

HIV Prevention Trials Network

LETTER OF AMENDMENT #2 TO:

HPTN 071

**Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART):
A cluster-randomized trial of the impact of a combination prevention package on population-level HIV incidence in Zambia and South Africa**

Protocol Version 3.0 dated 16 November 2015

DAIDS Protocol ID: 11865

Date of Letter of Amendment: 06 December 2016

Information/Instructions to Study Sites from the Division of AIDS

The information contained in this Letter of Amendment (LoA) impacts the HPTN 071 (PopART) study and must be forwarded to your Institutional Review Board (IRB) and/or Ethics Committee (EC) as soon as possible for their review and approval. This LoA must be approved by all responsible IRBs/ECs before implementation.

The information in this LoA affects the Sample Informed Consent Forms.

Upon receiving final IRB/EC and any other applicable regulatory entity approval(s) for this LoA, your site may implement immediately any activities included in the LoA that do not require consent, or that only require revision to consent forms you have previously registered with the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). For any activities included in this LoA that require the participant to sign a consent form that is newly introduced with this LoA (that is, that your site has not previously registered with PRO), your site must first submit the LoA registration packet to PRO, including any new consents, and receive notification of successful registration prior to commencing those activities. A copy of the LoA registration notification along with this letter and any IRB/EC correspondence should be retained in the site's regulatory files.

If the HPTN 071 (PopART) protocol is amended in the future, this LoA will be incorporated into the next version.

Summary of Revisions and Rationale

The HPTN 071 protocol v3.0, 16 November 2015 has been updated to reflect the changes listed in this Summary of Revisions and Rationale. All changes made are indicated in the next section, Implementation of the Protocol Modifications.

- 1) The description of the qualitative studies to be undertaken as part of the protocol has been revised. The sample informed consent for qualitative activities has been modified accordingly and an additional sample informed consent for parental/guardian consent has been added.

- 2) The sample informed consent for the Population Cohort (PC) has been revised to reflect the follow-up visit schedule for participants newly enrolling during the first or second round of follow up visits (PC12N and PC24N).
- 3) The sample informed consent forms for PC and for the intervention have been modified slightly to reflect the change in local guidelines for initiation of antiretroviral therapy (ART), which has eliminated the differences between the study's two intervention arms.
- 4) Administrative revisions were made to the protocol.

The reason for the first revision is to allow the team to merge two of the qualitative activities described in the originally-approved protocol into a single activity, to be more effective and efficient. Both of the original activities ('Qualitative Longitudinal Study in Arms A and B' and 'Ethnography of the HIV Landscape') proposed to follow a small number of participants in differing situations in relation to HIV (i.e. with and without HIV, having tested and not tested for HIV, on ART and not on ART). We have now combined these activities into a 'Qualitative Cohort' that will be followed longitudinally and which aims to describe the experiences of people living in the study communities generally alongside clients with different experiences of the PopART intervention. Linked to the case control studies, the cohort aims to explore in particular the reasons why clients do or do not accept Household Counselling and Testing (HCT), do or do not re-test in subsequent years and do or do not link to HIV care/initiate ART.

The reason for the second revision is to modify the PC consent to reflect the follow-up visit schedule for participants newly enrolling during the first or second round of follow up visits (PC12N and PC24). Since enrolling these participants was already approved as part of the prior LoA, this change merely brings the consents in line with that activity.

The reason for the third revision is that in both Zambia and South Africa, the standard HIV treatment guidelines in the areas where we work have now changed to include the offer of immediate treatment for HIV. This eliminated the difference between Arms A and B, and so the consents have been modified to reflect this change.

The reason for the fourth revision is to update the information for Dr. Christophe Fraser who has moved to a different institution and amend the Table of Contents and List of Tables and Figures to reflect the changes to the protocol described in the revisions above.

For the following sections, colored strikethrough (**example**) indicates text that has been deleted from the protocol. Colored underline (**example**) indicates text that has been added to the protocol. In the sample informed consent forms, bold text in brackets (**example**) indicates language that sites may alter, or not include, in their locally-adapted consent forms, depending on requirements. Ellipses within brackets ([...]) indicate areas where text from the protocol has not been shown, to reduce the length of this document.

Revision 1- Revision to Qualitative Activities

Section 5.4 Qualitative Studies

“In the second phase, the qualitative research will have ~~three~~two core components, ~~namely:~~ 1) qualitative research evaluating the acceptability of the intervention (**‘The Story of the Trial’**) including, critically, the acceptability and functioning of the CHiPs and the process of community engagement; and 2) a qualitative longitudinal study of representative individuals ~~nested within (the first Case-Control~~ **‘Qualitative Cohort’**) to describe the experiences of people living in the study described above; and an ethnographic component: communities generally (ethnography) and to understand the perspectives of clients with particular responses to the components of the PopART intervention (e.g. those who accept HIV testing and those who do not).”

Section 5.4.1 Evaluation of the Acceptability of the Intervention

Evaluation of the Acceptability of the Intervention: – The Story of the Trial

... This research component will be carried out throughout the intervention period at intervals linked to the intervention timeline – e.g. at the outset, ~~three months into every subsequent year~~ in the intervention, ~~a year into if there are any significant changes in~~ the intervention and, towards the end of the intervention and after the completion of the intervention implementation. Comparative research will also be carried out in Arm C – evaluating community response to HIV testing and treatment in the absence of trial interventions. Following full implementation of protocol version 3.0, social science research will be conducted on the transition to immediate eligibility for ART in Arm B and C communities and the continued response to this change over time. In addition, social science research now encompasses the inclusion of adolescents in the intervention.

