

Science, theory, and practice of engaged research: Good Participatory Practice and beyond

Guest Editors: Kathleen M MacQueen, Judith D Auerbach

Supplement Editor: Marlène Bras



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EDITORIAL

It is not just about “the trial”: the critical role of effective engagement and participatory practices for moving the HIV research field forward

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Engagement by and with affected people, communities, and other stakeholders has been a critical part of HIV treatment and prevention research since the earliest days of the epidemic [1,2]. It has been a force for moving important research forward through advocacy, as well as, a disrupter of research and its translation to practice when inadequate engagement creates possibilities of exploitation. Over the decades, there has been a gradual accumulation of experience on what engagement means, how to effectively engage diverse stakeholders, and how context influences the effectiveness of different engagement practices. We have also seen a gradual progression from engagement mainly as a consultative mechanism towards a fuller use of participatory practices. Advocates have led the way by creating independent structures such as the AIDS Coalition to Unleash Power (ACT UP) in 1987, Treatment Action Group (TAG) in 1992, AIDS Vaccine Advocacy Coalition (AVAC) in 1995, and the Alliance for Microbicides and the Global Campaign for Microbicides in 1998, as well as by pushing for leadership structures within major funding networks, such as the Community Partners [3] and the Legacy Project within the NIH Office of HIV/AIDS Network Coordination (HANC). Research advocacy organizations continue to emerge such as the New HIV Vaccine and Microbicide Advocacy Society (NHVMAS) in Nigeria, Africa free of New HIV Infections (AfnHI), and the International Rectal Microbicide Advocates (IRMA).

In parallel with this advocacy movement within HIV research, bioethicists historically have been engaged in a broader global discussion of the role of communities in research. UNAIDS called for the involvement of community representatives “in an early and sustained manner” in HIV vaccine trials in 2000 [4], and placed increased emphasis on community participation in guidance for biomedical HIV prevention trials more broadly in 2007 [5]. The Council for

International Organizations of Medical Sciences (CIOMS) provides detailed commentary on the need to engage research participants and communities “in a meaningful participatory process that involves them in an early and sustained manner” [6]. The National Health Research Ethics Council of South Africa recommends similar engagement by communities for health research generally and requires it for population-focused HIV prevention research specifically [7].

While the importance and legitimacy of engaged and participatory practices increasingly is recognized as a vital component of HIV and other health research, it nonetheless remains largely compartmentalized within the scientific process. For example, in many HIV research networks, community representation is mandated on protocol teams and implementing sites are required to have community advisory boards (CABs) or similar mechanisms in place, but representatives and CABs are not resourced or structurally supported in ways that parallel the contributions of laboratories, biostatistics, and clinical components. Protocol teams struggle to balance calls for substantive community participation in the early stages of research development and the pressure from funders to minimize costs and timelines to implementation. Advocates raise concerns that engagement practices are in danger of being reduced to window dressing, while researchers and funders raise equally important questions about the evidence that the time and resources invested in engagement ultimately enhance the ethical and scientific outcomes of the research. Systematic evaluation could assure advocates, researchers, and funders of the quality and value of engagement, yet it is rare. In fact, while the practice of engaged research has proliferated the science of it still is in early development [8-12].

Creating an evidence base for community and stakeholder engagement in HIV-related research is not an easy task. The

importance of understanding what will work, for whom, and under what conditions has increased as the boundaries between HIV prevention, treatment, and cure research have blurred and intervention strategies have become ever-more technological and differentiated [13]. This heightens the need to attend to context and its multiple dimensions—culture, politics, religion, history, economics, gender, family/kinship systems, and social hierarchies of race and ethnicity—in tandem with whatever specific HIV strategy is being explored.

While social scientists always argued for the need to pay attention to context, this generally fell on deaf ears in the biomedical HIV clinical trials world, until a few big controversies erupted in the 1990s and early 2000s. In 1994, the ACTG 076 trial demonstrated that AZT, the only retroviral treatment available at that time, was effective for preventing HIV transmission in utero and during birth [14]. The treatment regimen used in the trial was expensive, complex, and clinically demanding. Concerned that the treatment could therefore not be used in lower-middle income country (LMIC) settings where mother-to-child transmission rates were highest, a global effort began to field trials to test effectiveness of less intensive treatment regimens with a greater potential for scale-up in those settings. The trials were designed to compare the experimental regimens against a placebo, on the grounds that this reflected the current standard of care. The argument was that use of the ACTG 076 regimen as a comparator could result in rejection of effective new regimens that fell short of the ACTG 076 standard, and that such a design would also require both more resources and more time to implement [15]. As some analysts have argued, the trial design highlighted and sought to address global health inequities at one level, but failed to challenge them at another [16]. The trials raised important ethical questions about higher-income country (HIC) researchers' responsibilities to LMIC trial participants who lack access to effective interventions and treatment. The controversies led to revisions in international ethics guidelines, setting the stage for ongoing debates about the appropriate use of local versus global standards of care in the design of ethical trials, and who gets to decide what is appropriate and what is exploitative [17-20].

The controversial trials of simplified regimens to reduce mother-to-child HIV transmission were completed, despite the controversies, and showed efficacy. This led many HIV researchers to feel validated in their view of what constituted an appropriate balance between science and ethics in a research design. But for many advocates, the trials were just one more brick in a wall of global inequity that they were determined to tear down. By the early 2000s AIDS treatment activists built high-level support to expand antiretroviral treatment globally, despite widespread scepticism that such programmes could be successfully implemented in economically disadvantaged countries [21]. At the same time, the first pre-exposure prophylaxis (PrEP) trials were being planned in Cambodia and West Africa, but not in coordination with the effort to expand global treatment. For some treatment advocates, this raised several red flags: Why would researchers test a new, and at that time very expensive, antiretroviral drug in settings with limited access to similar drugs for treatment? Were poor women in poor countries being exploited, so that a drug company could profit from the sale of PrEP in rich countries? If antiretrovirals could be made available for a prevention trial, why couldn't participants who became infected in

that trial then be provided antiretroviral treatment aligned with global standards [22-24]? This new round of controversies led to the closure of a PrEP trial in Cameroon and prevented implementation of another in Cambodia [23]. Following this disruption, a three-year effort ensued during which UNAIDS, civil society representatives, advocates, researchers, funders, and bioethicists came together in a series of meetings that culminated in the creation of Good Participatory Practice (GPP) for HIV Prevention Trials, to parallel existing practice guidelines for clinical, laboratory, and epidemiological research [25,26].

This special supplement aims to explore the impact of GPP and broader community engagement efforts on the conduct and outcomes of HIV (chiefly prevention) research. We begin by looking at the state of engagement practice today. Day and colleagues conducted a scoping review of community engagement in HIV clinical trials, using benchmarks outlined in GPP guidelines: the variety of stakeholder engagement methods used, the variety of types of stakeholders engaged, and how engagement aligned with all stages of clinical research (pre-trial, implementation, and post-trial) [27]. The results are encouraging in that the benchmarks were met to at least some degree by all of the 108 studies included in the analysis. However, the authors found that many benchmarks were met using researcher-driven methods such as focus groups and interviews, rather than true participatory processes. They also found fewer studies reporting stakeholder engagement in LMIC than other income-status countries, and a general tendency to focus engagement on the early stages of trial planning rather than all along the trial's trajectory.

A challenge faced by Day and colleagues in their analysis is the fact that no standards exist for reporting on stakeholder engagement related to HIV (or other) clinical trials. Clinical trialists are fond of saying that "if it isn't documented, it didn't happen." The absence of documentation about stakeholder engagement efforts severely limits the systematic accumulation of knowledge and, therefore, opportunities to move the field forward. One option for both assuring a minimal standard for engagement and documenting the elements of that standard is regulatory oversight, as outlined by Slack and colleagues in this issue [28]. They describe consensus among extant guidelines that research ethics committees should review engagement for HIV prevention trials, but they note that there is a lack of consensus on what constitutes standards of excellence. At the same time, they note that regulatory oversight requires a delicate balancing act between ensuring compliance and respecting the need for research teams to maintain flexibility and responsiveness in their engagement practices. They argue that inclusion of engagement as part of the ethics review process should not result in a need for approval of amendments to the protocol that would undermine the concept of dynamic responsiveness.

Another aspect of community and stakeholder engagement that has received little attention in the literature is the set of challenges faced by research sites conducting multiple trials with multiple sponsors or other partners. Baron and colleagues present a unique case study highlighting lessons learned from a leading South African research institute in this regard [29]. Their analysis goes beyond assessing GPP implementation in the context of a single clinical trial, and documents the experience of implementing it on an institution-

wide level. They also attend to the impact of environmental factors beyond the control of the clinical trial team – in this case, the outcomes of two other trials in the area—on GPP implementation. Through self-reflection, the authors identify challenges, describe the long-term problem-solving strategies undertaken, and provide rich documentation about engagement that likely will prove useful to others.

Case examples and systematic reviews such as those described above are important contributions to building the evidence base for community and stakeholder engagement in HIV research. A persistent gap, however, centres on the need for generalizable data derived from the engagement experiences of multiple communities, research sites and clinical trials. The article by MacQueen and colleagues describes ongoing work aimed at filling this gap [30]. While focused on the example of GPP in the context of TB clinical trials, the process outlined by the authors for developing systematic measures is equally informative for the HIV research context. The article highlights the importance of developing a theory-based framework for evaluation of engagement practices, clarifying the goals of engagement, and engaging stakeholders in an iterative, participatory process to refine the measurement strategy.

Many of the challenges and gaps noted thus far reflect the outlier status of community and stakeholder engagement, that is, that it often is treated as ancillary to trials rather than as an integral dimension on par with clinical, laboratory, regulatory, and statistical components. This problem of viewing engagement narrowly as a tool or mechanism for supporting clinical trials has deeper implications. Pantelic and colleagues argue that engagement should not be viewed as a *method*, but rather as an *orientation* that should be built into the interventions being designed and tested [31]. They make the case for shifting the nature and orientation of HIV prevention research to be more aligned with the interests and needs of individuals and for addressing structural barriers to enhancing and integrating knowledge about community engagement in research through community-based participatory and person-centred research approaches.

Taking this mindset further, Wheeler and colleagues describe an HIV prevention study built on a long-term partnership among Black men who have sex with men (BMSM) communities and organizations in the United States, which included a multidisciplinary, multiracial research team led by BMSM together with a Black Caucus, comprised of highly respected multidisciplinary Black professionals [32]. The study, a PrEP demonstration project, included community consultations at all sites and staff trainings aligned with the person-centred research approach. The success of this project underscores the multiple layers of leadership and inclusion—from the grassroots to the institutional to the national—needed for true and effective engagement in communities where there are deep, persistent disparities in HIV and its syndemic co-travellers by race, ethnicity, and geography. This requires investing resources and building capacity, infrastructure, and scientific leadership within these communities to ensure substantive decision-making power is available to individuals from those communities who understand how these disparities are experienced.

As HIV research increasingly expands into the area of pragmatic and community-level interventions, the importance of engagement as more than an ancillary tool becomes even greater. Camlin and colleagues make the point that qualitative research methods can be an important “listening tool” in the

engagement process for large-scale clinical trials and can facilitate meaningful, productive dialogue that enhances intervention design and study implementation [33]. In one example, they describe uncovering gender differences in accessing HIV testing services from such qualitative research, and how the presentation of these findings to the clinical research team led to adjustments in the testing campaign. In another, they describe how ongoing qualitative research led to a deeper understanding of the impact of the intervention on the community which led to unanticipated positive social change that fuelled intervention effectiveness. This kind of finding would not be evident from a “typical,” quantitative clinical trial outcome analysis, and it has implications for future community-level trial design.

Lippman and colleagues carry this theme further in their description of theory-based community mobilization to reduce HIV acquisition among adolescent girls and young women (AGYW) in sub-Saharan Africa, where engagement and participatory practice were the intervention rather than merely the means for facilitating interventional research [34]. Their study is the first to show that community mobilization is associated with lower HIV incidence among AGYW. In highlighting the components of community mobilization that are protective—including, critical consciousness, leadership, social cohesion, and shared concerns around HIV—the authors point to social-level factors that can be harnessed for meaningful community engagement in HIV research, and, more importantly, for addressing fundamental inequities and disparities to better combat HIV and other health threats altogether.

