Protocol Title: TRAnsmission of Covid-19 in Crowded Environments
Short Title: The TRACE Study.

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TRaCE summary

The overarching objective of this protocol is to understand and mitigate household transmission of SARs-CoV-2 infection in a low income, high density South African community setting. Data over an 8-month period will be used to determine the Ro for SARS-CoV-2 infection, rate of symptomatic disease, and impact of a community healthcare worker (CHW) administered household infection mitigation intervention (STOPCOV intervention).

- Aim 1: To measure incidence and timing of transmission of SARS-CoV-2 to household contacts (HHC). SARS-CoV-2 transmission will be monitored using nasopharyngeal swabs for PCR and serology (IgM/IgG) assays in all Household Contacts (HHC) weekly for 1 month. Symptom checklists will be completed daily and collated weekly for each HHC. The proportion of patients and HHC who have symptoms vs asymptomatic disease will also be measured.
- Aim 2: To investigate the effect of an intensive infection mitigation intervention (STOPCOV) administered by lay health care workers on SARS-CoV-2 household transmission. The proportion of transmissions to HHC of COVID19 cases assigned to the infection mitigation intervention arm compared with the households in the Enhanced Usual Care (EUC) arm will be measured. In addition, we will evaluate the effectiveness of the STOPCOV intervention on uptake of infection mitigation strategies, loneliness, stigma and social impact among households.

Setting and population: The Klipfontein sub-district is a resource-limited, densely populated, high HIV disease burden areas in Cape Town. Newly diagnosed COVID19 cases will be identified from two sources: screening conducted in DTHF mobile screening units and local public sector clinics. Consecutive cases (n=120 and households) will be invited to participate. After enrolment, the household will be randomised to the STOPCOV intervention or enhanced usual care messaging.

Design: A cluster randomised controlled study with longitudinal follow up of SARS-CoV-2 infection in 120 households which have newly diagnosed positive cases. The index cases and their HHC will be invited and enrolled after informed consent. Baseline surveys and SARs-CoV-2 screening (PCR and IgM/IgG serology) and then weekly SARs-CoV-2 screening (PCR and serology) of HHC will occur at 0, 1, 2, 3 and 4 weeks. The households will be randomized to an intensified COVID19 infection mitigation intervention (n=60) administered by CHWs vs standard messaging currently being provided (n=60).

Analysis: The proportion of SARS-CoV-2 transmission from index cases to HHC over 4-week period will be calculated. The proportion of symptomatic and asymptomatic SARS-CoV-2 infection in a high density, low resourced community will be described. The impact of the STOPCOV intervention by assessed by measuring transmission, and clinical outcomes, in households randomised to intervention vs standard of care. A process evaluation will explore the feasibility, acceptability and contextual factors impacting the STOPCOV intervention delivery.

TRaCE Schema
Questions: 1 What is the transmission pattern (Ro number and timing of infection) of SARS-CoV-2 in a household in which a COVID-19 case has been identified in a low-income, high density community in Cape Town? 2 What is the burden of symptomatic versus asymptomatic SARS-CoV-2 cases in a high HIV/ TB disease burden setting in Cape Town, South Africa? 3 Can an intensified, infection mitigation intervention reduce the transmission in a household setting, improve clinical outcomes and reduce psychosocial impact of a COVID19 diagnosis?
Objective: The overarching objective of this protocol is to understand and mitigate household transmission of SARs-CoV-2 infection in a low income, high density community setting.
Aims: Specific Aim 1: To measure frequency and timing of transmission of SARS-CoV-2 to household contacts. The proportion of patients and household contacts who have symptoms vs asymptomatic disease will also be measured. Specific Aim 2: To investigate the effect of an intensive infection mitigation intervention (STOPCOV) administered by lay health care workers on the household transmission of SARS-CoV-2, clinical outcomes and psychosocial functioning.
Design: The study design is a type 2 hybrid cluster (household) randomised controlled trial, with outcomes assessed on index patients and their household contacts (Fig 1). 120 consecutively newly diagnosed index patients (GeneXpert SARS-CoV-2 PCR) and up to 8 household contacts will be invited to participate in the trial as part of the prospective observational study evaluating transmission and symptoms. After completing consent, households will be randomised in a 1:1 ratio in blocks of 10 (60 households per group; 360 patient and household contacts per group).
Study setting and population: Klipfontein is a resource-limited, densely populated, high HIV/TB disease burden areas in Cape Town. Newly diagnosed COVID19 cases will be identified from two sources: screening conducted in DTHF mobile screening units and local public sector clinics working closely with DTHF. Consecutive cases (n=120 cases and households) will be invited to participate in the randomised trial and prospective longitudinal follow up of up to ~6 -8 household contacts. The contacts will be followed up after informed consent to SARS-CoV-2 screening, symptomatic questionnaires weekly up to 1 month.
Study size: We will enrol n=120 SARS-CoV-2 positive and n=~6 their household contacts (n=~720).
Process: Newly diagnosed SARS-CoV-2 index patients will be identified and recruited from a mobile clinic and local community clinics conducting SARS-CoV-2 testing. Index cases and their households will be invited to enroll. After enrolment, the household will be randomised to the infection mitigation intervention or enhanced usual care messaging. Baseline demographic, household characteristics questionnaire will be administered, and each household occupant invited to participate. Following consent procedures, household contacts (HHC) will be screened at baseline and weekly for 4 weeks for evidence of COVID infection. Specifically, the research team will conduct SARS-CoV-2 GeneXpert PCR testing and antibody serology. They will collate self- administered daily symptom checks on a weekly basis. Six months after a positive SARS-CoV-2 antibody, the study nurse will visit the participant household to conduct SARS-CoV-2 serology to assess for the presence of antibodies.
Duration: We will recruit 120 households over 1-3 months. We will initiate a prospective longitudinal follow up of the household contacts of each case for 4 weeks in each case.
Analysis: Calculate proportion of SARS-CoV-2 transmission from index cases in each household over 4- week period. Describe the proportion of symptomatic and asymptomatic SARS-CoV-2 infection in a high density, low resourced community. Investigate the impact of the infection mitigation intervention by comparing Ro number in households randomised to intervention vs standard of care. Secondary outcomes for the trial will include clinical outcomes (hospitalisations, death), linkages to care for people, psychosocial functioning and stigma.