Building on the rapid formative research, qualitative insights will be collected in ~~a structured diary form throughout the intervention period from all communities using resident fieldworkers who would dedicate a few days a month to document local response. More in-depth work~~ annual 2-3 week blocks of mixed-method field research by social science graduates. This will also be carried out in communities of a certain type. In these communities, roughly 100 participants, including supplemented by a variety of observational data on study implementation (e.g. at annual CHiP training), in-depth interviews with key local stakeholders, CHiP teams personnel responsible for study implementation, and different age and gender groups from the community, discussions with residents in study communities. In Zambia, this will be questioned about the acceptability of the intervention, any problems experienced or foreseen, and suggested solutions to these problems, and findings will be fed back into community engagement and trial practice. supplemented by routine observations conducted by social science research assistants based in the study communities...

Section 5.4.2 Qualitative Longitudinal Study in Arms A and B – sub-set of Case-Control Study 1

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A small number (roughly 12 in each selected community) of representative individuals from *Case-Control Study 1* will be enrolled and seen longitudinally over the intervention period in selected communities across Arms A and B to explore and document the longitudinal trajectory of individual behavior in relation to uptake of HIV testing and treatment, complementing the findings of the case-control studies.

Individuals who have refused testing at baseline and individuals who have accepted testing with different outcomes (tested HIV-uninfected or HIV-infected) from different genders, age groups, and socio-demographic backgrounds will be selected and approached to participate in this longitudinal study. This cohort of individuals would be recruited following their participation in *Case-Control Study 1* with the first in-depth interview taking place after the *Case-Control Study 1* survey, and subsequent in-depth interviews being held at one to three-month intervals until the end of the intervention period. This research will document experiences over time and establish how the micro-level continuum of experiences influence decision-making processes related to uptake of HIV testing and treatment services. Additional locator information will be collected and separate informed consent obtained for the study for each visit.

A mix of methods will be used including semi-structured interviews, observations and respondent records of significant events pertaining to individual health and health-seeking behavior. In-depth interviews will be conducted by local social science research assistants supervised by a social scientist.

As a result of changes to the protocol in version 3.0, and in addition to the above, a small number of individuals in some Arm C communities representing different decisions concerning HIV testing and treatment (following the shift to immediate eligibility to ART) will also be recruited and followed to the end of the intervention period.

5.4.2 Qualitative Cohort

This component will be conducted in all nine study communities in South Africa and purposively selected study communities in Zambia (selected across Arms and geographical areas and according to key characteristics that influence uptake of the intervention). It has the dual goals of 1) providing contextual and comparative understanding of how communities are experiencing the roll-out of UTT, including immediate HIV treatment, and 2) understanding the perspectives of individuals from particular groups, including those who accept or do not accept HIV testing, those who test positive for HIV and those who test negative and those who have started ART and those who have not. The primary research activity with cohort participants is spending significant time with them and conducting a set of semi-structured participatory research activities as prompts for in-depth discussions. The social science team will interact with cohort participants frequently: approximately once a month or once every-other-month from the time of recruitment until the end of the study, or until completion of at least five core data collection modules (each module pertaining to a set of social factors influencing HIV service uptake). The cohort activities will be conducted by a team of graduate social scientists and local social science research assistants.

Recruitment of qualitative cohort participants will employ a range of strategies. These include: referral by local key informants and CAB members; referral by NGOs and local stakeholder groups; through Case Control study teams; through intervention and clinic data; and walking through the community. The aim is to identify particular groups and ages and to achieve qualitative representation for different types of HIV pathways and identities that have an influence on HIV.

Participants include adolescents aged 16 years and above in Zambia, and 12 years and above in South Africa – these are the respective ages of consent for HIV counselling and testing. Qualitative cohort participants will be recruited from approximately 50 households across four communities in Zambia and from approximately 110 households across nine communities in South Africa. In Zambia, the social science team will focus their efforts on one person in each cohort household. This will be the person who will provide data longitudinally through repeated in-depth interviews, although participatory qualitative activities, as described above, may take place that involve additional household members to provide context and broader ethnographic understanding. In South Africa, staff resources and the relatively short distances between communities will allow the social science team to spend more time with each cohort household. Because of this, multiple household members may be recruited to participate at various times in in-depth individual interviews, or in structured focus groups, or other activities.

Section 5.4.3 Ethnography of the HIV landscape

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This component aims to provide more contextual and comparative understanding of how communities are experiencing the roll-out of UTT, including immediate HIV treatment. The inquiry will build on and extend current knowledge of the impact of ART on HIV stigma, the long-term realities of ART in low-resource settings, the influence of alternative prevention options, the role of welfare and food insecurity in shaping uptake of ART, popular knowledge of ART, sexual risk disinhibition, alcohol and drug use, gender-based violence, HIV identity, the reproductive health of people living with HIV, the acceptability of and response to male circumcision, the influence of local systems, social networks and community morale, and the role of different stakeholders. This ethnographic research will use a mix of social research methods—with the most key method being the continued presence of a social scientist in a community over a period of 3–6 months, mostly likely 6–18 months into the intervention period. It will be carried out in two communities in each country and most of the inquiry will be carried out at household level

5.4.3 Consent for Qualitative Cohort Participation

The activities of the qualitative cohort are unlike the activities of a typical clinical trial in which pre-determined questions are asked, and biological samples collected, from an individual in a clinic setting according to a prescribed schedule. Conduct of the qualitative cohort, by contrast, will take place in the home or surrounding community of the individual or household participating, involves activities and discussions informed by and responsive to context, and occurs through repeated immersion of the social scientist into the lives of the participants. Because of this, at the start of every interaction, the research team asks verbal permission to visit again and to further explore new topics in the household's or individual's experiences of the world. At every point, any individual, or group of individuals, or the household as a whole can opt out of continuing participation altogether, or participation in a particular component of the activities. In practice, this happens in very organic ways. However, as part of a clinical research trial, the study team recognizes the importance of the formal documentation afforded by obtaining written informed consent prior to initiation of cohort activities. In both countries, adult participants who will participate in the more formal data collection activities, such as an individual interview or structured focus group, will therefore sign a standard informed consent form based on the sample informed consent in Appendix III, prior to participation. Younger people, below the age of independent research consent (but, as noted above, at least the age of legal consent for HIV testing locally) may also be invited to participate in more formal data collection activities. In these instances, the study will be explained to both the minor and the parent/guardian and consent will be sought from both. The minor will be asked to sign a