CONCLUSION

Clinical research is essential, challenging work that has brought us to a point where we can envision a world without HIV. But clinical research alone will not create that world. HIV is a disease that travels with stigma, disparity, and discrimination—social processes that unintentionally may be reproduced in the context of clinical research if appropriate engagement of stakeholders does not occur. The realization of a world without HIV will require political will, social support, and funding, to translate science into the day-to-day lives of people and communities, and to have the day-to-day realities of people inform science. Experience has taught us that this bi-directional translation must include stakeholders at all levels, from the streets to global board rooms, and across all stages of research, from the earliest concepts to demonstration projects and programme scale-up. Stakeholder and community engagement must be fully and systematically integrated into HIV clinical research, and the evidence of its contributions and effectiveness must move beyond anecdotal reporting.

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COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHORS' CONTRIBUTIONS

K.M.M. and J.D.A. wrote the paper. Both authors read and approved the final manuscript.

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DISCLAIMER

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REVIEW ARTICLE

Stakeholder engagement to inform HIV clinical trials: a systematic review of the evidence

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Abstract

Introduction: Stakeholder engagement is an essential component of HIV clinical trials. We define stakeholder engagement as an input by individuals or groups with an interest in HIV clinical trials to inform the design or conduct of said trials. Despite its value, stakeholder engagement to inform HIV clinical trials has not been rigorously examined. The purpose of our systematic review is to examine stakeholder engagement for HIV clinical trials and compare it to the recommendations of the UNAIDS/AVAC Good Participatory Practice (GPP) guidelines.

Methods: We used the PRISMA checklist and identified English language studies describing stakeholder engagement to inform HIV clinical trials. Four databases (PubMed, Ovid, CINAHL and Web of Science) and six journals were searched, with additional studies identified using handsearching and expert input. Two independent reviewers examined citations, abstracts and full texts. Data were extracted on country, engagement methods, stakeholder types and purpose of stakeholder engagement. Based on the GPP guidelines, we examined how frequently stakeholder engagement was conducted to inform clinical trial research question development, protocol development, recruitment, enrolment, follow-up, results and dissemination.

Results and discussion: Of the 917 citations identified, 108 studies were included in the analysis. Forty-eight studies (44.4%) described stakeholder engagement in high-income countries, thirty (27.8%) in middle-income countries and nine (8.3%) in low-income countries. Fourteen methods for stakeholder engagement were identified, including individual (e.g. interviews) and group (e.g. community advisory boards) strategies. Thirty-five types of stakeholders were engaged, with approximately half of the studies (60; 55.6%) engaging HIV-affected community stakeholders (e.g. people living with HIV, at-risk or related populations of interest). We observed greater frequency of stakeholder engagement to inform protocol development (49 studies; 45.4%) and trial recruitment (47 studies; 43.5%). Fewer studies described stakeholder engagement to inform post-trial processes related to trial results (3; 2.8%) and dissemination (11; 10.2%).

Conclusions: Our findings identify important directions for future stakeholder engagement research and suggestions for policy. Most notably, we found that stakeholder engagement was more frequently conducted to inform early stages of HIV clinical trials compared to later stages. In order to meet recommendations established in the GPP guidelines, greater stakeholder engagement across all clinical trial stages is needed.

Keywords: stakeholder engagement; community; HIV clinical trials; reporting quality; systematic review; advisory mechanisms

Additional Supporting Information may be found online in the Supporting Information tab for this article.

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1 | INTRODUCTION

Engaging stakeholders in the clinical trial research process has been well established as a method to improve research implementation, procedures, and outcomes [1,2]. Stakeholders can be defined broadly as any individual or group who can have an impact on or is affected by a clinical trial [3]. Some examples of stakeholders include trial participants, members of local communities in which a trial is conducted, governmental organizations and funders who shape the research process. Strong stakeholder engagement can potentially result in trials that more effectively address stakeholders' needs and perspectives [4], as well as improve health equity, access and participant

welfare [5]. Stakeholder engagement is particularly important in HIV clinical trials, which require careful consideration of the unique physical, psychological and social vulnerabilities associated with HIV infection [6] and subsequent ethical obligations towards trial participants [7]. In addition, despite the disproportionate impact of the HIV epidemic on minority communities, these populations are underrepresented in HIV research [8]. These factors make stakeholder engagement critical for building effective and sustainable collaborations.

The field of HIV research has championed innovative stakeholder engagement efforts, spurred partly by the activism of those living with HIV. Following the efforts of the ACT-UP movement, the National Institutes of Health (NIH) established

community advisory boards (CABs) in the 1980s to help design and implement research within the NIH trials network, making CABs one of the earliest mandated forms of stakeholder engagement in HIV trials in the United States [9]. The first CABs in low- and middle-income countries were established in the late 1990s [10]. Since these early efforts, further advancements in stakeholder engagement have included the development of guidance documents such as *Principles of Community Engagement* by the Centers for Disease Control and Prevention [11], as well as guidelines specific to the conduct of HIV research, including: *Respect, Protect, Fulfill*, a guidance document for researchers involving men who have sex with men (MSM) in the HIV research process [12]; the *Stakeholder Engagement Toolkit for HIV Prevention Trials* [13]; *Recommendations for Community Engagement in HIV/AIDS Research*, developed by community stakeholders partnering with the NIH [14]; and the *Good Participatory Practice* (GPP) guidelines for stakeholder engagement in biomedical HIV prevention trials [3]. Developed jointly by UNAIDS and the AIDS Vaccine Advocacy Coalition (AVAC) in 2007, the GPP guidelines established a framework for effective stakeholder engagement in HIV clinical trials that are applicable to a broad range of stakeholders and use of an array of engagement methods [3]. These guidelines were revised in 2011 based on extensive consultation and feedback with global stakeholders. The GPP guidelines recommend stakeholder engagement as a continual process throughout the stages of a clinical trial: research question development, protocol development, recruitment, enrolment, follow-up, trial results and dissemination.

Although the importance of stakeholder engagement for HIV clinical trials is widely recognized, little is known about how engagement strategies are being implemented in this field. Existing literature is limited to examining the historical development of stakeholder engagement [15], exploring single sites of stakeholder engagement [16] and reviewing implementation challenges [17]. The purpose of our systematic review is to examine stakeholder engagement for HIV clinical trials and compare it to GPP benchmarks. More data on how stakeholder engagement is being conducted in-practice could help inform GPP guidelines and local engagement strategies for specific HIV trials. Five primary research questions are used to guide our inquiry: (1) What are the geographical locations in which stakeholder engagement is conducted for HIV clinical trials? (2) What methods of stakeholder engagement have been used to inform HIV clinical trials? (3) What types of stakeholders have been engaged? (4) For what purpose has stakeholder engagement been undertaken in relation to informing HIV clinical trials? (5) What is the quality of reporting on stakeholder engagement for HIV clinical trials? By examining how stakeholder engagement for HIV clinical trials has been conducted and reported, our review aims to provide a better understanding of patterns and gaps in existing engagement efforts, pointing to opportunities for improvement in accordance with the recommendations established by the GPP guidelines.

2 | METHODS

2.1 | Search strategy

We used the PRISMA checklist for reporting systematic review findings (Figure 1). We searched English language

studies published before 9 August 2017. Search terms included variations to capture the concept of stakeholder engagement (community engage* OR community consult* OR participatory OR community advis* OR stakeholder*) in combination with the terms HIV and clinical trial*. We searched four databases: PubMed, OVID, CINAHL, and Web of Science. To supplement database results, we additionally searched six HIV journals using their respective journal search functions: *Lancet HIV*, *Journal of the International AIDS Society*, *AIDS*, *Journal of Acquired Immune Deficiency Syndromes*, *AIDS Research and Human Retroviruses* and *International Journal of STD & AIDS*. Finally, studies' reference lists were handsearched for additional articles to include. We also contacted three individuals with relevant expertise to recommend additional references for inclusion. These individuals were experts in the field of stakeholder engagement for HIV clinical trials and/or principal investigators on NIH-funded projects examining the conduct of HIV research.

2.2 | Study selection

To be selected for review, a study had to describe some form of stakeholder engagement undertaken for informing the design or conduct of an HIV clinical trial. Two reviewers independently screened all titles and abstracts returned from searches. Disagreements were resolved through discussion with a third reviewer. The full texts of selected abstracts were then read in full independently by two reviewers for final inclusion and again compared for agreement, with discrepancies resolved by third reviewer. Duplicates were removed and reasons for excluding abstracts and full texts were recorded at each selection stage. A two-reviewer selection process was similarly applied to studies identified via reference list searching and expert input.

As the purpose of our review was to provide an overview of stakeholder engagement for HIV clinical trials, we used a broad definition of stakeholder engagement. Adapting descriptions of stakeholders and advisory mechanisms for HIV prevention trials outlined in the GPP guidelines [3], we defined stakeholder engagement as any input sought from an individual or group with a stake in HIV clinical trials to inform the design or conduct of said trials. Our definition of clinical trials follows the NIH definition, which encompasses interventions in both biomedical and behavioural outcomes [18]. Using this definition allowed us to include studies describing stakeholder engagement to inform both biomedical HIV-related trials (e.g. vaccine and microbicide trials) and behavioural trials (e.g. trials of behavioural interventions for HIV prevention). Regardless of whether the trial was biomedical or behavioural, it had to be related explicitly to HIV in order to be included in the review; for example, we did not include behavioural trials for prevention of sexually transmitted infections in general.

Recognizing that stakeholder engagement takes place along a continuum from minimal to substantial involvement [2], we did not limit selection of studies based on the extent of stakeholder engagement in the studies identified. We also did not limit inclusion of studies solely to stakeholder engagement efforts undertaken for a current HIV clinical trial; studies describing stakeholder engagement to inform future and/or hypothetical HIV clinical trials (i.e. the field of HIV clinical trial research in general) were also included. Studies were excluded on the basis of not involving stakeholder engagement to

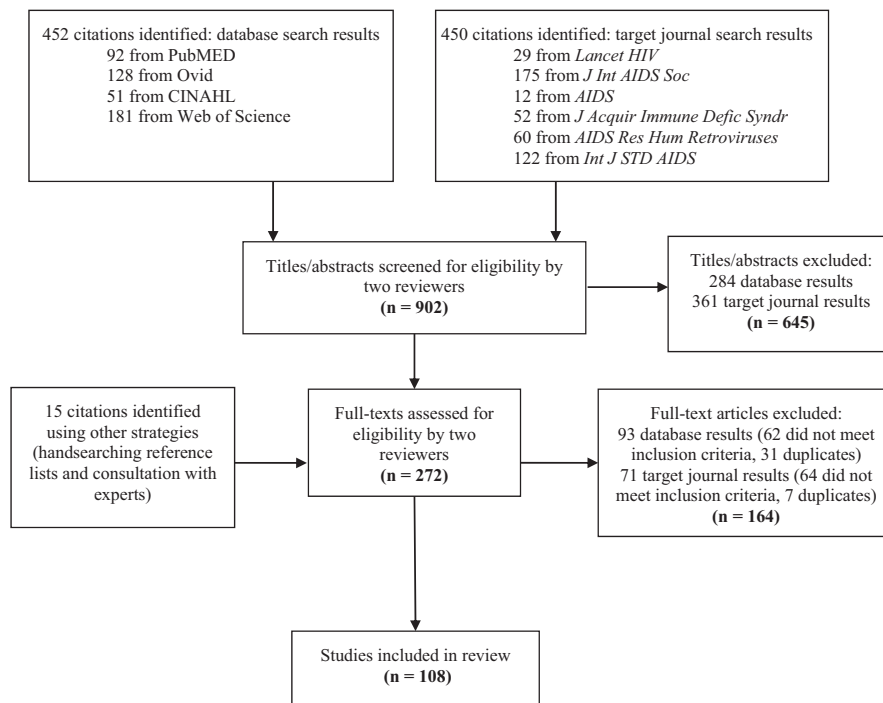


Figure 1. Search and selection strategy results for a systematic review of stakeholder engagement for HIV clinical trials.

inform HIV clinical trials as per our set definitions. We excluded editorials and reviews.