Background

South Africa currently has the largest COVID19 epidemic in Africa, with >205,721 cases reported in all nine Provinces (*COVID-19 South African Coronavirus News and Information Portal*, n.d.). The South African Department of Health has reported more than 3310 deaths of individuals infected with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the cause of coronavirus disease (COVID-19) to date (Karim, 2020). As screening and testing is scaled up, South African healthcare facilities are preparing for the mitigation stage in the epidemic, wherein people with severe COVID-19, mostly adults, may require hospitalization, and intensive care (Karim, 2020).

A large proportion of the 55 million people who make up the South African population live in low income, high density communities in peri-urban locations. These settlements may be formal or informal and often consist of crowded shack dwellings. Self-isolation and physical distancing may be impossible in these crowded environments (Davey et al., 2020). Many do not have water and need to stand in queues to get water or food. The major risk mitigation factors recommended by WHO and others – physical distancing and hygiene – are extremely difficult to implement in much of Africa (Joseph Davey et al., 2020; The Lancet, 2020).

The Desmond Tutu Health Foundation mobile HIV counselling and testing (HCT) service was designed, built and launched in Cape Town in 2008. Previous studies using active case-finding with the Tutu Tester Mobile clinic services have successfully identified undiagnosed cases of HIV and TB and linked these patients to care (Govindasamy et al., 2013; Kranzer et al., 2012; Smith et al., 2014). The mobile clinic has provided accessible, community-based, rapid HCT services in high HIV and TB disease burden communities. The mobile clinic team sought to destigmatise HCT by embedding HIV testing in a wellness service for a range of chronic diseases, including diabetes and hypertension. In addition to HIV testing, the service included point of care (POC) STI screening, CD4 T cell testing and TB screening of HIV infected clients. After 90,000 client contacts in numerous communities with high rates of HIV and TB infection in the Cape Metro district we have established that this service is feasible, acceptable, effective, non-stigmatising and cost effective (Bassett et al., 2014; Govindasamy et al., 2013; Smith et al., 2019). Additionally, the mobile has enhanced linkage to care among HIV infected individuals, rapid ART initiation for pregnant women reduced PMTCT to <1% (Black et al., 2013) and POC diagnostics were in a mobile clinic setting (Kranzer et al., 2013). Mobile clinics provide an opportunity to actively identify communicable disease and link patients to care (Kranzer et al., 2012).

With the advent of COVID19, the mobile services have added COVID testing to the suite of screening tests and has been conducting testing in partnership with the provincial health services since the beginning of April 2019. During the first three months of the pandemic the strategy had been to test all symptomatic individuals identified in a door to door community-based approach. Testing teams linked to the mobile and under armed police protection have been set up in “hotspots” in which a known COVID case has previously been identified. Community health care workers are trained to sweep through the immediate community administering a symptom questionnaire whilst community education via loud hailing is conducted. After completing a symptom questionnaire administered by community health workers, symptomatic individuals or people who have had known contact with a COVID case are screened by a clinician for symptoms and if confirmed, have been invited to undergo nasal swabbing in an outdoor gazebo linked to the mobile by a trained clinician. This has been done safely and with a reasonable yield. To date, the case fatality rate (CFR) is 354 per million in the Western Cape, which is over 7 times higher than the national mortality rate of 49 per million (https://www.totalanalysis.com/187). The CFR is projected to be 700 per million in the Klipfontein region (Timeslive, 2 July 2020).