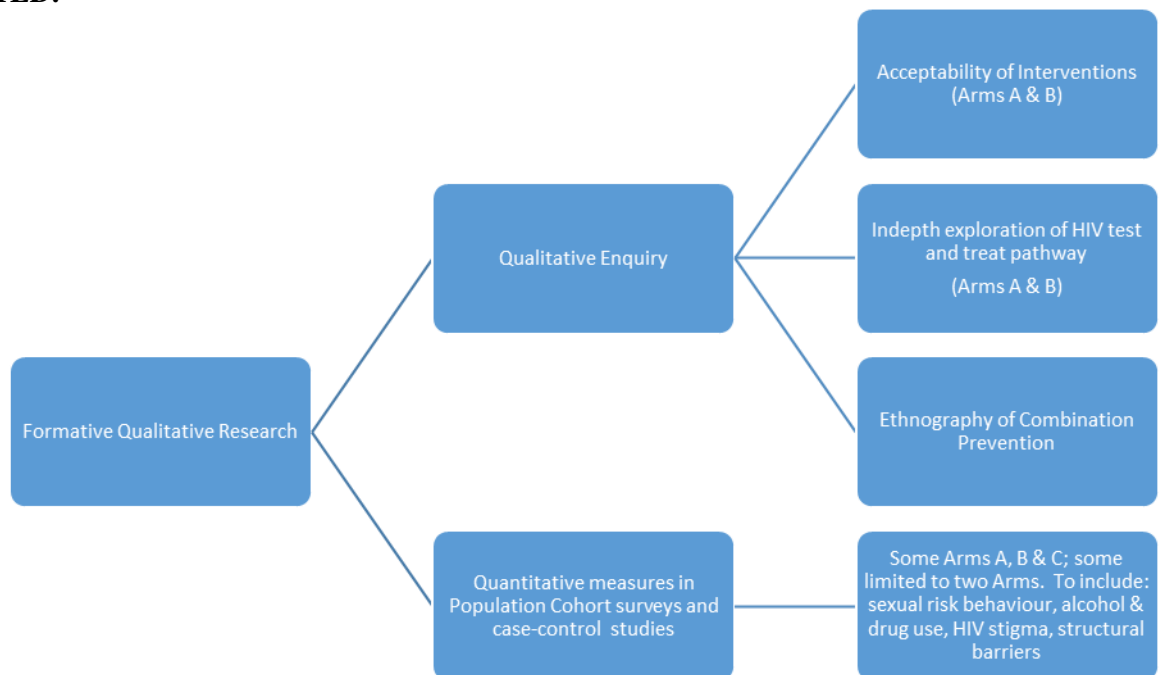
consent for him/herself in lieu of a verbal assent. A sample informed consent form for parental/guardian consent for minors has been included in Appendix IIIB. In both countries, but particularly in South Africa where there will be the opportunity for more extensive interactions between social scientists and household members, verbal consent from household members will be the standard for ethnographic work and for group participatory activities that involve the whole household, in keeping with standard practice for ethnography and local ethics committee recommendations.

Section 5.4.4 Graphical Summary of Qualitative Activities

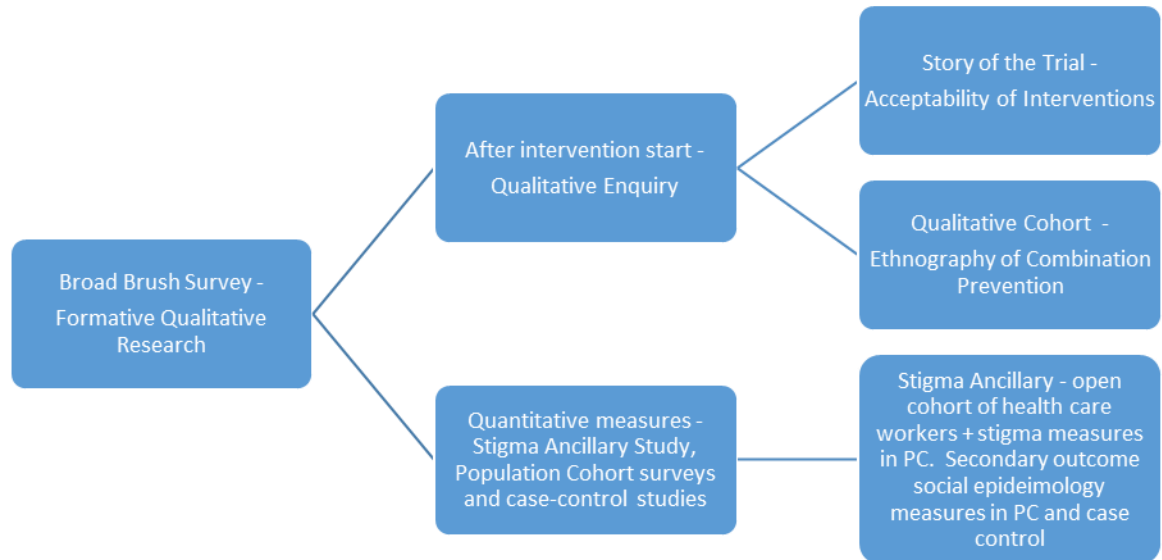
A summary of the timing, flow and logic of how the qualitative activities described fit into the wider social science of PopART is provided in Figure 4.

Figure 1- QualitativeSocial Science Activities in HPTN 071

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5.4.5- Integration of Data from Case-Control and Qualitative Components

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~~The social science team will be involved in helping to develop the themes and questions for the case control studies. Within the case control studies there is a qualitative component that aims to provide a more detailed picture of HIV testing and treatment pathways for a small number of representative individuals. The lead investigator for the case control studies will work closely with a social scientist who will carry out the qualitative component as well as supporting the quantitative measures/data collection. Broader ethnographic enquiry will also explore core themes (all related to secondary outcomes)~~

Appendix III - Sample Informed Consent Form – Qualitative Studies Participants

NOTE: Sample informed consent forms are adapted from NIH templates. It is understood that sites will modify these consents to meet the requirements of their setting and of their ethics committees. Modifications made locally to prior versions of the consents that have already been approved for use in-country are expected to be maintained in subsequent site-specific consent versions.