2.3 | Data extraction and analysis

A data extraction chart was developed to record four characteristics of studies included in the review: the geographical location of engagement activities, the methods used for stakeholder engagement, the types of stakeholders engaged and the purpose of stakeholder engagement. Geographical location was extracted based on the country where stakeholder engagement was conducted using World Bank classifications (high-, middle- or low-income countries) [19]. We did not extract data on the location of the clinical trial given our focus on stakeholder engagement. The purpose of stakeholder engagement refers to the reason that it was undertaken relative to informing the conduct of an HIV clinical trial. Our choice to extract descriptions of purpose rather than outcome was again due to our selection strategy: since we included studies of stakeholder engagement to inform future/hypothetical HIV clinical trials, it was not always possible to extract data on the impact or outcomes of stakeholder engagement. However, all studies described (in varying levels of detail) the purpose for which stakeholder engagement was undertaken relative to inform HIV clinical trials.

Following data extraction, a series of analytic codes were developed to categorize the purpose of stakeholder engagement in each study by the stage of the HIV clinical trial research process that stakeholder engagement was undertaken to inform. Broad coding categories were initially developed based on the seven stages of an HIV clinical trial process as outlined in the GPP guidelines: research question development, protocol development, trial recruitment, participant enrolment, follow-up, results and dissemination [3]. We then used an open coding process to develop and apply thematic codes to each study

based on the various reasons for which stakeholder engagement was undertaken to inform any given stage in the HIV clinical trial research process. Coding was conducted exhaustively to categorize the potentially multiple reasons for conducting stakeholder engagement in any one study. For example, if a study included stakeholder engagement to both enhance the ethical conduct of the trial as well as develop effective recruitment strategies, the study would receive both codes.

Data analysis involved comparing our extracted and coded data to three benchmarks outlined in the GPP guidelines [3]. First, given that GPP guidelines recommend use of an array of stakeholder advisory mechanisms beyond the clinical trial CABs, we identified and categorized all stakeholder engagement methods used and calculated the number of studies using each method. We did not assess the extent of stakeholder engagement in each study because there are no standardized metrics [20]. Second, GPP guidelines stress the identification of relevant trial stakeholders, noting a distinction between community stakeholders (i.e. stakeholders representing the interests of persons participating in the trial and/or affected by the trial) and other stakeholders with interests in HIV clinical trials more broadly (i.e. funders, government representatives). As such, our analysis aimed to identify and categorize the types of stakeholders presently engaged in HIV clinical trials, again calculating the number of studies engaging each stakeholder type. Finally, given that GPP guidelines recommend stakeholder engagement throughout the entire clinical trial, we categorized purpose of engagement according to the seven stages of the HIV clinical trial process.

2.4 | Quality of reporting on stakeholder engagement

To assess reporting quality, we adapted the short form of a checklist on Guidance for Reporting Involvement of Patients

and the Public (GRIPP) in health research [21] into a reporting quality assessment tool. All studies were assessed by one reviewer per study for inclusion of the following information: (1) description of stakeholder engagement purpose; (2) explanation for choice of stakeholder engagement method; (3) description of the development of stakeholder engagement methods used; (4) the number of stakeholders engaged; (5) the results of stakeholder engagement; (6) the impact of stakeholder engagement on trial design/conduct; and (7) discussion of limitations to the stakeholder engagement method used. In each study, these seven reporting details were assessed as being either present or absent. Analysis of reporting quality was conducted for all 108 studies overall, as well as by the type of trial that engagement was conducted to inform (i.e. behavioural prevention trials, biomedical prevention trials, treatment trials or combination/trial type not specified). Additionally, in accordance with the Sex and Gender Equity in Research (SAGER) guidelines [22], we assessed two indicators of the extent to which studies reported on stakeholders' sex and/or gender (depending on which variable was relevant to the study): the number of stakeholders engaged by sex and/or gender category, and reporting of stakeholder results disaggregated by sex and/or gender.

3 | RESULTS

As illustrated in Figure 1, a total of 452 titles and abstracts were returned for screening from our four database searches. Of these, 168 full texts were assessed, resulting in 75 studies included for review from the database search strategy. Our target journal search produced 402 titles and abstracts for screening, of which 89 full texts were assessed and 18 studies were retained for review. Our additional search strategies (handsearching of reference lists and inquiry with field experts) yielded an additional 15 studies for inclusion. In total, 108 studies were selected for final inclusion and data extraction. The oldest study included in our review was published in 1988 [23], and the most recent was published July 2017 [24]. Of the 108 studies in our review, 11 studies conducted stakeholder engagement to inform behavioural HIV prevention trials, 70 for biomedical HIV prevention trials and 10 for HIV treatment trials. In the remaining 17 studies, stakeholder engagement was conducted to inform either a combination of HIV-related trial types or an unspecified type of HIV clinical trial (i.e. HIV clinical trials in general, without specifying whether prevention or treatment, behavioural or biomedical) (see Appendix 1).

Analysis of the data extracted from these 108 studies was guided by our five research questions on the characteristics and reporting of stakeholder engagement to inform HIV clinical trials. The following subsections present in detail the results of each of these five analyses. In terms of the geographical location of stakeholder engagement, the majority of studies in our review described engagement conducted in high-income countries. Engagement methods used included both individual and group methods. We identified a wide array of stakeholders engaged, ranging from stakeholders directly involved in clinical trial processes to stakeholders on the periphery of HIV clinical trials. Engagement was found to be undertaken much more often for informing earlier stages of HIV clinical trials as compared to later stages. Finally, we found that reporting on the results of stakeholder

engagement and limitations associated with engagement are the main gaps in the quality of reporting.

3.1 | Location of stakeholder engagement

Of the 108 studies, 48 studies (44.4%) conducted stakeholder engagement in high-income countries [5,23,25-70]. In contrast, fewer studies conducted stakeholder engagement in middle- (30 studies; 27.8%) [71-100] and low-income (nine studies; 8.3%) [101-109] countries. The location of stakeholder engagement could not be discerned in six studies (5.6%) [110-115], and fifteen studies (13.9%) [16,24,116-128] conducted stakeholder engagement in multiple countries at different income levels.

3.2 | Methods of stakeholder engagement for HIV clinical trials

In addition to CABs, we identified 13 other methods of conducting stakeholder engagement across the studies in our review, for a total of 14 distinct methods (Table 1). Methods were separated into five individual methods (i.e. methods involving input or feedback by one stakeholder at a time, such as interviews) and nine group methods (i.e. methods involving input or feedback in a collective format, such as focus groups).

As shown in Table 1, individual methods appeared in 75 (69.4%) studies and group methods were used in 66 studies (61.1%). The most frequently used method for stakeholder engagement was stakeholder interviews, followed by focus group discussions. CABs were used as often as surveys/questionnaires. Five methods were used by only one study each: concept mapping [35], cognitive mapping [77], crowdsourcing [72] (having a group participate in solving a problem and then sharing the solution with the public), participatory mapping [102] and dramatic performances [112]. All five of these studies were published from the year 2005 onward, suggesting more recent diversification of stakeholder engagement methods. Additionally, many studies used a combination of both individual and group methods for stakeholder engagement; for example, 19 studies (17.6%) paired focus group discussions with stakeholder interviews [5,16,27,32,33,79,82,89,90,96,98,100,101,106,108,109,116,125,128].

3.3 | Types of stakeholders engaged for HIV clinical trial research

Table 2 presents our analysis of the types of stakeholders engaged throughout all studies reviewed. We identified 35 unique types of stakeholders, which can be grouped into eight subcategories under three broader categories: trial-related stakeholders, community stakeholders and broader stakeholders. Similar to the categories of stakeholders identified in the GPP guidelines as being relevant to HIV clinical trial research [3], we found that the types of stakeholders engaged ranged from individuals or groups in close proximity to the trial (e.g. trial participants themselves) to broader stakeholders who hold an interest in HIV trial outcomes more generally (e.g. policymakers).

As shown in Table 2, 29 studies included participant trial-related stakeholders in their engagement efforts and 36 studies engaged non-participant trial-related stakeholders, the latter of which included community advisory board/group members, trial staff, and trial funders. Collectively these

Table 1. Methods of stakeholder engagement (n = 108)

Methods of stakeholder engagement		Method description	Studies using each method	Number of studies using each method ^a (%)	
Individual engagement methods	Stakeholder interviews	Interviews conducted with individuals identified as key stakeholders	[5,16,26-28,32,33,44,49,54,56,58,62,68,69,72,76,79,82,86,88-91,93,95-98,100-102,106,108-111,113,116,117,124,125,128]	43 (39.8%)	75 (69.4%)
	Surveys/questionnaires	Surveys or questionnaires about stakeholder perspectives administered by mail, online or in-person	[24,26,30,31,43,48,49,52,53,56-58,62-67,80,81,83,87,114,123]	24 (22.2%)	
	Individual stakeholder consultations	Consultations on trial issues/processes sought with specific key informants	[30,34,40,45,50,72,103-105,118-121]	13 (12.0%)	
	Cognitive mapping	Mixed-methods approach involving stakeholder interviews, map sketching and observational techniques	[77]	1 (0.9%)	
	Concept mapping	Mixed-methods approach involving initial stakeholder idea generation and subsequent stakeholder-led categorization and ranking of submitted ideas.	[35]	1 (0.9%)	
Group engagement methods	Focus group discussions	Multiple stakeholders led in a group discussion by a facilitator	[5,16,27,32,33,37-39,45-47,50,55,60,71,74,79,82,85,89,90,94,96,98,100,101,106-109,116,125,128]	33 (30.6%)	66 (61.1%)
	Community advisory boards/groups	A formally established group of stakeholders representing community interests and providing a link between trial researchers and the broader community	[23,25,26,28-30,34,36,37,42,50,51,75,80,84,92,102,112,115,118-122]	24 (22.2%)	
	Community forums or meetings	Public or invitational meetings held to inform the community about trial issues/processes and obtain feedback from community members	[30,34,61,70,75,92,99,103,108,112,118,121,122,126,127]	15 (13.9%)	
	Stakeholder workshops/education sessions	Events where stakeholders are convened to solve specific trial-related problem(s) and/or build capacity to understand trial issues/processes	[26,30,41,75,78,102,108,115,118,126]	10 (9.3%)	
	Community working groups	Group of stakeholders convened to solve or advise on trial-related problems	[59,75,120]	3 (2.8%)	
	Media outreach campaigns	Informing the broader community about trial issues/processes through mass media and inviting commentary/feedback from stakeholders reached through media messaging	[34,73,92]	3 (2.8%)	

Table 1. (Continued)

Methods of stakeholder engagement	Method description	Studies using each method	Number of studies using each method ^a (%)
Crowdsourcing	Having a group participate in solving a problem and then sharing the solution with the public	[72]	1 (0.9%)
Participatory mapping	Community members collaborate with field workers to develop a map depicting local knowledge and community needs	[102]	1 (0.9%)
Dramatic performances	Skits or plays performed to inform about trial-related issues/processes and prompt feedback from the audience	[112]	1 (0.9%)

^aFor totals and percentages of overall individual versus group methods, studies that used multiple types of individual or group methods were only counted once for each of the two method categories.

stakeholders are in closest proximity to the HIV clinical trial research process.

The community stakeholders category presented in Table 2 comprises stakeholders drawn from communities (socially or geographically defined) in which HIV clinical trials may be embedded. Approximately half of all studies included HIV-affected community stakeholders in their engagement efforts, a subcategory of community stakeholders which encompassed key populations of interest, people involved in HIV advocacy, people living with HIV, and partners and family members of people living with HIV. The most frequently engaged type of stakeholder was populations of interest (40 studies; 37.0%), defined on the basis of socio-demographic characteristics, occupation, relationship status, HIV risk status or other factors that made a population of particular interest to an HIV clinical trial. In contrast to this targeted approach in defining stakeholders, members of the general public were engaged in just 12 studies (11.1%). Thirteen studies (12%) described engagement conducted with community stakeholders or community representatives without specifying further as to what aspect of the community these stakeholders represent [29,30,56,59,70,92,98,108,112,120,122,125,128].

Stakeholder types encompassed by the broader stakeholders category in Table 2 differ substantially from lay community members. Studies engaging broader stakeholders sought input from medical, academic and governmental experts, including three types of healthcare stakeholders (23 studies), eight types of research stakeholders (13 studies) and three types of governmental stakeholders (12 studies). It is important to note that while these are not the most frequently engaged stakeholders in HIV clinical trials, limiting investigation of engagement to ‘community’ members/representatives would fail to capture the involvement of these groups.

3.4 | Purpose of stakeholder engagement for HIV clinical trials

Table 3 presents the results of our coding for the purpose of stakeholder engagement in the studies reviewed, organized by the seven stages of HIV clinical trial research.

