time and transport, we will include verbal consent to maximize transparency.

Index TB patients, household contacts: Stepped-Wedge Trial Contact Investigation

According to 45 CFR 46.116(f)3, effective 19 July 2018, investigators may ask an IRB to approve a waiver of informed consent if several conditions are met. We list these criteria in bold below, accompanied by explanations of how and why they apply to the proposed study:

i. **The research involves no more than minimal risk to the subjects.** All participants will be offered standard contact investigation procedures, and the additional services provided during the intervention phase of the study do not pose any additional risks beyond those encountered in everyday life.
ii. **The research could not practicably be carried out without the waiver or alteration.** It is not practical for community health workers to obtain informed consent during the process of routine care. In addition, informed consent procedures change the care context for participants in ways that may reasonably alter their behavior. For these reasons, including consent procedures could compromise the scientific validity of the study which seeks to identify best strategies for implementation under real-world conditions.
iii. **The research could not practicably be carried out without using identifiable private information**. Collection of name, age, telephone number, residence, information about health status and other personal health information is required to carry out TB contact investigation according to existing Uganda public health guidelines. It is not possible to evaluate the implementation of these services without collection of this information.
iv. **The waiver or alteration will not adversely affect the rights and welfare of the subjects.** The rights of patients to accept or decline care are similar to their rights in everyday medical practice and are not altered by the research.
v. **When appropriate, the subjects will be provided with additional pertinent information after participation.** All pertinent results of TB evaluation will be communicated to patients via routine or enhanced processes of care.

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.
We will be requesting a waiver of consent for data collection activities related to health workers opinions and actions in delivering contact investigation. However, as is done in routine medical settings, community

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health workers will obtain permission before conducting routine TB evaluation services. Health workers participating in study related activities will be informed that they can choose at any time to end participation or not answer any question that they do not feel comfortable answering.

Research staff with human subjects protection training will assess whether individuals have capacity to provide verbal consent based on appropriate answers to questions about the purpose of the procedures (i.e. to get information to improve services for community members) and their affirmation to participate.

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.
All health workers speak both English and Luganda, the most common local language spoken. Health workers will converse with index TB patients and household contacts in the language of their preference as is done in the health facilities. We will not recruit those who do not speak English or Luganda for qualitative data collection.

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? N/A 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 (Note that an information sheet may be required.)

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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 ☒

We are working on quality improvement proceedings and no data collected is outside of routine public health proceedings for community health workers. For index, contact participants and community members, we will obtain verbal consent for interviews or focus group discussions. Signed consent would be the only record linking these participants to the research and the breach of confidentiality is the principal risk to subjects.

☐ Requesting a waiver of consent:

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

☐ Entire Study

For a full waiver of consent, please address all of the following:

- Does the research pose greater than minimal risk to subjects?
  ☐ Yes *If you answered yes, stop. A waiver cannot be granted.*
  ☐ No
- Will the waiver adversely affect subjects' rights and welfare? YES ☐ NO☐
- Why would the research be impracticable to conduct without the waiver?
- Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date?

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 the following information:
   - Names
   - Dates
   - Postal addresses
   - Phone numbers
   - Medical record numbers

2. How will the research data be collected, recorded and stored? All data will be collected using mobile tablets equipped with a customized survey software application such as a CommCare (Dimagi, Cambridge, MA) or RedCap application. Quantitative data will temporarily be stored on these devices during collection but will then be uploaded via a 3G connection to a remote, cloud-based, encrypted server. We will ensure that all safety features have been reviewed and approved by an independent security expert. Data on the server will be password protected. Only study staff will have access to identifiable data collected. As many journals now require a data repository in order to publish findings, we will de-identify all data at the earliest possible moment

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after trial completion and subsequently create a de-identified data repository using one. We will have at least 2 study team members verify that the dataset is completely de-identified and that there exists no way of connecting the data to individual participants prior to submitting the data to a data repository. No one outside of the study team will have access at any point to identifiable data.

Qualitative data in the form of digital recordings and written transcripts will be stored on password protected cloud-based servers and backed up on secured institutional servers. Recordings will be carefully destroyed once transcriptions have been completed. Transcription will be conducted by professional transcribers with signed NDA's and confidentiality agreements. English transcripts may be transcribed by a verified transcription service such as Rev or similar transcription service that protects participant confidentiality while producing quality transcriptions. We will create a data repository for qualitative data as well however, as transcripts pose a greater challenge in de-identification due to people referencing specific individuals or places throughout their interview that may be used to identify that participant, we will only do this upon request by a journal for publication and only if possible to completely de-identify the transcripts. We may submit a limited subset of the transcripts instead of the full transcripts to ensure that re-identification is impossible. We will only submit transcripts if at least 2 study team members have verified that all transcripts, or parts of transcripts if only a subset of the data is to be kept in a repository, are completely de-identified and there exists no way to re-identify participants. No one outside of the study team will have access to identifiable data including the original audio recordings and the raw transcripts produced from these recordings.

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

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? *All data will be stored on encrypted servers with password protection. Only approved study staff will have access to data collected.*

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.
   All data will be stored securely on password protected servers. Data will be de-identified once enrollments are complete and the personal health identifiers destroyed under the direction of the principal investigator.

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.)
Health workers may gain additional satisfaction from participating in research and helping to generate new knowledge to improve care and from delivering better quality care. Indirectly, the study may benefit future TB

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patients, their households, and health workers involved on contact investigation for TB by improving the quality of TB contact investigation and evaluation.

SECTION VI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. Alternatives: What other alternatives are available to the study subjects outside of the research?
   The only alternative would be to decline participation.
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.
   We will provide appropriate compensation for health workers, community health riders, contacts and index patients participating in qualitative data collection activities designed for quality improvement and evaluation of contact tracing implementation. Health workers, community health riders, community members, index patients and their contacts who participate in the focus group discussions and/or interviews or surveys outside of routine health data collection (e.g. CHW and CHR surveys on psychological safety) may be compensated a small amount of money (~20,000 Ugandan shillings, equivalent of ~$5.66USD) for their time and/or transportation reimbursement. As costs have risen due to the pandemic, the stated amount is more appropriate than what has been used pre-pandemic (increase of ~10,000 UGX).
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.
   Study participants will not be charged for participation.

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).

   All participants will be offered standard TB contact investigation procedures and the additional services provided during the intervention phase of the study do not pose any additional risks beyond those encountered in everyday life. Therefore, this section is N/A due to the minimal risk posed.

   a. Will medical treatment be available if research-related injury occurs? *Write here*

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

IMPORTANT REMINDERS

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

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

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