NOTE: As described in the protocol, youth below the age of legal research consent but at least the age of consent for HIV testing in-country may be invited to participate in certain qualitative activities requiring written consent as a community member. Their written consent will be solicited using the standard site-specific consent form for that activity, with parental consent obtained in addition.

SUBJECT INFORMATION AND CONSENT FORM

Title of Research Study: **Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART): A cluster-randomized trial of the impact of a combination prevention package on population-level HIV incidence in Zambia and South Africa**

Protocol #: HPTN 071, Version 3.0 16 November 2015
DAIDS ID: 11865

Sponsor: National Institute of Allergy and Infectious Diseases
National Institute of Mental Health
(U.S. National Institutes of Health)
Office of the United States Global AIDS Coordinator
Bill and Melinda Gates Foundation

Investigator of Record: *(insert name)*

Research Site Address(es): *(insert address)*

Daytime telephone number(s): *(insert number)*

24-hour contact number(s): *(insert number)*

Subject Information and Consent Form

Please ask the study investigator or the study staff to explain any words or procedures that you do not clearly understand.

Purpose of the Research in the Communities

The HPTN 071 or PopART study is testing a program to try to reduce HIV infection in ~~a community~~ communities like yours. Twenty one communities that include about 600,000 adults are included in this research (about 400,000 adults in twelve Zambian communities and 200,000 adults in nine South African communities).

~~In some communities, the level of care that people are used to will stay the same, in terms of HIV testing, and care of those who have HIV.~~

~~In other communities, to make HIV testing easier, each community health care workers will go to all homes and will offer to do an HIV test on each adult (or younger people with permission of guardian) wishing to have a test. For anyone infected with HIV, they will be offered to start taking drugs to treat HIV according to the standard treatment guidelines that are in place for doing so in your country. The health workers will visit every home again once a year for up to three more years to repeat the HIV testing and to refer people to care.~~

~~In other communities, health care workers will go to all houses offering HIV testing, as was just described. In these communities if someone tests HIV positive however, they will be offered to start taking medicines to treat HIV right away. The health workers will visit every home again once a year for up to three more years to repeat the HIV testing and to refer people to care.~~

~~At the end of the study, the researchers will see if offering HIV tests in each household and offering people the chance to start HIV treatment right away has reduced HIV infection.~~

~~Your community is one of the communities participating in this research. If health care workers are visiting homes in your community, you will notice that they provide some other information and services to people, but the most important thing is the testing and HIV treatment they offer.~~

~~In each community, around 2,700, some people will be asked to participate in additional activities such as completing questionnaires and providing additional samples for laboratory testing. These questionnaires and tests will let the researchers participating in discussions, being interviewed, being observed while they work or go about their day, or being documented in photos. The goal of these activities is to help us understand the community better. It will help us know how the community feels people feel about the HPTN 071 (PopART) program and if the how people in this community meet their health needs. It will also help us understand why people do or do not participate in different parts of the PopART program is working like HIV testing. You have been selected to be one of the people from your community who we are asking to participate in these additional activities. That is why you are being asked to read this document.~~

Why were you selected?

You are being asked to participate because you are a resident or working in a community that is a part of the PopART study.

What will happen during this study?

[For participants providing a single interview]

~~If you agree to participate in this study, you will have one interview today. We will ask you questions about the reasons why people in this community chose to test for HIV or not to test for HIV. We will also ask about how people in this community experience HIV treatment and any other HIV prevention methods.~~

[For participants being followed longitudinally]

~~If you agree to participate in this study, we will interview you every three months until the end of the study. We will ask you questions about the reasons why people in this community chose to test for HIV or not to test for HIV. We will also ask about how people in this community experience HIV treatment and any other HIV prevention methods.~~

[For individuals participating in a focus group]

~~You have been selected to participate in this group discussion because of either your knowledge of the community or your association with HIV/AIDS related programs and activities in this community. If you agree to participate in this study, you will be a part of a group and questions will be directed~~

towards the group, but you are free to answer any question and comment on the answers of others. In some instances, the facilitator may ask you to elaborate on your answer for the benefit of others but you may choose not to if you are not entirely comfortable with the request. The questions will be broad/general in nature and will touch on many aspects of the community's experiences with HIV.

Single In-Depth Interview (may include: community member, health worker)

You are being asked to participate in an interview with a study staff member who will ask you questions about [*Consent may include any or all of the following elements depending on local implementation: “**how the PopART study intervention is being implemented; how the community is responding to the intervention; how study communities participate and experience HIV ‘combination prevention’; major events that have happened as a result of the PopART study; your thoughts and opinions on HIV and PopART related topics**”*]. [*Depending on local implementation: “**You may be asked to do some activities (like ranking of alternatives)**”*]. This interview is expected to last about [*Will be adjusted depending on local implementation: “**30” - “90”**”*] minutes. The staff member will record the discussion and take notes [*Depending on local implementation: “**and, with your permission, may photograph all or parts of the interview. We may ask if we can spend a bit more time with you outside of the interview to observe and better understand your perspective**”*].

Longitudinal In-Depth Interviews (may include: community member, health worker)

You are being asked to participate in multiple interviews with a study staff member who will ask you questions about [*Consent may include any or all of the following elements depending on local implementation: “**how the PopART study intervention is being implemented; how the community is responding to the intervention; how study communities participate and experience HIV ‘combination prevention’; major events that have happened as a result of the PopART study; your thoughts and opinions on HIV and PopART related topics**”*]. [*Depending on local implementation: “**You may be asked to do some activities (like ranking of alternatives)**”*]. These interviews are expected to last about [*Will be adjusted depending on local implementation: “**30” - “90”**”*] minutes and will take place about every 3-4 months until the end of the study (June 2018). The staff member will record the discussion and take notes [*Depending on local implementation: “**and, with your permission, may photograph all or parts of the interview. We may ask if we can spend a bit more time with you outside of the interview to observe and better understand your perspective**”*].