We identified 25 distinct purposes for which stakeholder engagement was undertaken. The most frequently reported purpose for stakeholder engagement was for understanding factors affecting trial recruitment (29 studies). This includes studies that examined how stakeholders’ attitudes about HIV trial participation may impact recruitment; for example, examining how stakeholders’ perceptions of early trial termination might affect willingness to participate in future vaccine trials [33,62]. Additional examples of studies using stakeholder engagement for this purpose include studies investigating barriers and facilitators to trial participation among specific populations [55,87]. The second and third most frequent purpose for conducting stakeholder engagement was to inform the ethical conduct of the trial (16 studies) and to develop trial tools (15 studies) respectively. In informing the ethical conduct of trials, stakeholders were engaged for providing input on ethics-related concerns, either in terms of the overall trial process [70,76,88,99] or in relation to particular aspects of the trial; for example, trial stopping rules [78], trial communication strategies [123] and concepts of fairness in the research relationship [94].

By examining the purpose of stakeholder engagement by research stage in Table 3, we observed that stakeholder engagement was conducted more often to inform the earlier stages of trials. More studies described undertaking stakeholder engagement to inform the trial protocol development stage (49 studies; 45.4%) than any other research stage. Nearly the same volume of studies (47; 43.5%) undertook stakeholder engagement to inform trial recruitment. Stakeholder engagement to inform the final two stages of the research process was described least frequently, with just three studies engaging stakeholders to inform the trial results stage and eleven to inform dissemination of trial results. This disparity in studies conducting stakeholder engagement for purposes across the seven stages of research is more clearly visualized by Figure 2.

3.5 | Quality of stakeholder engagement reporting

Table 4 summarizes the results of our assessment of reporting quality, indicating the number of studies meeting seven

Table 2. Types of Stakeholders Engaged (n = 108)

Types of stakeholders engaged			Studies engaging each stakeholder type	Number of studies engaging each stakeholder type ^a (%)		
Trial-related stakeholders	Participant trial-related stakeholders	Trial participants (past or current)	[16,30,31,36,49,56,62,70,74,79-81,83,86,87,91,98,101,103,106,108,112,113,116,118,125,128]	27 (25.0%)	29 (26.9%)	
		Partners of trial participants	[75,79,106]	3 (2.8%)		
		Potential trial participants (not further specified)	[81,94]	2 (1.9%)		
	Non-participant trial-related stakeholders	Community advisory board/group members (not further specified)	[28,30,35,37,71,74,77-79,84,85,88,89,92,98,101,108,115,116,118-120,124,127]	24 (22.2%)	36 (33.3%)	
		Trial research team members (e.g. site staff, recruitment officers)	[16,30,56,58,71,74,76,78,88,89,98,101-103,108,112-114,116,124,127,128]	22 (20.4%)		
		Trial sponsors	[61,78,83,88]	4 (3.7%)		
Community stakeholders	HIV-affected community stakeholders	Populations of interest (e.g. based on race, sexual orientation, occupation, geographical location, risk status)	[16,28,33,37-39,41-45,47,48,50,52,54,55,63-69,72,77,85,90,93,95-97,100,102,109,117,121,123,125,128]	40 (37.0%)	60 (55.6%)	
		People involved in HIV advocacy (e.g. community outreach)	[16,23,25,28,30,33,34,36,51,57,61,78,96,100,105,118,127]	17 (15.7%)		
		People living with HIV (not further specified)	[5,26,27,32,36,53,57,60,109]	9 (8.3%)		
		Partners of people living with HIV	[101]	1 (0.9%)		
		Family members/guardians of people living with HIV	[23,104]	2 (1.9%)		
		Local community stakeholders	Community leaders (e.g. political, traditional, religious)	[5,16,23,29,32,36,45,60,75,82,93,96,98,100,102,105,106,109,112,121,122]	21 (19.4%)	41 (38.0%)
		Community stakeholders/representatives (not further specified)	[29,30,56,59,70,92,98,108,112,120,122,125,128]	13 (12.0%)		
		General community members (general public)	[26,30,46,48,72,73,82,92,99,107,115,121]	12 (11.1%)		
		Local media representatives	[29,79,88]	3 (2.8%)		
		School teachers/principals	[75,85]	2 (1.9%)		
		Food/recreation facility owners/managers	[102]	1 (0.9%)		
	Organizational community stakeholders	Non-governmental organizations	[16,29,75,76,88,92,102,106,110,111,121,122]	12 (11.1%)	20 (18.5%)	
		Community-based organizations/groups serving people living with HIV	[5,16,26,32,36,79,82,111,118]	9 (8.3%)		
Community-based organizations (not further specified)		[29,36,75,79,85,102,121,122]	8 (7.4%)			
Human rights groups		[111]	1 (0.9%)			
Broader stakeholders		Healthcare stakeholders	Healthcare providers	[27,29,33,34,36,42,57,60,75,82,93,96,100,106,109,118,121,126,128]	19 (17.6%)	23 (21.3%)
			Healthcare facility managers/staff	[23,75,85,93,94,126]	6 (5.6%)	
	Drug industry representatives		[61]	1 (0.9%)		
	Research stakeholders	IRB/Ethics Committee Members ^b	[27,30,70,83,88]	5 (4.6%)	13 (12.0%)	
		HIV researchers	[24,61,76,118]	4 (3.7%)		
	Clinical researchers	[70,94]	2 (1.9%)			

Table 2. (Continued)

Types of stakeholders engaged		Studies engaging each stakeholder type	Number of studies engaging each stakeholder type ^a (%)	
	Ethics experts (not further specified)	[70,120]	2	(1.9%)
	Survey design experts	[72]	1	(0.9%)
	Research advocates	[70]	1	(0.9%)
	Women's health researchers	[34]	1	(0.9%)
	Anthropologists	[72]	1	(0.9%)
Governmental stakeholders	Government health research organizations	[30,35,40,61,127]	5	(4.6%)
	Government health officials	[40,61,70,102,118]	5	(4.6%)
	Policymakers and government representatives (not further specified)	[29,76,88,122]	4	(3.7%)
			12	(11.1%)

^aFor totals and percentages of subcategories of stakeholders, studies that engaged multiple types of stakeholders within the same subcategory were only counted once per subcategory.

^bEngagement of IRB/Ethics Committee Members refers to engagement efforts outside of the standard IRB/Ethics review process.

criteria adapted from the GRIPP2 checklist to improve reporting of stakeholder involvement in health research [21]. We also disaggregated our analysis of stakeholder engagement reporting quality by the type of HIV-related trial that the stakeholder engagement was meant to inform (see Appendix 1).

While all 108 studies included in the review described at least one purpose for conducting stakeholder engagement, Table 4 demonstrates that most studies also provided details on the development of the engagement methods, the number of stakeholders engaged and the results of stakeholder engagement. 'Results of stakeholder engagement' refers to reporting the information obtained through a study's engagement method, such as reporting findings from focus group discussions [27,71,101]. This differs from reporting the *outcome* of stakeholder engagement, which we defined as reporting on the impact that stakeholder engagement made on the design or conduct of an HIV clinical trial, such as describing how the results of crowdsourcing were subsequently used to develop a clinical trial's intervention [72]. We found that stakeholder engagement outcomes were assessable among 41 studies (67 studies included in the review conducted stakeholder engagement to inform future/hypothetical trials); however, among these 41 studies, only 29 (70%) met the reporting criteria, meaning 30% of studies with the opportunity to report on stakeholder engagement outcomes did not do so. Additionally, of all 108 studies reviewed, 60 (55.6%) reported the number of engaged stakeholders by sex and/or gender category; however, only four studies reported stakeholder engagement results disaggregated by sex and/or gender category [38,52,74,87].

4 | DISCUSSION

This systematic review described stakeholder engagement for HIV clinical trials and compared this engagement to GPP recommendations. Our review suggests critical gaps in

stakeholder engagement that should be examined and addressed in the field of HIV clinical trial research.

First, we found more of the studies included in our review conducted stakeholder engagement in HICs compared to LMICs. This finding is consistent with a review of clinical trial priority setting processes [129]. One potential explanation for these results may be that there is a greater proportion of HIV clinical trials conducted in HIC settings, as a review of infectious disease trials registered with ClinicalTrials.gov found that the greatest proportion of all registered HIV trials were located in North America and Europe [130]. In addition, conducting stakeholder engagement in LMICs may be hindered by limited resources, communication barriers, and mistrust of research [16]. However, while stakeholder engagement may be challenging to conduct in LMICs, these are also the contexts in which stakeholder engagement may be most important [131]. Our results demonstrate a need for more evidence to inform HIV clinical trials in LMICs.

Second, our data suggest that while many methods are used, most stakeholder engagement is conducted using researcher-driven, top-down methods. This often involves formal social science methods such as in-depth interviews or focus group discussions. It is unclear how effective these methods are for fostering meaningful partnerships and continuous dialogue as the GPP guidelines recommend [3]. Additionally, the extent to which top-down engagement methods can inform the design and conduct of HIV clinical trials depends entirely on trial researchers. Thus, while the GPP guidelines recommend that trial researchers carefully consider and select from the range of possible advisory mechanisms [3], the reliance on top-down, expert-driven stakeholder engagement suggests the need for these and other guidance documents to consider innovative, bottom-up engagement strategies. For example, crowdsourcing approaches that allow community members a more participatory role in informing HIV clinical trials could supplement existing stakeholder engagement strategies [132]. Engagement methods that follow a participatory model can help to achieve

Table 3. Purpose of stakeholder engagement (n = 108)

Purpose of stakeholder engagement, by research stage		Studies using stakeholder engagement for each purpose	Number of studies using each purpose ^a (%)	
Research question development	Understanding stakeholder perspectives on trial feasibility/acceptability	[5,27,30,32,82,106,112,121,122]	9 (8.3%)	15 (13.9%)
	Setting research priorities/goals	[36,40,61,84,117,118]	6 (5.6%)	
Protocol design	Informing ethical conduct of trial (e.g. participant rights, stopping rules, communication, IRB submission, confidentiality, concepts of fairness)	[23,36,67,68,70,76,78,88,94,99,115,117,120,123,125,127,128]	17 (15.7%)	49 (45.4%)
	Developing trial tools (e.g. interventions, measurements, training materials, participant education materials)	[24,25,29,35-39,42,72,74,103,106,107,119]	15 (13.9%)	
	Developing stakeholder engagement strategies for trial	[16,50,57,59,70,75,76,102,110,111,113,116,122,124]	14 (13.0%)	
	Developing trial protocol (in general or not further specified)	[29,34,36,51,109]	5 (4.6%)	
	Selecting trial sites	[34,37,105]	3 (2.8%)	
	Determining trial participation incentives/compensation	[25,94]	2 (1.9%)	
	Securing healthcare services for trial participants	[126]	1 (0.9%)	
	Developing trial site management strategies	[114]	1 (0.9%)	
Recruitment	Understanding factors affecting trial recruitment (e.g. attitudes about trial participation)	[31,33,43,45,46,48,52-55,58,60,62-66,69,85,87,89,90,95,97,98,100,106,109,110]	29 (26.9%)	47 (43.5%)
	Building community education/awareness to enhance recruitment and/or community support for trial	[26,29,30,41,73,75,92,112,115,121,122]	11 (10.2%)	
	Developing trial recruitment strategies	[29,34,47,50,68,77,93]	7 (6.5%)	
	Building credibility for trial among community to enhance recruitment	[37]	1 (0.9%)	
Enrolment	Enhancing the informed consent process	[49,53,56,71,80,81,96,99,101,108,112,120,128]	13 (12.0%)	13 (12.0%)
Follow-up	Developing retention strategies	[34,36,50,77,93,104]	6 (5.6%)	17 (15.7%)
	Understanding factors affecting trial adherence/retention	[28,31,44,79,91]	5 (4.6%)	
	Addressing participants' concerns as they arise in trial	[75,108,118,122]	4 (3.7%)	
	Understanding participants' expectations about the trial	[86]	1 (0.9%)	
	Building community education/awareness to enhance retention	[115]	1 (0.9%)	
Results	Developing post-trial processes (e.g. post-trial access to medication)	[62,83]	2 (1.9%)	3 (2.8%)
	Reviewing/interpreting trial results	[29]	1 (0.9%)	
Dissemination	Communicating results to broader stakeholders	[23,25,36,110,117,118,122]	7 (6.5%)	11 (10.2%)
	Communicating results to trial participants	[62,75,86,110,118,122]	6 (5.6%)	
	Developing academic products based on trial results	[29]	1 (0.9%)	

^aFor totals and percentages by research stage, studies that conducted stakeholder engagement for multiple purposes within the same research stage were only counted once per research stage.