These services have therefore already shown to be ideal for strategically identifying and following up cases and contacts of SARS-CoV-2 and triaging patients to quarantine, isolation, and hospital care as appropriate. The overall objective of this proposal is to understand and mitigate the transmission of SARS-CoV-2 in high density townships. We plan to do this by establishing the Ro number for SARS-CoV-2 in low-income high-density households, and evaluating the effect of a lay health worker administered risk mitigation strategy on transmission, clinical outcomes and psychosocial functioning compared with enhanced usual care.

Approach:

Overall Objective: The overarching objective of this protocol is to understand and mitigate household transmission of SARs-CoV-2 infection in a low income, high-density community setting. Data over an 8-month period will be used to determine the Ro for SARS-CoV-2 infection, the rate of symptomatic disease and the impact of a lay health care worker administered infection mitigation intervention (STOPCOV) in low income, high-density communities in South Africa.

Specific Aim 1: To measure frequency and timing of transmission of SARS-CoV-2 to household contacts. The proportion of patients and household contacts who have symptoms vs asymptomatic disease will also be measured.
Specific Aim 1 Endpoints: SARS-CoV-2 transmission will be monitored using nasopharyngeal swabs for SARS- CoV-2 PCR and serology (IgM/IgG) assays in all HHC weekly for 1 month. Symptom checklists will be completed daily and collated weekly for each HHC.

Specific Aim 2: to investigate the effect of an intensive infection mitigation intervention known as STOPCOV administered by lay health care workers, compared with enhanced usual care, on SARS-CoV-2 household transmission.
Specific Aim 2 Primary Endpoint: The proportion of transmissions to HHC in the households of COVID cases assigned to the infection mitigation intervention arm compared with the households in the enhanced usual care (EUC) arm.

Population and Sample: We will consecutively recruit n=120 SARS-CoV-2 positive index patients 12 years and older. The index patients will be identified from referrals from associated public sector clinic screening in a high-density community in Cape Town. Each household is estimated to have 6-8 occupants. We will invite HHC (n=~6-8) household contacts of each of the index patients (n=~720).

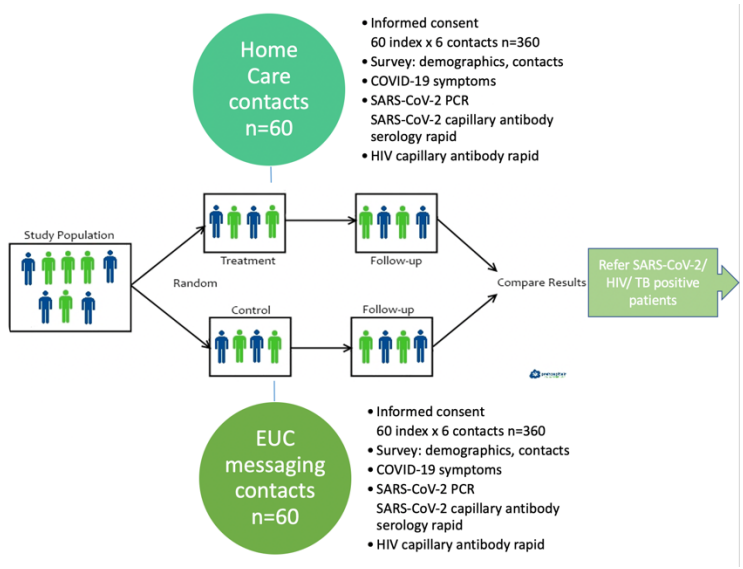
Duration: The study will be conducted for eight months from June 2020 and last until Jan 2021.

Setting: The study will be conducted in KMP. The community is a resource-limited, densely populated, high HIV/TB disease burden area in Cape Town. The DTHF Tutu Tester Mobile Clinics offer mobile HIV testing days in various locations in KMP. Specifically, there are four high HIV disease burden communities in the district; Philippi (population n=200,803), Crossroads (n=36,043), Gugulethu (n=98,468) and Nyanga (n=57,996). In addition to our well-established relationship with community organisations such as an independent advisory board, we have provided HIV testing services and linkage to treatment from the mobile clinic since 2008 and are currently partnering with the K/MP subdistrict health team in providing COVID screening and testing. Given our long-term relationship with and service in the community, our relationships with the Provincial Department of Health, and our experience with the research platforms, it is feasible for us to successfully execute the proposed

research. The mobile clinic team will provide a screening service and SARS-CoV-2 polymerase chain reaction (PCR) testing with the GeneXpert or courier samples to accredited laboratories and rapid testing with the SARS-CoV-2 antibody COVID-19 lgG/lgM Rapid Test Device. Additionally, the mobile clinic team will offer screening for HIV, TB, STI and chronic diseases (e.g. diabetes, hypertension, and obesity).