Focus Groups (may include: community member, health worker)

You are being invited to participate in a group discussion related to health, HIV and related issues in the HPTN 071 (PopART) study communities. Typically, these discussions include several people and last [*Will be adjusted depending on local implementation: “**30”-“180” – “240”**”*] minutes. During the discussion, the research team will ask you questions, may ask you to clarify or elaborate on your responses, and encourage you to talk to others. The research team will record the discussion and make notes of what they see and hear [*Depending on local implementation: “**and with your permission, may photograph all or parts of the discussion**”*].

Observing/Shadowing (community member)

The social science field team would like to spend time with you as a representative of people living in the HPTN 071 (PopART) study communities. In order to properly understand your life, we would like to spend a significant portion of time with you (at your home, in the places you go to during the day and evening, and anywhere else you think that would help us to clearly understand your life). For most participants, we will spend time observing their daily life, conduct a follow-up phone call or visit in about one month, and have at least one in-person follow-up visit a few months later. During this time, the research team will observe your life and ask you questions. The research team will make notes of what they see and hear [*Depending on local implementation: “**and will also keep records like audio recordings and photographs of relevant parts of their observations. The research team would also**”*].

like you to refer us to other people who are significant to you and may help us better understand your life.”]

Observing/Shadowing (health worker)

The social science field team would like to spend time with you as you do your work for the day, being at your side as you interact with clients or customers, joining you if you are on breaks and so on. During this time, they may ask you questions, and they will make notes of what they see and hear. Some of the questions might be particular to health and HIV, but in general the conversation is about better understanding your work and how the PopART intervention is being implemented. They will also keep records like audio recordings and photographs of relevant parts of their observations.

Photo-journal (may include: CAB member, health worker) (SA only)

The social science field team would like to work with certain members of this community such as CAB members or health workers to develop a photo-journal about health, HIV and HPTN 071 (PopART). This process will include spending about an hour at a meeting discussing the photo-journal, then a day walking through the study community with you taking photographs, and then another hour at a subsequent meeting to discuss the outcome of the day of taking photographs. During this time, the research team will ask you questions, make notes of what they see and hear, and will also keep records like audio recordings and photographs of relevant parts of their observations.

What are the possible risks or discomforts?

The risk to you in participating in this study is that some of the questions may be uncomfortable and may make you feel worried or embarrassed. If any of the questions make you feel upset, the interviewer may go to another question or totally stop the interview.

There is also a risk that following up individuals at home may lead to rumors in the community. To minimize this risk we will ask you to propose places where we can talk in private.

What are the potential benefits?

You will not receive any direct benefit from being in this study. You or others may benefit in the future from the information learned in this study.

Are there any alternatives to participation?

If you decide not to participate in this study, you can still receive HIV tests and other services from your local health center.

How will my confidentiality and privacy be protected?

We cannot guarantee absolute confidentiality. However, we will do everything possible to protect your confidentiality if you join this study. We do this by giving you a study number and any information you provide will be labeled with this number only, not your name. Only the research staff will be able to link this number to your name. Your personal information (name, address, phone number) will be protected by the research staff. This information will not be used in any publication of information about this study.

To protect your privacy, you will meet with the researcher in a private area where others cannot overhear conversations with you.

People who may review your records include: [insert name of site IRB/EC], local regulatory agencies, US National Institutes of Health (NIH), study staff, and study monitors. Institutional Review Boards (IRBs) or Ethics Committees (ECs) are committees that watch over the safety and rights of research participants.

[Information and related waiver of consent re: long term storage and social science databank to be included only if applicable and approved by the local ethics board:]

Long term storage of the data and inclusion in a social science databank

If you sign the consent document, you are agreeing to allow the researchers to use the information you share with them to answer the questions of this study, as described above. Hard copies of the data will be stored in secure, lockable cabinets and soft copies on secure, password-protected computer platforms. The data will be stored for a minimum of 7 years and destroyed after 7 years or after study completion.

Unless you indicate otherwise, you are *also* agreeing to allow researchers to store your data in what is called a ‘social science databank’. Storing your data in the databank means it can be used to answer additional relevant research questions besides the ones described above. All data stored in this way will be treated as confidential as described in the section above on “participant confidentiality and privacy”. We ask to store the data and use the data in this way for four reasons:

- (a) To reduce the burden on research communities because multiple researchers do not have to ‘keep coming back’ asking very similar questions**
- (b) To enable researchers to understand patterns over a much longer time scale than is usually possible because we will have contributions like this from multiple research studies**
- (c) To offer opportunities to students to analyse real data that it would usually be too logistically challenging for them to collect and thus improve social science training**
- (d) To help ensure that all such social science research is conducted with the same rigor and at the same high standard**

Every new study or analysis that wants to use the data you contribute will still need to receive approval to do this from an appropriate ethics review committee. There are strict controls in place as to who may access such stored data and for what purpose.

If you *DO NOT* want your data to be included in this databank, please indicate this to the research staff now and they will show you how to indicate this on the consent form when you sign consent. Otherwise, it will be assumed that you are happy for the data to be included as described.]

What happens if I am injured by participating in this study?

It is very unlikely that you could be injured as a result of participating in this study. However, if you are injured while participating in this study, you will be given immediate treatment for your injuries. You [will/will not] have to pay for this care. There [is a/is no] program for compensation either through this institution or the United States NIH. You will not be giving up any of your legal rights by signing this Subject Information and Consent Form.

What are some reasons why I may be withdrawn from this activity without my consent?