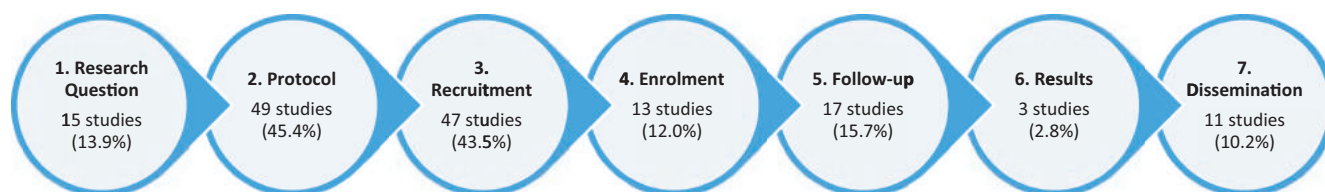


Figure 2. Summary of the purpose of stakeholder engagement by clinical trial research stage.

more meaningful inclusion of stakeholders and greater opportunities to change the status quo [2].

Third, we found that stakeholder engagement was predominantly conducted to inform early trial stages. These findings are comparable to those of studies examining stakeholder engagement in other fields of health research [133,134]. Both of these studies emphasize the importance of engaging stakeholders throughout all stages of the research, a recommendation also posed by the GPP guidelines for HIV clinical trials [3]. In order to meet these benchmarks for GPP, our results suggest that greater efforts are particularly needed to engage stakeholders in the later stages of HIV clinical trial research. Future research should examine innovative methods to foster opportunities for stakeholder contributions at these points in the research process. Additionally, while multiple guidance documents exist to promote meaningful and effective stakeholder engagement [3,11-14], HIV clinical trial teams should consider how to tailor these recommendations so that engagement efforts account for the specificities of the type of trial being conducted as well as for local contexts (e.g. social, political). These efforts by HIV researchers could help to establish models for stakeholder engagement in clinical trial research more broadly.

Our findings should be considered alongside broader factors that inform the engagement process and researcher-stakeholder relationship in HIV clinical research. The extent to

which stakeholders are engaged is shaped not only by the clinical trial team, but also by the structural contexts within which clinical trial research is embedded. As noted by others [15], it is important to consider how funders and corporate interests influence stakeholder engagement. For example, the funding of many HIV trials by high-income countries may inadvertently assert norms and activities (e.g. community advisory boards) that are not locally driven. The impact of global resource disparities on stakeholder engagement should also be considered, particularly for the potential to reproduce inequalities in terms of which stakeholders are engaged [16]. Thus, while the results of our review help to make visible some of the gaps in current stakeholder engagement for HIV clinical trials, more research is needed to account for why these gaps occur and how best to address these gaps as a product of broader structural contexts.

There are several important limitations to this review. First, we did not assess quality of engagement. However, there is a notable lack of quality measurement tools for stakeholder engagement [20], as well as disagreement regarding whether and how to determine what level of engagement is appropriate [135]. Second, our review does not examine the outcomes of stakeholder engagement; however, only 41 studies (38%) in our review provided information on engagement outcomes. Future reviews should focus on systematically assessing

Table 4. Quality of stakeholder engagement reporting (n = 108 studies)

Reporting quality criteria		Studies meeting reporting quality criteria	Number of studies (%)
Aim	Describes the purpose of stakeholder engagement	[5,16,23-128]	108 (100%)
Methods	Explains reasons for choice of stakeholder engagement method(s)	[23,27,29,35,36,38,39,41,63,69,72,73,77,78,81,86,88,92,99,101,102,104-106,115,116,120-122,124]	30 (27.8%)
	Describes development of engagement method(s) used	[5,16,23,26,27,29,30,32-36,38-41,43-49,52-60,62-64,66,69,70,72,73,75,77-83,85-90,92-106,108-111,114,116,119,120,122,124-126,128]	82 (75.9%)
	Reports the number of all stakeholders engaged	[16,24-33,35,36,38-40,43-49,52-57,59,60,62-69,71,74-83,85-103,106,108-111,113,114,116,123-125,127,128]	82 (75.9%)
Results	Describes results of stakeholder engagement	[5,16,23,24,26-36,38-41,43-46,48,49,52-83,85-102,104-106,108-111,113,114,116-128]	97 (89.8%)
Outcomes ^a	Discusses impact of stakeholder engagement on HIV clinical trial (where applicable)	[23,25,29-31,34,36,39,41,47,49,50,61,72,73,75,78,92,103-105,108,109,115,118-122]	29 (70%) ^a
Reflections	Discusses limitations of stakeholder engagement	[5,16,24,26-29,31-36,41,43-46,48,52-56,58,60,62-64,68,71,73-76,78-83,87,88,90,91,93-96,98-102,110,111,114,116,120,123,125,127]	62 (57.4%)

^aReporting on outcomes was assessed only among 41 studies that were not related to future/hypothetical trials.

engagement outcomes in relation to methods used and stakeholders engaged. Third, our finding that fewer studies conducted stakeholder engagement in LMICs may be attributable in part to our search strategy being limited to English language studies only. Manuscript selection bias (i.e. the overrepresentation of scientific publications from HICs) may also play a role [136]. Fourth, the extent to which this review can provide an overview of stakeholder engagement for HIV clinical trials is necessarily dependent on the extent to which these activities are reported. It is possible that more engagement takes place “behind the scenes” of clinical trial research without making its way into published accounts of trial results. Improved reporting standards in accordance with guidance documents such as those used in our analysis of reporting quality [21] may help to provide further evidence for all research teams seeking to enhance their own engagement approaches, regardless of HIV trial type.

5 | CONCLUSIONS

The results of this systematic review of stakeholder engagement for HIV clinical trials have implications for research and policy. First, our finding of fewer studies conducting stakeholder engagement in LMICs suggests the need for further reporting on stakeholder engagement in these settings [131]. Additional resources and regulations to support and sustain stakeholder engagement in these settings may be necessary to address potential barriers to engagement. Second, despite engagement recommendations outlined in comprehensive guidelines [3] and funding allocated on the part of national and international funding bodies to support engagement activities [20], our findings suggest that stakeholder engagement is not being conducted evenly to inform all stages of the HIV clinical trial process. More research is needed in order to understand barriers and facilitators to involving stakeholders in the later stages of HIV clinical trial research specifically, as well as which methods of engagement would be most conducive to involving stakeholders in trial results and dissemination processes. Funders should additionally consider adding specifications to stakeholder engagement requirements to help address this gap, such as requiring clinical trial researchers to include detailed engagement plans for each stage of the trial process. Future research could then examine whether and how stakeholder engagement changes over time in response to such efforts. Finally, to address gaps identified in reporting quality, HIV research journals should consider implementing policies about reporting stakeholder engagement. Checklists for reporting on stakeholder engagement [21,133] may help to promote greater transparency as to what engagement efforts are undertaken in trials and how this engagement shapes the research process. This information will be particularly valuable for undertaking future research to evaluate the quality of stakeholder engagement.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

S.D., J.T. and R.S. conceived of the idea for this review. S.D. designed the review protocol, and S.D. and M.B. conducted the search. S.D., Y.Z., M.B. and T.V. read and selected the citations, abstracts and full texts. S.D., Y.Z. and T.V. extracted the data. S.D. with assistance from M.B. and T.V., as well as in consultation with S.R. and J.T. conducted the coding and analysis. S.D., M.B. and T.V., with substantial contributions and edits provided by Y.Z., S.R. and J.T., prepared the manuscript. All authors reviewed, provided feedback and approved the final manuscript.

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AUTHORS' INFORMATION

The authors are part of a working group examining the social and ethical aspects of research on curing HIV (searchHIV). More information about our working group is available at: <http://searchiv.web.unc.edu/>

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Quality of Reporting on Stakeholder Engagement, by Type of HIV Clinical Trial.

REVIEW ARTICLE

Strengthening stakeholder engagement through ethics review in biomedical HIV prevention trials: opportunities and complexities

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Abstract

Introduction: Clinical trials of biomedical HIV prevention modalities require the cooperation of multiple stakeholders. Key stakeholders, such as community members, may have stark vulnerabilities. Consequently, calls for HIV prevention researchers to implement “stakeholder engagement” are increasingly common. Such engagement is held to benefit inter-stakeholder relations, stakeholders themselves and the research itself. The ethics review process presents a unique opportunity to strengthen stakeholder engagement practices in HIV prevention trials. However, this is not necessarily straightforward. In this article, we consider several complexities. First, is stakeholder engagement a legitimate component of what Research Ethics Committees (RECs) should review for HIV prevention trials? Second, what are the core features of engagement that should be under ethics review? Third, what are the key practices that should be highlighted in ethics review?

Methods: To address these questions, we examined the international ethics guidelines specialized for such trials (UNAIDS 2012, UNAIDS-AVAC GPP 2011) and directly applicable to such trials (CIOMS 2016; WHO 2011). Thematic analysis was used to code and analyse these guidelines.

Results and discussion: Ethics guidelines support REC review of engagement. Guidance recommends that engagement be broad and inclusive; early and sustained; and dynamic and responsive. Broad engagement practices include evaluating the context, planning in writing, and resourcing. RECs should assess engagement as part of a comprehensive review, and recommend revisions where necessary. Researchers should profile key elements of engagement valued in ethics guidance, when they draft ethics submissions. Importantly, the ethics review process should not undermine the ‘dynamic responsiveness’ required for excellent engagement in this field.

Conclusions: As evidence-informed engagement strategies emerge, these should inform the ethics submission and review process. Both parties in the review process should strive to avoid a superficial, check-list type approach that caricatures what should be a thorough, nuanced ethics review of a rich, responsive engagement process.

Keywords: Stakeholder engagement; community engagement; ethics review; Research Ethics Committee; Institutional Review Boards; HIV prevention trials

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1 | INTRODUCTION

HIV prevention trials are complex endeavours. Ethics guidelines recognize several background complexities with such trials that trigger the need for stakeholder engagement. UNAIDS [1] notes the pragmatic need for “collaboration” between multiple role-players for trial success, for example, affected populations, research institutions, industry, government and health sectors (p. 11). Also, there is the vulnerability of key stakeholders, such as participants and community stakeholders, who are at increased risk of potential harm because of marginalization or HIV stigma and discrimination [1]. They might be exploited because of disparities in wealth, scientific experience, power, and technical capacity relative to researchers [1]. Even host countries are identified as at risk of potential exploitation because of such disparities. Ethics guidelines

recognize that when sponsors and researchers engage relevant stakeholders, potential risks and harms can be mitigated.

Ethics guidelines recognize several potential benefits of engagement. *First*, there are beneficial outcomes of engagement for *inter-stakeholder relations* – that is, relations between researchers and stakeholders that are more trusting, “collaborative,” involve “partnership,” are “mutually beneficial” and “equitable” so that power imbalances are reduced [2]. *Second*, there are several beneficial outcomes *for stakeholders themselves* – these include improved knowledge, understanding or literacy; increased trust in research(ers); increased ownership of research [2]; and increased acceptance of research [1]. *Third*, UNAIDS-AVAC GPP [2] states there are beneficial outcomes of engagement *for research* – that is, research that is “shap[ed]... collectively” (p.16); that has received effective and expert contributions from stakeholders [2]; that is relevant

[1]; that is culturally appropriate, successfully conducted, where the likelihood of application is enhanced and where a firmer foundation for future research has been laid [2].

Finally, UNAIDS [1] recognizes the “right” of key stakeholders, such as communities, to participate fully as partners in the research, and to make decisions about the nature of their participation (p. 21). Even host countries are identified as having such rights. This rationale is rooted less in the positive consequences of engagement (i.e. reducing risk and enhancing benefits) and more in the inherent “rightness” of involving stakeholders.

The ethics review process presents a unique opportunity to strengthen stakeholder engagement in such trials. Despite rich scholarship on stakeholder engagement [3-8] little has been written on this specific issue. Ethics review of engagement is not necessarily straightforward. One could question whether review of engagement in HIV prevention trials falls within a Research Ethics Committees’ (RECs) “purview” of responsibility [9]. Also, one could question whether any consensus exists about the core features and practices of “excellent” engagement in such trials, such that researchers could highlight these, or RECs could look for these, in the ethics review process.