Design: A cluster randomised controlled study with longitudinal follow up of SARS-CoV-2 infection in 120 households which have newly diagnosed SARS-CoV-2 positive cases. The index cases and their household contacts will be invited to participate in the study after informed consent. Baseline surveys and screening and then weekly screening of HHC will occur (Table 1). These household contacts will be tested at 0, 1, 2, 3 and 4 weeks.
The study design is a type 2 hybrid cluster (household) randomised controlled trial, with outcomes assessed on index patients and their household contacts (Diag 1). 120 consecutively newly diagnosed index patients (GeneXpert SARS-CoV-2 PCR) and up to 8 household contacts will be invited to participate in the trial as part of the prospective observational study evaluating transmission and symptoms. After completing consent, households will be randomised in a 1:1 ratio in blocks of 10 (60 households per group; 360 patient and household contacts per group).

Diagram 1: Study flow



Control group households will receive standard Western Cape Department of Health COVID-19 recommendations for transmission mitigation at the time of diagnosis. Currently this includes advice on physical distancing, hand and respiratory hygiene and cleaning. Information has been distributed through dissemination of written pamphlets, WhatsApp messages, telephone hotlines and websites. Home care is only recommended if there is a separate room. Facility isolation and quarantine services are available for households without separate rooms, and are strongly advised should members of the household be considered at risk for severe COVID-19 (age ≥ 55 years and/or underlying chronic conditions especially diabetes). But uptake of such services has been lower than expected and beds are being decommissioned. Intervention group households will receive intensive support delivered by CHWs (See Table 1). This will comprise an initial household assessment to assess needs for facility isolation or quarantine referral, explain infection control measures and help the household adapt

them to their homes, provision of basic supplies (masks, hand sanitiser and bleach) and written materials at appropriate literacy levels and in local language. The same CHWs will follow-up household members daily for the first two weeks and three times a week during weeks 2-4, as well as distribute pre-prepared twice daily text messages. Two CHWs will be assigned per household to sustain intensive support and prevent burnout.

Table 1: Interventions

Characteristic	**Usual care (outside study)**	**Enhanced Usual Care**	**StopCov intervention**
Testing of household contacts	Not routinely available. Limited to symptomatic individuals at risk of severe COVID-19.*	At baseline and weekly for up to 8 household contacts ≥ 12 years.	At baseline and weekly for up to 8 household contacts ≥ 12 years.
Facility based isolation and quarantine	Available but uptake limited.	Available but uptake limited.	Counselled to take up service if isolation at home not possible and person in household at risk for severe COVID-19.
Hospital care	Available through clinical services/ hotline	Available through clinical services/ hotline	Available through clinical services/ hotline
Written material	Extensive content available online. Limited content available as pamphlets and WhatsApps. No systematic distribution of WhatsApp messaging.	Printed copies of PACK Home Volume 1 (Be coronavirus safe) and Volume 2 (COVID-19 Caring at home).	Printed copies of PACK Home Volume 1 and 2. WhatsApp optimised versions of content delivered daily.
Community Health Worker visits	Mainly alongside chronic medication delivery.	Mainly alongside chronic medication delivery.	Additional one off household assessment to establish relationship at baseline.
Equipment	Distributed through drives.	Masks and hand sanitiser at enrolment.	Masks, hand sanitiser, bleach, gloves (to wear when using bleach). Plus on demand during follow-up.
Telephonic and text message support	On demand hotline service.	On demand hotline service	Scheduled support: Active phase (until 14 days after last person in household diagnosed): daily.

			Follow-up phase: 3 times a week for 7-14 days. Close-out: 5 days (to facilitate full integration into usual services).

* As of 06/07/2020 patients are considered at risk of severe COVID-19 if they are: 55 years or older or of any age with any one of the following: diabetes, on TB treatment, HIV, kidney disease, hypertension, previous TB, chronic clung disease, on cancer treatment.