You may be withdrawn from the study without your consent for the following reasons:

- The research study, or this part of the study, is stopped or canceled
- The study staff feels that completing the study or this part of the study would be harmful to you or others

Persons to Contact for Problems or Questions

If you have any questions about your participation in this research study, your rights as a research subject, or if you feel that you have experienced a research-related injury, contact:

Investigator of Record Name: *(site insert name of the investigator or other study staff)*

Research Site Address(es): *(site insert physical address of above)*

Daytime telephone number(s): *(site insert telephone number)*

24-hour contact number(s): *(site insert telephone number)*

If you have any questions or concerns about your rights as a research subject or want to discuss a problem, get information or offer input, you may contact:

Independent Review Board/Ethics Committee: *(site insert name or title of person on the IRB/EC or other organization appropriate for the site)*

Address of Independent Review Board:*(site insert physical address of above)*

Daytime Telephone Number: *(site insert telephone number of above)*

SUBJECT'S STATEMENT OF CONSENT

Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART): A cluster-randomized trial of the impact of a combination prevention package on population-level HIV incidence in Zambia and South Africa

- I have been given sufficient time to consider whether to take part in this study.
- My taking part in this research study is voluntary. I may decide not to take part or to withdraw from the research study at any time without penalty or loss of benefits or treatment to which I am entitled.
- The research study may be stopped at any time without my consent.
- I have had an opportunity to ask my study investigator questions about this research study. My questions so far have been answered to my satisfaction.
- I have been told how long I may be in the research study.
- I have been informed of the procedures and tests that may be performed during the research study.
- I have been told what the possible risks and benefits are from taking part in this research study. I may not benefit if I take part in this research study.
- I do not give up my legal rights by signing this form.
- I have been told that before any study related procedures being performed, I will be asked to voluntarily sign this Subject Information and Consent Form.
- I will receive a signed and dated copy of this Subject Information and Consent Form.

If you have either read or have heard the information in this Subject Information and Consent Form, if all of your questions have been answered, and if you agree to take part in the study, please print and sign ~~and~~ your name and write the date on the line below.

I voluntarily agree to take part in this research study.

Subject's Name (print)

Subject's Signature and Date

[To be included only if optional language above regarding data banking is part of the local sites's consent:

I, the participant, indicate my preference that the data I contribute be EXCLUDED from the social science databank (that is, the data I contribute will only be used for the HPTN 071 (PopART) study and NOT other research) by signing again here: (otherwise leave blank)

I certify that the information provided was given in a language that was understandable to the subject.

Name of Study Staff

Study Staff Signature and Date

Conducting Consent Discussion (print)

Witness' Name (print)
(As appropriate) Date

Witness' Signature and Date

Appendix IIIB - Sample Informed Consent Form – Parent/Guardian Consent for Participation of a Minor in Qualitative Studies

NOTE: Sample informed consent forms are adapted from NIH templates. It is understood that sites will modify these consents to meet the requirements of their setting and of their ethics committees. Modifications made locally to prior versions of the consents that have already been approved for use in-country are expected to be maintained in subsequent site-specific consent versions.

SUBJECT INFORMATION AND CONSENT FORM

Title of Research Study: **Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART): A cluster-randomized trial of the impact of a combination prevention package on population-level HIV incidence in Zambia and South Africa**

Protocol #: **HPTN 071, Version 3.0 16 November 2015**
DAIDS ID: 11865

Sponsor: **National Institute of Allergy and Infectious Diseases**
National Institute of Mental Health
(U.S. National Institutes of Health)
Office of the United States Global AIDS Coordinator
Bill and Melinda Gates Foundation

Investigator of Record: **(insert name)**

Research Site Address(es): **(insert address)**

Daytime telephone number(s): **(insert number)**

24-hour contact number(s): **(insert number)**

Subject Information and Consent Form

Please ask the study investigator or the study staff to explain any words or procedures that you do not clearly understand.

The purpose of this form is to give you information about a research study that the minor in your care is being asked to join. If you sign this form, you will be giving your permission for that minor to take part in the study. The form describes the purpose, procedures, benefits, and risks of the research study. You should agree for the minor to take part in the study only if you want to do so. You may choose not to allow the minor to join the research project, or withdraw your permission for the minor's participation in this study at any time. Choosing not to have the minor take part in this research will not in any way affect the health care or benefits that the minor, or you, or your family will receive. Please read this Subject Information and Consent Form and ask as many questions as needed. You should not sign this form if you have any questions that have not been answered to your satisfaction.

This study is being funded by the U.S. National Institutes of Health, the Office of the United States Global AIDS Coordinator, and the Bill and Melinda Gates Foundation

Participation is voluntary

The minor in your care does not have to take part in this study. If you give permission today for the minor to take part in this research project, you may decide not to let the minor take part in any portion of the study or stop participating at any time without reducing or affecting any care that you or the minor receive at the health centers in your community.

Purpose of the Research in the Communities

The HPTN 071 or PopART study is testing a program to try to reduce HIV infection in communities like yours. Twenty one communities that include about 600,000 adults are included in this research (about 400,000 adults in twelve Zambian communities and 200,000 adults in nine South African communities).

In each community, some people will be asked to participate in activities such as participating in discussions, being interviewed, being observed while they work or go about their day, or being documented in photos. The goal of these activities is to help us understand the community better. It will help us know how people feel about the HPTN 071 (PopART) program and how people in this community meet their health needs. It will also help us understand why people do or do not participate in different parts of the PopART program like HIV testing. The minor in your care has been selected to be one of the people we are asking to participate in these activities. That is why you are being asked to read this document.

Why was the minor in your care selected?

The minor in your care is being asked to participate because the minor is a resident in a community that is a part of the PopART study.

What will happen during this study?

Single In-Depth Interview

The minor in your care is being asked to participate in an interview with a study staff member who will ask questions about [Consent may include any or all of the following elements depending on local implementation: **“how the PopART study intervention is being implemented; how the community is responding to the intervention; how study communities participate and experience HIV ‘combination prevention’; major events that have happened as a result of the PopART study; the minor’s thoughts and opinions on HIV and PopART-related topics”**]. [Depending on local implementation: **“The minor may be asked to do some activities (like ranking of alternatives)”**]. This interview is expected to last about [Will be adjusted depending on local implementation: **“30” - “90”**] minutes. The staff member will record the discussion and take notes [Depending on local implementation: **“and, with your permission, may photograph all or parts of the interview. We may ask if we can spend a bit more time with the minor outside of the interview to observe and better understand the minor’s perspective”**].