In this article, we consider several complex questions about leveraging the ethics review process to impact on stakeholder engagement in biomedical HIV prevention trials. *First*, is stakeholder engagement really a legitimate component of what RECs should review?; *second*, what core engagement features should be under ethics review?; and *third*, what core engagement practices should be under ethics review? Given that ethics guidance is central to determining the acceptability of researchers’ practices and of RECs’ practices, we looked to ethics guidance to address these questions.

2 | METHODS

We aimed to find ethics guidelines that would be relevant to any researcher or REC involved in HIV prevention trials anywhere in the world, regardless of host country, institutional affiliation or network membership. We conducted a Google search using a combination of the following key terms – *ethics guidelines* OR *ethics guidance* AND *community* OR *stakeholder* AND *engagement* OR *consultation* OR *participatory* OR *consultation* OR *partnership* OR *involvement* OR *collaboration* AND *biomedical HIV prevention trials* OR *HIV vaccine trials* OR *HIV prevention trials* AND *research ethics committees* OR *ethics review* OR *ethics review committee* OR *institutional review board*.

We included those ethics guidelines *specialized* for HIV prevention trials and those *applicable* to HIV prevention trials conducted internationally. That is, we included UNAIDS (2012) *Ethical Considerations In Biomedical HIV Prevention Trials* which provide guidance on all ethical aspects of such trials [1]. We also included UNAIDS-AVAC GPP (2011) *Good Participatory Practice Guidelines For Biomedical HIV Prevention Trials* [2] which provide guidance on engagement in such trials. We also included the CIOMS (2016) *International Ethical Guidelines for Health-Related Research Involving Humans* [10] which provide guidance relevant to HIV prevention trials, as a subset of health research with humans. Lastly, we included WHO (2011) *Standards and Operational Guidance For Ethics Review Of Health-Related Research With Human Participants* [11]. We

excluded ethics guidelines applicable to specific nations (e.g. South African MRC 2003) [12] or to specific networks (e.g. HPTN 2009)[13] or non-HIV diseases (e.g. GPP EP 2016; GPP TB-Vax 2017; GPP TB-drug 2012) [14-16].

Guided by Braun and Clarke’s [17] process for Thematic Analysis, each ethics guideline was closely read and coded by two coders, guided by the questions above. For example, for question 2, text we coded as “early” included “at the outset” and “at the earliest opportunity”. Text we coded as “sustained” included “ongoing” or “long-term.” We clustered codes that had shared meaning to form “sub-themes” (“early and sustained”). We clustered sub-themes (“early and sustained,” “broad and inclusive” and “dynamic and responsive” into major themes (“features” of sound engagement). We defined qualitative characteristics of engaged research as “features”; and we defined observable conduct or behaviour as “practices.” Discrepancies between coders were resolved by discussion [18]. We conducted the search and review during the period June 2017 to May 2018.

3 | RESULTS

3.1 | Is “stakeholder engagement” a legitimate part of what RECs should review?

RECs should evaluate engagement when HIV prevention trials are ethically reviewed, according to all ethics guidelines reviewed here. UNAIDS [1] states that ethics review should consider “community participation and involvement” (p. 24). CIOMS [10] states that RECs should receive a “description of the plan for community engagement” (p. 25) (community equates to stakeholder in both cases). WHO [11] states that REC ethics review criteria include “community considerations” (p.14). UNAIDS-AVAC GPP [2] allow that RECs *can* require the ethics document to be followed, in line with this documents’ tendency to avoid prescriptive language when making recommendations. (It is worth noting but not central to our review that, increasingly, national guidelines also recommend that engagement be reviewed by RECs [19-21]).

3.2 | What core engagement features should be under ethics review?

Our review identified three broad features. See Table 1.

3.2.1 | Broad and inclusive

Engagement in HIV prevention trials should involve a broad range of diverse role-players, according to most ethics guidance reviewed here. CIOMS [10] recommends engaging those who can “influence or are affected by” the study (p. 25). UNAIDS-AVAC GPP [2] similarly recommends engaging those who “have a stake” (p. 14). UNAIDS [1] recommends a broad definition of community. This means engagement should extend beyond community stakeholders who reside locally and represent the interests of participants [2].

3.2.2 | Early and sustained

Engagement in such trials should be prompt and continuous, according to all ethics guidelines reviewed here. UNAIDS-

Table 1. Key features of engagement in ethics guidance

Broad and inclusive	
CIOMS (2016)	"Stakeholders are individuals, groups, organizations, government bodies, or any others who can influence or are affected by the conduct or outcome of the research project. The process must be fully collaborative and transparent, involving a wide variety of participants, including patients and consumer organizations, community leaders and representatives, relevant NGOs and advocacy groups, regulatory authorities, government agencies and community advisory boards" (p. 25)
UNAIDS-AVAC GPP (2011)	"any individual or collection of individuals who have a stake in a biomedical HIV prevention trial" (p. 14)
UNAIDS (2012)	"the concept [of community] needs to be broadened to civil society so as to include advocates, media, human rights organizations, national institutions and governments, as well as researchers and community representatives from the trial site" (p. 18)
Early and sustained	
CIOMS (2016)	"Researchers, sponsors, health authorities and relevant institutions should engage potential participants and communities in a meaningful participatory process that involves them in an early and sustained manner in the design, development, implementation, design of the informed consent process and monitoring of research, and in the dissemination of its results" (p. 25)
WHO (2011)	"Researchers should actively engage with communities in decision-making about the design and conduct of research" (p. 15)
UNAIDS-AVAC GPP (2011)	"activities required for the development, planning, implementation, and conclusion of a trial, including dissemination of trial results" (p. 5), "a long-term process that extends throughout and beyond the life-cycle of any single clinical trial" (p. 66)
UNAIDS (2012)	"engage in consultations with communities who will participate in the trial from the beginning of the research concept, in an open, iterative, collaborative process" (p. 17)
Responsive and dynamic	
CIOMS (2016)	"In the design and conduct of the research[...] the researchers and the sponsors must be responsive to the concerns of the community" (p. 63)
UNAIDS-AVAC GPP (2011)	"The application of each practice or set of practices will vary by location, the type of trial being conducted, and trial site experience" (p. 26), "stakeholders interests, priorities, perspectives, and culture may change over time" (p.16), "Stakeholder identification and inclusion considers the dynamic stakeholder landscape" (p. 31)
UNAIDS (2012)	"engage in consultations with communities [...] in an open, iterative, collaborative process" (p. 17), "find solutions to unexpected issues that may emerge once the trial is underway" (p. 17), "Defining the relevant community for consultation and partnership is a complex and evolving process" (p. 18)

AVAC GPP [2] recommends that it be early and long-term. CIOMS [10] recommends engagement from design through to dissemination. UNAIDS [1] takes a similar approach. By recommending engagement for "design", WHO [11] implies early engagement (p.15).

3.2.3 | *Dynamic and responsive*

Engagement in such trials should respond to context, and change across time where needed, according to most ethics guidance reviewed here. UNAIDS-AVAC GPP [2] acknowledges diverse interests and perspectives that may change across time, and recommends diverse strategies and mechanisms that vary accordingly. UNAIDS [1] recommends an "iterative process" of engagement (p. 18). CIOMS [10] recommends responsiveness to stakeholder concerns. See Table 2.

3.3 | **What core engagement practices should be under ethics review?**

Our review identified three broad practices. See Table 3.

3.3.1 | *Evaluating the context*

Researchers should understand the context for an HIV prevention trial, according to most ethics guidelines reviewed here. UNAIDS-AVAC GPP [2] recommends a "multifaceted" understanding (p.16) largely through formative evaluation. CIOMS [10] recommends that engagement "appreciate the research context" (p.5). UNAIDS [1] recommends a socio-political analysis of background factors. WHO [11] recommends sensitivity to cultural and traditional practices. Such understanding can be achieved informally or formally through dedicated protocols [2], and the latter may require ethics review [2,10]. Researchers should demonstrate in ethics applications to RECs a commitment to evaluating the context so such understanding will be achieved.

3.3.2 | *Planning in writing*

Engagement should be carefully planned and purposeful, according to most guidelines reviewed here. UNAIDS-AVAC GPP [2] repeatedly recommends planning for engagement.

Table 2. Examples of engagement strategies/mechanisms from ethics guidance

UNAIDS (2012) & UNAIDS-AVAC GPP (2011)	Meetings
UNAIDS (2012) & UNAIDS-AVAC GPP (2011)	Consultations
UNAIDS-AVAC GPP (2011)	Local events
UNAIDS-AVAC GPP (2011)	Suggestion boxes
UNAIDS-AVAC GPP (2011)	Call-in radio shows
UNAIDS-AVAC GPP (2011)	Focus group discussions
UNAIDS-AVAC GPP (2011)	Interviews
CIOMS (2016) & UNAIDS (2012)	A continuing forum
UNAIDS-AVAC GPP (2011)	A formal Stakeholder Advisory Mechanism (SAM) e.g. Community Advisory Board (CAB)

CIOMS [10] and UNAIDS [1] and WHO [11] explicitly recommend that Research Ethics Committees consider engagement, which endorses the requirement for written planning. Plans should include various engagement strategies and mechanisms, depending on the trial and its context. See Table 2 for a non-

exhaustive, non-prescriptive list. These strategies can elicit concerns, objections, advice, experiences, expectations, needs, preferences, perceptions, perspectives, beliefs, inputs, feedback, responses, recommendations and suggestions and other crucial information relevant to trials [1,2,10]. Researchers should demonstrate in ethics applications to RECs that their engagement is carefully planned.

3.3.3 | Resourcing

Engagement should be sufficiently resourced, according to most ethics guidelines reviewed here. UNAIDS-AVAC GPP [2] strongly endorses funding and staffing for engagement, in no less than 15 places, spanning site selection to post-trial access. CIOMS [10] recommends that resources allocated for engagement be declared to RECs. UNAIDS [1] simply recommends that logistics for consultations be addressed. Researchers should demonstrate in ethics applications that they have carefully considered the issue of resources for engagement.

4 | DISCUSSION

RECs should review engagement because ethics guidelines governing or applicable to HIV prevention trials explicitly

Table 3. Core practices of engagement from ethics guidance

Evaluating the context	
CIOMS (2016)	“Active community involvement [...] helps the research team to understand and appreciate the research context” (p.5)
UNAIDS-AVAC GPP (2011)	“Successful stakeholder engagement requires a broad, inclusive, and multifaceted understanding of the context in which a biomedical HIV prevention trial is conducted” (p.16) “Formative research activities can be conducted informally to gather information about local populations and research areas or formally as a part of approved, funded protocols” (p.27)
UNAIDS (2012)	“A social and political analysis should be carried out early on in planning the research process, to assess determinants of vulnerability, such as poverty, gender, age, ethnicity, sexuality, health, employment, education, and legal conditions in potential participating communities”(p.32)
WHO (2011)	“Researchers should actively engage with communities [...] while being sensitive to and respecting the communities’ cultural, traditional and religious practices” (p.15)
Planning in writing	
CIOMS (2016)	“The research protocol or other documents submitted to the research ethics committee should include a description of the plan for community engagement, and identify resources allocated for the proposed activities. This documentation must specify what has been and will be done, when and by whom” (p.25)
UNAIDS-AVAC GPP (2011)	“A comprehensive stakeholder engagement plan enables research teams to collaborate with stakeholders and facilitate a more participatory approach to biomedical HIV prevention research” (p. 35)
UNAIDS (2012)	“Scientific and ethical review prior to approval of a trial protocol should take into consideration these issues [...] community participation and involvement” (p. 24)
WHO (2011)	“Duties to respect and protect communities require examining by the REC” (p.14)
Resourcing engagement	
CIOMS (2016)	“The research protocol or documents sent to the research ethics committee should [...] present resources allocated for the community engagement activities” (p.102)
UNAIDS-AVAC GPP (2011)	“Trial sponsors ensure sufficient funding and research teams allocate resources and time to support stakeholder engagement” (p.45), “Research teams designate trial site staff responsible for [engagement]” (p. 28)
UNAIDS (2012)	“The principal investigator and site research staff should work with representatives of affected communities to identify needs related to their participation, including logistical requirements such as transportation to the meeting site” (p.19)

assign this responsibility to RECs. Both researchers and RECs should understand this. However, in order to deliver “well-reasoned judgements” (p. 457) [22] and avoid “poorly justified responses” or “unjustified variations” [23] (p.15) in judgements we hope that RECs will use norms in guidance to render their judgements (more below), while not undermining “efficient processes” [22,23]. We also argue that review of engagement is supported by a leading ethics framework, namely, the “Emanuel Framework” [24,25]. The Emanuel Framework [24] provides a comprehensive and coherent way for “ethics reviewers” to “evaluate a protocol and to determine whether it fulfils ethical standards” (p. 131-132). It explicitly provides ethics reviewers with an organized way to conceptualize “what [they] already do” (p. 132). It positions stakeholder engagement (termed “collaborative partnership”) as the first component of ethical research [5], thereby firmly situating it as part of a comprehensive ethics review. “Collaborative partnership” recognizes community stakeholders and policy-makers as critical stakeholders for consultation, in order to fully realize the potential benefits of research.