Outcomes will be independently assessed by research staff who are also collecting biological samples at 0, 1, 2, 3, and 4 weeks. Baseline surveys will collect information on demographics, COVID-19 symptoms, household tracing information and home/ dwelling characteristics that impact transmission (size, rooms, ventilation, access to safe water, laundry facilities). Patient and household contact surveys will also include standardised measures to assess psychosocial functioning: General Health Questionnaire; UCLA Loneliness Scale and a version of the Brief AIDS-Related Stigma scale adapted for COVID-19. Research staff will complete a checklist documenting uptake of infection control measures at all follow-up contacts (1, 2, 3, 4 weeks). A sample size of 120 households (60 per group; 320 patient and household contacts per group) will provide 80-99% power to detect a 40% reduction in R0 (2.5 to 1.5) varying the intra-cluster correlation efficient from 0.90 (80%) to 0.05 (99%) (Table 3). Index patients and their contacts will be reimbursed with R150 for their time at the baseline and final study visits.

A mixed methods process evaluation will explore acceptability, feasibility and contextual factors impacting intervention delivery guided by the Consolidated Framework for Implementation Research. Qualitative data collection during the first 4 weeks will be curtailed to minimise exposure of research staff completing qualitative interviews (high risk for COVID-19 transmission) and will be limited to observation of CHW training and up to 5 initial CHW household assessments. We will explore the feasibility of recording and analysing telephone interactions between CHWs and households. Once a household has been determined to be COVID-19 free (2 weeks after last symptoms in a diagnosed person) trained qualitative interviewers will conduct interviews with patients, household contacts and caregivers. These in-depth interviews will be limited to a purposive sample of 5 households per group. CHWs and community leaders will also be interviewed.

Assessing SARS-CoV-2 transmission: The research team will conduct SARS-CoV-2 testing with household contacts at baseline and weekly for 1 month. SARS-CoV-2 transmission will be monitored using nasopharyngeal nostril swabs for SARS-CoV-2 GeneXpert PCR and antibody COVID-19 lgG/lgM Rapid serology assays. Nasopharyngeal samples will be collected in a well-ventilated sputum collection space and staff will have adequate protective equipment. Venepuncture will be used to obtain dried blood spots. The test results will be delivered telephonically to household contacts within 24 hours of the test. HHC will complete a daily symptom checklist and symptom data will be collated weekly by the research team. Six months after a positive SARS-CoV-2 antibody, the study nurse will visit the participant household to conduct SARS-CoV-2 serology to assess for the presence of antibodies.

Eligibility of index case:

Inclusion:

Individual >12 years
Able to give assent if <18 years with parental/guardian consent
Able to give consent> 18 years
Self-isolating at home at the time of COVID diagnosis
Exclusion:
<12 years
Unable to give consent

Eligibility of HHC
Inclusion:
Living in the same household as index case
Able to give assent if 12-17 years with parental/guardian consent
Able to give consent≥ 18 years
Exclusion:
Unable to give consent

Table 2: Study procedures

Study participant	Procedure	Baseline	Week 1	Week 2	Week 3	Week 4
Index						
	ICF	x				
	Demography survey	x				
	Symptom check	x	x	x	x	x
	Follow up surveys	x		x		x
Household Contacts (HHC)						
	ICF	x				
	Demography survey	x				
	Symptom check	x	x	x	x	x
	COVID19 PCR	x	x	x	x	x
	COVID serology	x	x	x	x	x
	Follow up surveys	x		x		x

Data Collection and Management: Data will be collected by study staff on handheld devices. Data will be downloaded daily to a central database housed at the DTHF head office. Further details are available in Work Package 5 and the Data Management document.

Statistical Analysis and sample size: We will describe and compare the characteristics and survey outcomes, isolation, and linkages of participants. We calculated the different effect sizes (Table 2). Based on exponential test for comparing hazards, assuming 120*6=720 subjects, different intraclass correlation coefficients (ICCs) and comparing R0=2.5 (with resulting incidence of 0.208 among 720 subjects) to a reduced R0 of 0.9 (64% reduction, with resulting incidence of 0.075 among 720 subjects) or 1.25 (50% reduction) or 1.5 (40% reduction).

Table 3: ICC calculations

ICC	R0 2.5 to 0.9	R0 2.5 to 1.25	R0 2.5 to 1.5
	64% reduction	50% reduction	40% reduction
0.05	1.00000	1.00000	0.999944
0.25	1.00000	0.999891	0.991312
0.50	0.999993	0.995042	0.935880
0.75	0.999729	0.972942	0.846222
0.90	0.999033	0.951485	0.792745

The analyses will be determined by the study analysis plan. These analyses include the calculation of the proportion of SARS-CoV-2 positive individuals screened over a 3-month period, the transmissibility of the virus by determining the proportion of SARS-CoV-2 transmitted to household contacts of the identified COVID19 cases over a 4-week period, the period of infectiousness by correlating the time to transmission and clinical symptoms of the index cases, and the symptomatic/asymptomatic ratio among transmitted SARS-CoV-2 in household contacts. The Ro will be determined by both looking at new cases among the population in contact with the index cases and the total population (both in our service and other clinics in the area) diagnosed over time. The main outcome relates to the incidence of new cases of COVID19. These will be analysed using mixed effect Poisson regression models and frailty models to take the clustering by household into account. Both these regression models take the duration of follow up into account. Scores (e.g., GHQ) will be baseline adjusted. Qualitative data will be transcribed, translated and inductively analysed for themes.