Longitudinal In-Depth Interviews

The minor in your care is being asked to participate in multiple interviews with a study staff member who will ask questions about [Consent may include any or all of the following elements depending on local implementation: **“how the PopART study intervention is being implemented; how the community is responding to the intervention; how study communities participate and experience HIV ‘combination prevention’; major events that have happened as a result of the PopART study; the minor’s thoughts and opinions on HIV and PopART related topics”**]. [Depending on local implementation: **“The minor may be asked to do some activities (like ranking of alternatives)”**]. These interviews are expected to last about [Will be adjusted depending on local implementation: **“30” - “90”**] minutes and will take place about every 3-4 months until the end of the study (June 2018). The staff member will record the discussion and take notes [Depending on local implementation: **“and, with your permission, may photograph all or parts of the interview. We**

may ask if we can spend a bit more time with the minor outside of the interview to observe and better understand the minor’s perspective”].

Focus Groups

The minor in your care is being invited to participate in a group discussion related to health, HIV and related issues in the HPTN 071 (PopART) study communities. Typically, these discussions include several people and last [Will be adjusted depending on local implementation: “30”-“180” – “240”] minutes. During the discussion, the research team will ask the minor questions, may ask the minor to clarify or elaborate on their responses, and encourage the minor to talk to others. The research team will record the discussion and make notes of what they see and hear [Depending on local implementation: “and with your permission, may photograph all or parts of the discussion”].

Observing/Shadowing

The social science field team would like to spend time with the minor in your care as a representative of people living in the HPTN 071 (PopART) study communities. In order to properly understand the life of the minor, we would like to spend a significant portion of time with the minor (at his/her home, in the places he/she goes to during the day and evening, and anywhere else that would help us to clearly understand your minor’s life). For most participants, we will spend time observing people’s daily lives, conduct a follow-up phone call or visit in about one month, and at least one in-person follow-up visit a few months later. During this time, the research team will observe the minor’s life and ask the minor questions. The research team will make notes of what they see and hear [Depending on local implementation: “and will also keep records like audio recordings and photographs of relevant parts of their observations. The research team would also like the minor to refer us to other people who are significant to them and may help us better understand their life.”]

What are the possible risks or discomforts?

The risk to your minor in participating in this study is that some of the questions may be uncomfortable and may make the minor feel worried or embarrassed. If any of the questions make the minor upset, the interviewer may go to another question or totally stop the interview.

There is also a risk that following up individuals at home may lead to rumors in the community. To minimize this risk we will ask you to propose places where we can talk in private.

What are the potential benefits?

Neither you nor the minor in your care will receive any direct benefit from being in this study. The minor in your care or others may benefit in the future from the information learned in this study.

Are there any alternatives to participation?

If you decide not to have the minor in your care participate in this study, you and the minor can still receive HIV tests and other services from your local health center.

How will confidentiality and privacy be protected?

We cannot guarantee absolute confidentiality. However, we will do everything possible to protect the confidentiality of the minor in your care if he or she joins this study. We do this by giving the minor a study number and any information the minor provides will be labeled with this number only, not their name. Only the research staff will be able to link this number to the minor’s name. The minor’s personal information (name, address, phone number) will be protected by the research staff. This information will not be used in any publication of information about this study.

To protect the minor’s privacy, he or she will meet with the researcher in a private area where others cannot overhear the conversation when discussing confidential topics.

People who may review study records include: [insert name of site IRB/EC], local regulatory agencies, US National Institutes of Health (NIH), study staff, and study monitors. Institutional Review Boards (IRBs) or Ethics Committees (ECs) are committees that watch over the safety and rights of research participants.

[Information and related waiver of consent re: long term storage and social science databank to be included only if applicable and approved by the local ethics board:]

Long term storage of the data and inclusion in a social science databank

If you sign the consent document, you are agreeing to allow the researchers to use the information that the minor in your care shares with them to answer the questions of this study, as described above. Hard copies of the data will be stored in secure, lockable cabinets and soft copies on secure, password-protected computer platforms. The data will be stored for a minimum of 7 years and destroyed after 7 years or after study completion.

Unless you indicate otherwise, you are *also* agreeing to allow researchers to store these data in what is called a ‘social science databank’. Storing the minor’s data in the databank means it can be used to answer additional relevant research questions besides the ones described above. All data stored in this way will be treated as confidential as described in the section above on “participant confidentiality and privacy”. We ask to store the data and use the data in this way for four reasons:

1. To reduce the burden on research communities because multiple researchers do not have to ‘keep coming back’ asking very similar questions
2. To enable researchers to understand patterns over a much longer time scale than is usually possible because we will have contributions like this from multiple research studies
3. To offer opportunities to students to analyse real data that it would usually be too logistically challenging for them to collect and thus improve social science training
4. To help ensure that all such social science research is conducted with the same rigor and at the same high standard

Every new study or analysis that wants to use the data contributed by the minor in your care will still need to receive approval to do this from an appropriate ethics review committee. There are strict controls in place as to who may access such stored data and for what purpose.

If you *DO NOT* want your minor’s data to be included in this databank, please indicate this to the research staff now and they will show you how to indicate this on the consent form when you sign consent. Otherwise, it will be assumed that you are happy for the data to be included as described.]

What happens if the minor in my care is injured by participating in this study?

It is very unlikely that the minor could be injured as a result of participating in this study. However, if the minor is injured while participating in this study, they will be given immediate treatment for their injuries. You [will/will not] have to pay for this care. There [is a/is no] program for compensation either through this institution or the United States NIH. You will not be giving up any legal rights of you or your minor by signing this Subject Information and Consent Form.

What are some reasons why the minor in my care may be withdrawn from this activity without my consent?