Researchers should state their engagement plans to RECs in a way that facilitates review of key elements valued in ethics guidance (more below). They may also need to assess national ethics guidelines to see if unique, additional local recommendations exist for researchers and sponsors. Certain RECs, or members, may not necessarily have the expertise in stakeholder engagement, and may find this paper helpful in crystalizing core ethics recommendations from ethics guidance. They should use ethics norms to evaluate whether the planned engagement is acceptable. More specifically, ‘*broad and inclusive*’ means RECs can assess whether engagement appears overly focussed on any one stakeholder (e.g. CABs) and inquire about other stakeholders, where necessary. This broadened understanding resonates with key literature [5,6]. CABs may provide a formal mechanism for soliciting the views of various community stakeholders, as well their expertise [26]. However, ethics submissions should describe engagement that is “beyond CABs.” Ethics submissions could describe sponsor or network efforts to date to engage international and national stakeholders (or “multiple-level” engagement) [27].

‘*Early and sustained*’ means RECs can assess whether engagement appears overly focussed on any one stage (e.g. recruitment or results-dissemination). Post-recruitment engagement has been the focus of recent scholarship [8]. “Dynamic responsiveness” means RECs can evaluate whether engagement practices are appropriately tailored to the study and context, and whether plans can accommodate unexpected issues. Several commentators have recommended that engagement strategies be tailored and flexible [8], be improved via constant feedback [4], be revised in response to unfolding issues and realities [6] and take into account the dynamic, transient nature of various groups [28].

In terms of key practices, RECs can address ‘*evaluation of the context*’ by helping researchers to judge whether evaluation activities constitute “formal research,” and where they do, ethics reviewers could evaluate whether such activities meet norms for research, such as social value or scientific validity [24]. The importance of researcher understanding of the socio-economic-political context has been strongly endorsed [5]. Seeing ‘*planning*’ as a core practice means RECs should seek evidence of this in the ethics submission. RECs should

recognize that ethics guidelines do not take a firm stand on which ethics submission document should outline engagement plans nor in what detail [10]. RECs should recognize that sufficient information is needed for them to assess whether ethics norms are met, while preserving researchers’ needs for responsiveness [29]. In order to satisfy the ‘*resourcing*’ aspect, RECs should recognize various ways to satisfy this - e.g. declarations by the applicant that engagement is funded; or review of the actual budget. Because funding for engagement might detract from funding for other aspects (e.g. data collection) researchers should follow a transparent, fair process in budget allocation and RECs should ensure that an appropriate balance has been struck.

Researchers and RECs should not inadvertently undermine ‘*dynamic and responsive*’ engagement through their actions in the review process. Researchers should describe plans to RECs in a way that preserves nimble future responses, and be forthcoming that their engagement plans will, and should, be adjusted in an attuned manner to a dynamic context. Various commentators such as Tindana et al. [30] recommend that engagement is flexible to “meet changing needs” (p. 1453), and MacQueen et al. [5] recommend “a dynamic process that is imbued with feedback loops” (p. 7). RECs should not require amendments to be submitted (as they might for trial procedures), because they should promote rapid engagement responses to future unforeseen developments. In certain instances, RECs may wish to be notified of new engagement efforts, for example, where the rights and welfare of community or other stakeholders are substantially affected, and where additional ethics paperwork is justified. RECs should not routinely insist on submission of granular operational ‘*living documents*’ best left to research sites, such as CAB membership lists. Both parties should draw on analogies with the review of consent processes – where RECs assess broad plans for consent strategies (e.g. regular review of consent concepts) while enabling researchers to implement consent practices that respond to the needs of individual participants in context.

Ideally, when RECs judge that planned engagement does not meet ethics recommendations, they should not recommend rejection of a protocol but rather make constructive recommendations for improvement so plans resonate better with ethics guidance. RECs can try to recruit persons with such expertise, or consult such experts as *ad hoc* reviewers if need be, or utilize the expertise of community members. Also, key REC documents should accommodate review of engagement. For example, application forms for initial review should have questions that will “trigger” researchers to describe their engagement practices in a way that is ‘*broad and inclusive*’ (e.g. more than permission from “institutional gatekeepers”) [31]. Renewal forms (progress reports) should enable researchers to describe progress in the preceding year, to promote ‘*sustained*’ engagement. This might impact the percentage of inquiries that RECs raise about engagement [32-34].

Ethical responses evolve over time, requiring researchers and RECs to stay abreast of concerns affecting their responsibilities. Both might benefit from training that highlights engagement as a legitimate focus of *ethics review* [35]. This might complement existing research ethics modules [36-41] developed by several institutions [42-48] that highlight practical skills using interactive features [36,39,41,49-56]. This might also complement existing modules featuring engagement as a key part of ethical research (FHI 360) [46]; of

ethical HIV vaccine trials, of ethical adolescent trials, and of public health research (TRREE) [42].

Ideally, evidence-based “best practices” for engagement should inform ethics submissions, as data become available, including for monitoring such practices. It is recognized that more evidence is needed for the impact of engagement on key outcomes, and several studies report on perceived impact [57-60]. There is also renewed commitment to building an evidence base [61]. Ethics guidelines, however, are clear that engagement holds potential benefit for inter-stakeholder relations, stakeholders themselves and research itself. This issue may have an historical parallel in the consent arena, where ethics guidance called for participant understanding before evidence existed about effective strategies [62].

Our review has several limitations. First, by limiting ourselves to cross-nation, cross-network, cross-institution ethics guidance, several features and practices relevant to ethics review of engagement under specific circumstances may have been excluded, for example monitoring and evaluation. Also, because our coding was driven by our specific questions related to ethics review of engagement, it is possible that alternate questions may have yielded new or additional codes [17].

5 | CONCLUSIONS

Ethics review of HIV prevention trials affords researchers and RECs an opportunity to highlight core elements of engagement valued in ethics guidance. We found that ethics guidance recommends that engagement for such trials be broad, sustained, responsive, based on nuanced understanding of the context, carefully planned, and importantly be adequately resourced. Both parties in the review process should strive to avoid a superficial, check-list type approach [6] that caricatures what should be a nuanced, sensitive ethics review of a rich, reflexive engagement process.

COMPETING INTEREST

The authors declare that they have no competing interests.

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AUTHORS CONTRIBUTIONS

CS designed the paper, reviewed ethics guidelines and drafted the manuscript; AW reviewed ethics guidelines and drafted the manuscript; JS helped interpret the review and revised the manuscript for important content; PN helped interpret the review and revised the manuscript for important content.

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COMMENTARY

Collateral benefits: how the practical application of Good Participatory Practice can strengthen HIV research in sub-Saharan Africa

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Abstract

Introduction: The *Good Participatory Practice (GPP): Guidelines for Biomedical HIV Prevention Trials, second edition (2011)* were developed to provide clinical trial sponsors and implementers with a formal stakeholder engagement framework. As one of the largest African research institutes, Wits Reproductive Health and HIV Institute (Wits RHI) became an early adopter of GPP by implementing its principles within large-scale national and regional clinical trials. This article examines Wits RHI's lessons learned from implementing GPP, its ongoing efforts to institutionalize GPP, and the yet to be realized potential in creating fully sustainable structures for meaningful stakeholder engagement in HIV prevention research, implementation science and beyond.

Discussion: For the past seven years, Wits RHI has undertaken both centralized leadership roles in implementing GPP across multi-party regional research consortia as well as overseeing GPP for smaller investigator-driven trials. Through this iterative roll-out of GPP, key lessons have emerged. Obtaining upfront funding to support GPP activities throughout and between the research life cycle, and a trained multi-disciplinary team of GPP practitioners have helped facilitate an enabling environment for GPP implementation. We further recommend formally integrating stakeholder engagement into study documents, including monitoring and evaluation plans with indicators and performance metrics, to assist teams to track and refine their GPP strategies. Finally, institutionalizing resources and supporting organization-wide GPP along with ongoing support can help build efficiencies and maximize economies of scale toward a pragmatic and innovative application of the GPP Guidelines.

Conclusions: Thanks to a growing global network of GPP practitioners and a burgeoning GPP Community of Practice, there has been substantive progress in making GPP an integral component of clinical HIV prevention research. The Wits RHI experience highlights the possibilities and the challenges to translating the GPP principles into concrete practices within specific clinical trials and across a research institute. Realizing the full potential of GPP, including direct and indirect – 'collateral benefits' will require the collective buy-in and support from sponsors, implementers and community stakeholders across the research field. As the HIV prevention research field expands, however, a more conscious and systematic implementation of GPP is timely.

Keywords: GPP; stakeholder engagement; HIV; prevention research; Africa

Additional Supporting Information may be found online in the Supporting Information tab for this article.

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1 | LOCATING GPP WITHIN HIV PREVENTION RESEARCH

While clinical trials have long engaged with trial communities and other stakeholders as a matter of course, these efforts have often been *ad hoc*, unstructured and reactive. In the field of HIV prevention research, the need for a more systematic approach to community engagement became evident in the

aftermath of the early and controversial closure of two oral pre-exposure prophylaxis (PrEP) clinical trials in 2004 to 2005 [1-4]. These premature closures in Cambodia and Cameroon highlighted the inherent power differentials within HIV biomedical clinical trials, and the complexity of undertaking effective stakeholder engagement in such settings. They also revealed how insufficient stakeholder engagement across the life cycle of a clinical trial may result in a number of damaging

consequences. In this instance, the trial closures delayed clinical findings and subsequent product licensure, essentially derailing the product development and roll-out timeline for PrEP as an additional tool that high-risk individuals can employ to stay HIV-uninfected.

In contrast to early AIDS treatment activism, which was led by people living with HIV and premised on the distinct “nothing about us without us” principle [5,6], the constituency for HIV prevention activism is less well defined. The beneficiaries of biomedical HIV prevention trials include a diverse range of invested and affected individuals, from trial participants and civil society to governments and product developers. Even prospective end-users vary widely. Some identify with high-risk key populations, such as sex workers, men who have sex with men (MSM) or injection drug users, while others are at risk largely because of their geographical location and regional gender dynamics, such as women living in high prevalence communities. In short, while AIDS treatment activism was able to transcend these differences, no comparable over-arching identity has yet formed to unify those in the field of HIV prevention. While trial participants remain at the centre of advocacy and engagement activities, there are diverse stakeholder groups and multiple partnerships involved, all of which exert varying degrees of influence in prevention trials.

The *Good Participatory Practice (GPP) Guidelines for Biomedical HIV Prevention Trials* developed by UNAIDS and AVAC in 2007 and revised in 2011 [7] have provided a much-needed, formalized framework to describe how clinical trial sponsors and implementers should engage with multiple stakeholders through deliberate, thoughtful and thorough mechanisms. The GPP Guidelines contribute to an overall body of normative guidelines and ethical goals of community engagement in research [8]. At its core, GPP is premised on the same ethical principles of respect, beneficence, accountability and transparency that underlie Good Clinical Practice (GCP) [7,9]. While the primary focus of GCP falls on how clinical trials should be conducted with prescriptive guidance on the relationship between investigators and trial participants, GPP focuses more broadly on the relationships between *all* stakeholders in a trial [7]. The GPP Guidelines offer a series of recommended steps for applying core principles, but few practical tools to guide stakeholder involvement in the often unpredictable social environment in which many HIV prevention trials are set. In this Commentary, we share the experiences of Wits RHI, a research institute at the University of the Witwatersrand, Johannesburg, South Africa, which became an early adopter and champion of GPP in HIV prevention research. Established in 1994, Wits RHI has a long history of community engagement, participatory research methods and working with local, national, regional and global partners [10-12]. By leading GPP initiatives across multi-site studies and regional research consortia, Wits RHI has been uniquely positioned to advance GPP implementation within research, and to develop models aimed at rendering GPP part of its institutional fabric.