Study Management: This project will be managed by a protocol team led by the overall PI, Prof Linda-Gail Bekker. There will be a safety team made up of clinicians from the protocol team. This group will convene fortnightly. The protocol team, chaired by Prof Bekker, will constantly review study progress and outcomes.

Ethical Review and Human Subjects Protection – The study will be reviewed and approved by the University of Cape Town Health Science Research Ethics Committee.

Our research focuses on investigating transmission of SARS-CoV-2 in a crowded environment in the Klipfontein district in Cape Town, South Africa. In keeping with the urgency to understand the local COVID19 epidemic, we formally and respectfully request an expedited human subjects ethical review. The protocol meets the Common Rule criteria as the research study is expected to pose no more than minimal risk to subjects AND the procedures fall within “category 2” outlined the Human Research Protections (OHRP) and in compliance with 45 CFR 46.110(b)(1). According to the OHRP category 2, the proposed research poses no more than minimal risk with collection of blood samples through fingerprick, venepuncture and nasal swabs as per national standard operating procedures.

Risk Mitigation: Staff will be given appropriate PPE and where possible all processes will be carried out in well ventilated spaces- outdoors where possible, whilst observing confidentiality. Cases and contacts will be invited to participate 24 hours before the mobile visit. Staff will invite contacts to attend the screening in small carefully controlled groups which will observe physical distancing. There are support services for participants at the site, including staff who are able to counsel participants, or telephonically, as well as established referral routes to external counselling resources. Participation in the study is voluntary. Participants may refuse participation, which will not affect further treatment. Participants will have the option to opt out of the study at any time. All information is anonymous and will be kept confidential. The name of investigators who are responsible for conducting the study and

direct contact details (telephone, address, e-mail) will be made available on the informed consent forms. The Site Investigator or designee will maintain, and store securely, complete, accurate, and current study records throughout the study, in accordance with local regulations. All records will be stored confidentially for five years from the beginning of the study.

Overall Risk – The greatest risks here are exposure of staff or among potential participants to undiagnosed cases of COVID and or TB (which may mimic COVID symptoms). Every effort will be made to enhance and adequately implement infection control measures.

Risks to participants: COVID-19 diagnosis has the potential to be stigmatized in communities. Although the study site will make every effort to protect participant privacy and confidentiality, including conducting testing and counselling in a private space, it is possible that participants' involvement in the study could become known to others. Social harms will be monitored and documented throughout the duration of the study. Should additional support be required for some participants due to study-related harms, referrals will be made to community-based services as needed. DTHF has worked in the setting of HIV and TB for 20 years. The staff and policies are well developed to mitigate risk related to stigmatization. The DTHF mobiles for this reason conduct health screening that is multi-disease related with an emphasis on wellness. The mobile units, known as 'Tutu Testers' are a loved brand and well known in communities. Confidentiality is highly regarded and carefully maintained. Good participatory practices are also carefully followed by all. Risk and benefits will be carefully conveyed at the time of recruitment and enrolment. Cases and household contacts will participate voluntarily and can withdraw at any time. All data will be treated confidentially and after consent, participants will be assigned participant identifiers for all study related documents. Study related impacts and harms will be solicited weekly and where necessary participants will be referred for support.

Risk to Staff: The risk of SARS-CoV-2 infection exists for research staff. All staff will be fully informed of risks. They will be provided with protective personal equipment to reduce infection risk including appropriate respirators, scrubs, aprons, goggles, gloves and sanitiser. The mobiles have running water for regular hand washing. The specimens will be collected in outdoor gazebos which allow adequate natural ventilation where possible. Where privacy is needed, the specimen collection will occur in the mobile clinic with only a single participant and adequate sanitisation and ventilation both before and after specimen collection. Staff providing the infection mitigation intervention will also be given appropriate counselling, training and equipment. Staff will be checked for symptoms daily and tested as needed. The mobile vehicle will be sanitised after each participant and decontaminated daily.

Benefits: Participants will benefit from SARS-CoV-2 testing by knowing their status. Participants and others may benefit in the future from information learned from this study. Participants may appreciate the opportunity to collaboratively contribute to the field of SARS-CoV-2 research. Information learned in this study may lead to the development of interventions to prevent onward SARS-CoV-2 transmission in an HIV endemic community. Participants who test HIV/ TB positive will be referred to the nearest clinic for rapid ART and/ or TB treatment start.