The minor may be withdrawn from the study without your consent for the following reasons:

- The research study, or this part of the study, is stopped or canceled
- The study staff feels that completing the study or this part of the study would be harmful to the minor or others

Persons to Contact for Problems or Questions

If you have any questions about participation of the minor in your care in this research study, their rights as a research subject, or if you feel that the minor has experienced a research-related injury, contact:

Investigator of Record Name: _____ *(site insert name of the investigator or other study staff)*

Research Site Address(es): _____ *(site insert physical address of above)*

Daytime telephone number(s): _____ *(site insert telephone number)*

24-hour contact number(s): _____ *(site insert telephone number)*

If you have any questions or concerns about the rights of your minor as a research subject or want to discuss a problem, get information or offer input, you may contact:

Independent Review Board/Ethics Committee: _____ *(site insert name or title of person on the IRB/EC or other organization appropriate for the site)*

Address of Independent Review Board:*(site insert physical address of above)*

Daytime Telephone Number: _____ *(site insert telephone number of above)*

STATEMENT OF CONSENT

Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART): A cluster-randomized trial of the impact of a combination prevention package on population-level HIV incidence in Zambia and South Africa

- I have been given sufficient time to consider whether to give permission for the minor in my care to take part in this study.
- Permitting the minor in my care to take part in this research study is voluntary. I may decide not to let them take part or to withdraw them from the research study at any time without penalty or loss of benefits or treatment to which they or I am entitled.
- The research study may be stopped at any time without my consent.
- I have had an opportunity to ask my study investigator questions about this research study. My questions so far have been answered to my satisfaction.
- I have been told how long the minor in my care may be in the research study.
- I have been informed of the procedures and tests that may be performed during the research study.
- I have been told what the possible risks and benefits are from taking part in this research study. Neither I nor the minor in my care may benefit from participation in this research study.
- I do not give up any legal rights for myself or the minor in my care by signing this form.
- I have been told that before any study related procedures being performed, I will be asked to voluntarily sign this Subject Information and Consent Form.
- I will receive a signed and dated copy of this Subject Information and Consent Form.

If you have either read or have heard the information in this Subject Information and Consent Form, if all of your questions have been answered, and if you agree to allow the minor in your care to take part in the study, please print and sign your name and write the date on the line below.

I voluntarily agree to allow the minor in my care to take part in this research study.

Name of Parent or Guardian (print)

Parent or Guardian's Signature and Date

[To be included only if optional language above regarding databanking is part of the local sites' consent:

I indicate my preference that the data contributed by the minor in my care be *EXCLUDED* from the social science databank (that is, the data the minor contributes will only be used for the HPTN 071 (PopART) study and *NOT* other research) by signing again here: (otherwise leave blank)

_____]

Revision 2- Revision to Sample Informed Consent for the Population Cohort (PC) to Accommodate Additional Enrollment

Appendix II- Sample Informed Consent Form – Population cohort

[...]

What will happen during this study?

If you participate in this study, you will have up to four [~~“three”~~ for participants enrolling at PC12N; “two” for participants enrolling at PC24N] study visits: today, in 12 months, in 24 months, and possibly a final visit in 36 months- [~~“in 12 and 24 months”~~ for PC12N participants; “in 12 months” for PC24N participants]. We will contact you to remind you about your visits. For example, we may call you or send a short text message (SMS). Today’s visit will take approximately 2 hours. Future visits may be slightly shorter.

[...]

Revision 3- Revision to Sample Informed Consent for the Population Cohort (PC) and Intervention to Reflect Changes in Local ART Guidelines

Appendix II- Sample Informed Consent Form – Population cohort

[...]

Purpose of the Research in the Communities

The HPTN 071 or PopART study is testing a program to try to reduce HIV infection in a community like yours. Twenty one communities that include about 600,000 adults are included in this research (about 400,000 adults in twelve Zambian communities and 200,000 adults in nine South African communities).

In some communities, the level of care that people are used to will stay the same, in terms of HIV testing, and care of those who have HIV.

In other communities, to make HIV testing easier, community health care workers will go to all homes and will offer to do an HIV test on each adult (or younger people with permission of guardian) wishing to have a test. ~~For anyone~~Anyone infected with HIV, ~~they will be offered to start taking~~receive a referral to the local health facility where drugs to treat HIV ~~according to the standard treatment guidelines that are in place for doing so in your country. The health workers will visit every home again once a year for up to three more years to repeat the HIV testing and to refer people to care.~~

~~In other communities, health care workers will go to all houses offering HIV testing, as was just described. In these communities if someone tests HIV positive however, they will be offered to start taking medicines to treat HIV right away~~offered. The health workers will visit every home again once a year for up to three more years to repeat the HIV testing and to refer people to care.

[...]

Appendix VI- Sample Informed Consent Form – CHiP Team Activities

[...]

How is the study being carried out?

- The PopART study has 3 Arms (Arms A, B and C). In each arm a package of HIV prevention services will be available including HIV testing, care and treatment, male circumcision, PMTCT and condoms:
 - In Arm C all of these activities will be available at the health facility. In arms A and B, community HIV workers (called CHiPs) will visit each household and offer HIV testing in the home and help people to link to care services at the health facility or in the community.
 - ~~In all arms of the study, people who are HIV positive will receive ART from the health facility. In Arms B and C this will be for all people who have a CD4 cell count below the threshold set by local guidelines. In Arm A, ALL people who are HIV positive will be offered ART at any CD4 cell count.~~
 - In Arms A and B, the CHiP teams will encourage pregnant women who are met during regular household visits, to attend an antenatal clinic in their community.
- The 21 study communities were put in these arms using a process called randomization, which is like a lottery. **Your community was put in Arm [A/B].**

[...]

Revision 4- Administrative Revisions

- Adjustments were made to the Table of Contents and List of Tables and Figures to reflect new page numbers and section headings.
- A revision was made to the Protocol Team Roster:

Christophe Fraser
Mathematical Modeler
~~Imperial College London~~
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