Data safety and monitoring: Information about study subjects will be kept confidential and all who choose to participate will complete an informed consent form. DTHF has standard operating procedures for data security and confidentiality procedures at collection, entry and storage levels, and will only release this information to study team members who have HREC/ IRB approval. All study data will remain securely stored by DTHF for the duration of the study. No participant identifiers will be included on any data forms; names and signatures will only be on the consent

forms, which will be kept under lock and key by the DTHF study. At the end of the study, data will be kept for up to 5 years for electronic version, and up to 2 years for paper forms, including consent forms at the DTHF office. The TRACE study will not begin until all the relevant staff members have been trained on the study specific procedures (see Work Package E: Training and Capacity Building and Work Package D: Data Management). All staff who have contact with human subjects will have completed an acceptable Human Subjects Protection training. Enough is known about the procedures in this proposal to evaluate and determine anticipated risks and these will be explained to participants. In addition, the TRACE management team will routinely evaluate adverse events and assess for any social harms occurring during the study period. The site staff will intervene, at the participant's request, to mitigate or resolve any social problems. Local phone numbers are provided on the consent form that participants can use to access resource persons for questions relating to social harms. The team will conduct HIV, TB, and SARS-CoV-2 risk reduction counselling to lower the chances of exposure for study participants.

Trial registry. The TRACE study protocol team will register and post-trial information to the Pan African Clinical Trial registry, which is based in South Africa and can be found at: https://pactr.samrc.ac.za/

Potential impact of the proposed research. The findings from this project have relevance to SARS-CoV-2 prevention and management in HIV and/ or TB co-infected patients. The findings will inform prevention methods to reduce SARS-CoV-19 infection acquisition and onward transmission in close crowded environments. Understanding the household and community transmission of SARS-CoV-2 will contribute to policy for effective prevention measures. Research on scalable interventions is urgently required. The proposed study may influence large scale, community-based SARS-CoV-2 testing and triage to circumvent COVID-19 patients overburdening hospital facilities. Understanding community viral transmission can facilitate decision making around prognosis and treatment. Additionally, COVID-19 treatment development is ongoing and mobile testing facilities would be ideal platforms for the targeted delivery of rapid-initiation treatment that does not require COVID-19 patients to travel in public transport. DTHF is aware and committed to support the requirements of ensuring timely publications of results, that publications are placed in the public domain, and sharing of scientific results with scientists interested in SARS-CoV-2/ COVID-19 services that improve health outcomes. Materials generated under this project will be disseminated consistent with University policies regarding data sharing. Opportunities for secondary analyses will be available following completion of the project and publication of the main study findings. These findings will be available to the public through scientific meetings or peer-reviewed journals, as well as through a structured policy dissemination process.

Management plan: timelines, milestones, and deliverables

Activities	Mo 1	Mo 2	Mo 3	Mo 4	Mo 5	Mo 6	Mo 7	Mo 8
Protocol development, Ethics Committee application, staff training (2 months)								
Aim 1 Accrual period (including first participant in and last participant in)								
Aim2: Randomised controlled trial intervention								
Aim 1: Household contact follow up								
End of data collection - last participant out								

Data lock								
Planned dissemination meetings and webinars								
Clinical study report: final report and primary manuscripts submitted for publication.								

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CLIENT SITE CODE:_____
E.G. ABCD1234 or STICKER

University of Cape Town - Department of Medicine
Informed Consent Form – index patient

Research Study: TRACE

Invitation and Purpose: We are researchers from the Department of Medicine at the University of Cape Town. You are invited to take part in a research study where you will be asked questions about COVID-19 symptoms. We would like to understand SARS-CoV-2 transmission and the impact of improved information on preventing SARS-CoV-2 transmission. You may receive a standard message or an improved message about SARS-CoV-2 transmission prevention. Your participation will help us understand if people who receive enhanced messaging decreases SARS-CoV-2 transmission.

Procedures: If you decide to take part in this study, we will ask you survey questions about your experience of symptoms, which will take 15 minutes. As part of the usual clinic service, you will receive HIV and TB testing and counselling. If you test positive for TB or HIV, we will refer you for treatment at the nearest clinic. If you agree, we will follow up medical records to see if you access treatment at the facility. You will be reimbursed with a R150 voucher at this visit and at the last study visit (visit 5). Lastly, we will contact you six months after the study to test for COVID-19 antibodies.

Risks, Discomforts & Inconveniences: There are no risks or discomforts over the standard survey, and HIV testing procedure. The fingerprick/ venepuncture blood draw may be painful. Additionally, it may be distressing to receive an HIV positive result. All information you give is confidential. We will not share your results with anyone.

Benefits: This study will not benefit you directly. However, the knowledge we gain from it will be used to help develop improved messaging for SARS-CoV-2/ COVID-19 management.

Alternatives (Other Options): You do not have to participate in this study—it is up to you.

Privacy and Confidentiality: We will take strict precautions to safeguard your personal information throughout the study. Your information will be kept without your name or personal identifiers. Your information will be identified with a code on a password-protected computer. Study data will be kept on a password-protected, secure server in the Department of Medicine at the Desmond Tutu HIV Foundation. Only the researchers will be able to access your personal information.

Questions: If you have questions, concerns, or complaints about the study, please contact Dr Philip Smith on 021 650 1895. If you have any questions about the rights you have while taking part in this study, call Prof. M Blockman, Chairperson for the University of Cape Town, Faculty of Health Sciences Human Research Ethics Committee, Old Main Building, Groote Schuur Hospital, Anzio Road, Observatory, Cape Town, 7925, South Africa, tel 021 406 6338; fax 021 406 6411) which is an independent committee established to help protect the rights of research participants. This is a group of scientific and non-scientific individuals who review research studies with the safety and welfare of research participants in mind and gave their positive opinion to this research study.

Signatures: {Participant's name}_____ has been informed of the nature and purpose of the procedures described above including any risks involved in its performance. He or she has been given time to ask any questions and these questions have been answered to the best of the investigator's ability. A signed copy of this consent form will be made available to the participant.

I have been informed about this research study and understand its purpose, possible benefits, risks, discomforts and that the researchers will follow up my medical records, including:

- Fingerpick/ venepuncture blood draw (weekly) to test for SARS-CoV-2 antibodies
- Nose and throat swabs (weekly) SARS-CoV-2 – to test for the virus
- Access to medical records
- Consent to samples and data to be stored and used in future research
- Follow up visits (1 visit every week), additional visits if randomised to the StopCov arm

I agree to take part in this research as a subject. I know that I am free to withdraw this consent and quit this project at any time, and that doing so will not cause me any penalty or loss of benefits that I would otherwise be entitled to enjoy.

I consent (please check) ☐ I do not consent (please check) ☐

Participants name: _____ Participants signature: _____ Date: _____

Investigators name: _____ Investigators signature: _____ Date: _____

CLIENT SITE CODE:_____
E.G. ABCD1234 or STICKER

University of Cape Town - Department of Medicine
Informed Consent Form – household contact

Research Study: TRACE

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Procedures: If you decide you to take part in this study, we will ask you survey questions about your experience of symptoms, which will take 15 minutes. As part of the usual clinic service, you will receive HIV, STI, blood pressure, blood glucose, and TB testing and counselling at baseline and SARS-CoV-2 testing at each visit. If you test positive for any of the tests, we will refer you for treatment at the nearest clinic. If you agree, we will follow up your medical records to see if you access treatment at the facility. You will be reimbursed with a R150 voucher at this visit and at the last study visit (visit 5). Lastly, we will contact you six months after the study to test for COVID-19 antibodies.

Risks, Discomforts & Inconveniences: There are no risks or discomforts over the standard survey, nasopharangeal swabs, and HIV testing procedure. There is risk of discomfort and a mild nosebleed with nasopharyngeal swabs. The fingerprick/ venepuncture blood draw may be painful. Additionally, it may be distressing to receive a positive result for HIV/ COVID19/ TB and staff are trained to provide counselling. All information you give is confidential. We will not share your results with anyone.

Benefits: This study will not benefit you directly. However, the knowledge we gain from it will be used to help develop improved messaging for SARS-CoV-2/ COVID-19 management.

Alternatives (Other Options): You do not have to participate in this study—it is up to you.

Privacy and Confidentiality: We will take strict precautions to safeguard your personal information throughout the study. Your information will be kept without your name or personal identifiers. Your information will be identified with a code on a password-protected computer. Study data will be kept on a password-protected, secure server in the Department of Medicine at the Desmond Tutu HIV Foundation. Only the researchers will be able to access your personal information. If you test positive for SARS-CoV-2, your result will be notified to the NICD.

Questions: If you have questions, concerns, or complaints about the study, please contact Dr Philip Smith on 021 650 1895. If you have any questions about the rights you have while taking part in this study, call Prof. M Blockman, Chairperson for the University of Cape Town, Faculty of Health Sciences Human Research Ethics Committee, Old Main Building, Groote Schuur Hospital, Anzio Road, Observatory, Cape Town, 7925, South Africa, tel 021 406 6338; fax 021 406 6411) which is an independent committee established to help protect the rights of research participants. This is a group of scientific and non-scientific individuals who review research studies with the safety and welfare of research participants in mind and gave their positive opinion to this research study.

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Participants name: _____ Participants signature: _____ Date: _____

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