In Follow-on African Consortium for Tenofovir Studies (FACTS) 001, a phase III licensure trial of tenofovir 1% gel conducted at nine sites across South Africa [13], Wits RHI deliberately and systematically implemented the GPP Guidelines. Building on HIV prevention research studies’ community-level stakeholder experience in the context of the GPP

Guidelines [14], we reflect on how Wits RHI has applied GPP at local, national, regional and global levels. As the field evolves, Wits RHI continues to expand and adapt its original GPP tools in studies that have followed FACTS 001. Ultimately, Wits RHI is striving towards organization-wide institutionalization of GPP, which will require re-framing GPP beyond the scope and time frame of a single trial. In closing, we reflect on the ongoing challenges and advantages of embracing stakeholder engagement – which we characterize as “collateral benefits” – and the as yet unmet potential of GPP in HIV prevention research as a whole.

2 | DEVELOPING A MODEL TO OPERATIONALIZE THE GPP GUIDELINES

Launched in 2011, the same year as the revised GPP Guidelines, FACTS 001 was the first large HIV prevention trial to formally implement these guidelines. As the FACTS 001 Coordinating Team (led by Wits RHI) began to engage with the GPP Guideline’s 16 topic areas that roughly follow the life cycle of a typical clinical trial [7], a rational clustering of these 16 areas into three manageable phases emerged. These phases comprised (1) study planning – including securing funds, developing protocol and study procedures, completing approvals processes, and securing study and site readiness; (2) implementing the study – including all time points in which study participants are actively being screened, enrolled or attending follow-up visits; and (3) preparing for and disseminating study results – including data analysis, dissemination and research uptake, and policy influence work when applicable (See Figure 1). In addition to outlining a range of stakeholder engagement strategies, mechanisms, and tools, this model illustrates the value-added outcome of attaining GPP – namely, the creation and sustaining of an enabling environment for research studies. While there is some overlap between the three phases, this division helps to facilitate the practical work of planning, resource allocation and oversight. How, then, has the model been implemented? And how has it evolved since FACTS 001? In the remainder of this Commentary, we describe how the model has been applied beyond the traditional placebo-control HIV prevention clinical trial context to open-label studies, observational cohorts and implementation science studies at Wits RHI, each application contributing towards the larger goal of institutionalizing GPP. See Table 1 for a summary of referenced clinical trials and implementation studies with Wits RHI-led GPP implementation.

3 | PUTTING THE GPP GUIDELINES TO WORK IN SUB-SAHARAN AFRICAN CLINICAL TRIALS

Working in partnership with AVAC, the FACTS 001 Coordinating Team formally incorporated GPP from the early planning phase of the trial. A GPP section in the study-wide Manual of Procedures (MOP) outlined the strategy, tactics and support that would be employed, and a series of novel tools were developed to support stakeholder engagement throughout the trial. Staff and community advisory board (CAB) trainings were convened before activation and during

	GPP Topic Areas	Tools & Participatory Strategies*	Stakeholders Engaged and Output*	GPP Principles and Value-Added Outcome
PLANNING / READINESS PHASE		GPP included in grant proposals/study budgets	GPP staff hired, resources allocated, training and activities budgeted upfront into clinical research/implementation project.	Research / project held accountable to optimal engagement when resources are sufficient.
	Formative Research Activities	Stakeholder mapping and analysis	Stakeholders identified and prioritised, which informs engagement platforms and strategies	Research team's socio-cultural competency strengthened contributing to mutual understanding
		Informal focus groups, formal qualitative research pilot testing	Prospective end users, community leaders, gate-keepers and influencers' input inform protocol / project development	
	Stakeholder Advisory Mechanisms*	Youth, Prevention and Treatment CABs, Global CABs	Research design, data collection, implementation informed and reviewed by Community Reps (Key Pops, NGOs, faith-based, police, students).	Ongoing stakeholder engagement contributes to scientific and ethical integrity, accountability, transparency and mutual understanding. Enabling environment improves protocol / project design, implementation and oversight.
		Structured consultations, events, workshops, call-in info		
	Stakeholder Engagement and Education Plans ^o	Structured template plans, Partner MOUs, research literacy and issues-based trainings	Stakeholders receive understandable (and translated) materials and resources; Research literacy capacity strengthened.	
	Communications Plan*	Strategic communications plans, media training, social media, comms campaigns	Selected staff and CAB media trained. Local, national and global stakeholders engaged via media, presentations, papers.	Equipped stakeholders to proactively manage communications and issues transparently and accountably.
	Issues Management Plan*	SOPs and systems to prevent, manage and escalate issues	As appropriate, sponsor, staff, participants, CABs notified; guidance sought if issues arise.	
Site Selection*	GPP included in site selection process and REC application	Research sites assessed on track record and (if new site) commitment to GPP	Stakeholder engagement mechanisms developed and/or assessed	
Protocol Development*	Protocol development stakeholder consultations	Broader stakeholder input considered into protocol before implementation.	Stakeholders maintain autonomy; process promotes respect. Consultation reports aim to provide transparency and mutual understanding (even if agreement not always reached).	
	GPP incorporated into study protocol and documents	Research team formally committed to upholding GPP principles and undertaking GPP.		
IMPLEMENTATION PHASE (PARTICIPANTS ON STUDY)	Informed Consent Process (ICP)	Informed Consent SOP; ICP assessment of understanding	Staff trained on ICP. Trained CABs and advocates review and provide input/ feedback to ensure ICP is age and culturally-appropriate for the intended community and participants.	Locally acceptable, understandable and transparent informed consent procedures and materials developed.
		ICP Stakeholder review		
	Trial Accrual, Follow-up and Exit*	Recruitment / Retention SOPs	Range of: retention events; clubs/support groups for participants and care-givers; male partner engagement events; community dialogues utilised as appropriate.	Multiple engagement mechanisms ensure suitable interventions respond to needs of participants and families.
		Community Engagement Work Plans	Libraries, free wi-fi, baby cots, children's area, refreshments improve clinic environment.	Informed socio-culturally acceptable ways of recruiting, retaining and exiting participants strategies.
		Community-friendly clinics	Flexible clinic hours based on participant cohorts' needs improve accessibility.	
	Standard of HIV Prevention	Prevention packages align with national guidelines, including oral PrEP where applicable	Participants receive comprehensive protocol-specified HIV prevention package.	Up-to-date prevention packages maintain respect and accountability of research teams to participants.
	Access to HIV Treatment and Care	Counselling; robust referrals; peer navigators; linked database	Participants who sero-convert are transferred to care and treatment programme of choice.	Strong linkage to HIV and non-HIV related care provided to participants' as needed fosters respect, greater trust and accountability of research teams to participants.
	Non HIV-related Care	Study protocols and / or national guidelines	STI testing and treatment, contraception, psycho-social support services.	
	Policies on Trial-related Harms	Counselling; Referral SOP; CBO partnerships; Resource guide	Support services / resources provided directly and discreetly available to participants.	Staff offer holistic care and respect participant's right to use or refuse referral, within legal reporting obligations.
		Social harms reporting; safety planning as needed	Participants counselled, offered referrals, and followed-up with support.	
Trial Closure and Results Dissemination*	Outcome scenario planning, dialogues, workshops, webinars	Civil society, researchers and communicators prepared for possible outcomes; Q&As and messages developed.	Dissemination strategies informed and stakeholders' expectations managed through transparent engagement.	
	Dissemination strategy and activities	Publications, media, events, webinars, films used to disseminate to range of stakeholders.	Research outcome disseminated widely using multiple platforms – ensuring scientific integrity, transparency and contribution to the evidence base.	
	Research uptake strategy; policy briefs, technical working groups	Policy, guidelines, public health programmes and training tools informed and developed.		
Post-trial Access to Trial Products or Procedures*	Post-trial access in: protocol; open-label extension; or negotiated with partners	Post-trial access for participants is protocol (and often donor) dependent and time-bound.	Aim to maximise benefits post-trial to participants maintains accountability.	
Key:				
+ For Column 2 (Tools & Participatory Strategies) and Column 3 (Stakeholders Engaged and Output), the Shaded boxes = Implemented in selected research studies and projects; Solid boxes = Institute-wide initiatives.				
* Highlights areas where novel GPP tools, approaches and / or structured plans were introduced, which formalised application of stakeholder engagement.				
^o Based on our experience, we have combined two topic areas, Stakeholder Education Plan and Stakeholder Engagement Plan, to reflect the inseparable nature of these strategies and activities, and subsequent overlapping outputs and intended outcomes.				

Figure 1. Wits RHI's Good Participatory Practice Implementation Model.

Table 1. Clinical trials and studies with wits RHI-led GPP implementation

Trial Name (Years active)	Description	Sites and Countries	# and Characteristics of Participants	Wits RHI's GPP Role
Follow-on African Consortium for Tenofvir Studies (FACTS 001) (2011 to 2014)	Phase III, multi-centre, randomized controlled trial that assessed the safety and effectiveness of the vaginal microbicide tenofovir gel in the prevention of HIV-1 and HSV-2 infection.	Nine sites run by eight independent research institutes in 4 South African (SA) provinces	Enrolment: 2 059 Population: Women, ages 18 to 30 years, at risk of HIV	Wits RHI coordinated this SA-research consortium, and led the development of GPP tools, training and templates with support from AVAC. Consortium partners designed and implemented GPP plans at site level, with technical support and guidance from Wits RHI.
Treatment and Prevention for Sex Workers (TAPS) (2015 to 2017)	Prospective, observational cohort study with two arms delivered in existing service settings: 1) PrEP for HIV-negative Female Sex Workers (FSWs) and 2) early ART for HIV-positive FSWS.	Two sites in Gauteng, SA	Enrolment: 358 (219 HIV-negative and 139 HIV-positive FSWS) Population: Women, 18 years or above, who identified themselves as FSWS	As part of this Wits RHI-sponsored and led study, the study team developed and implemented a GPP strategy, adopted GPP tools from FACTS 001 and established a CAB for Sex Workers and allies.
Evidence for Contraceptive Options and HIV Outcomes (ECHO) (2015-ongoing)	Large-scale open-label randomized clinical trial that aims to compare three highly effective, reversible methods of contraception – (injectable depot medroxyprogesterone acetate – DMPA, progestogen implant-Jadelle and copper IUD) to evaluate any differences in the risk of HIV acquisition among women using these methods.	12 sites run by independent research institutes in Kenya (n=1), SA (n=9), Swaziland (n=1), and Zambia (n=1)	Enrolment: 7 630 Population: Sexually active HIV-uninfected women, ages 16 to 35 years, who were seeking contraception	Through the ECHO research consortium, Wits RHI oversees GPP strategy and implementation by providing all 12 sites with training, tools and ongoing technical support in stakeholder engagement and education, trial accrual, follow-up and exit, communications and other GPP topic areas.
Enhancing Methods of Prevention and Options for Women Exposed to Risk (EMPOWER) (2016-2018)	Multi-site prospective, randomized cohort study to assess a combination HIV prevention intervention that includes oral PrEP for adolescent girls and young women.	Two sites run by independent research institutes: one in SA and one in Tanzania	Enrolment: Up to 500 PrEP acceptors Population: Women, ages 16 to 24 years at substantial risk for HIV infection	As part of this Wits RHI-sponsored and led study, the team incorporated GPP into the protocol, developed a GPP plan with stakeholder engagement and education, established referral systems and a dissemination/evidence into action plan.
Girls Achieve Power (GAP Year) (2015 to 2020)	Cluster randomised controlled trial testing the implementation of an afterschool intervention to empower adolescent girls by improving their overall health, safety, and wellbeing through an increase in their Educational, Health, Social and Economic Assets. The study also seeks to shift gender attitudes and encourage positive behaviour among adolescent boys.	26 schools in Western Cape and Gauteng provinces in SA, with 13 intervention schools compared to 13 control schools	Enrolment: Minimum 2600 adolescent girls and minimum 1850 adolescent boys Population: Grade 8 cohort of adolescents attending selected mixed sex, public secondary schools	Wits RHI's implementation Science team led the application and adaptation of the GPP framework into adolescent research and programming. Consortium partners (Grassroot Soccer and Sonke Gender Justice) implement the GPP framework at site level, with technical support and guidance from Wits RHI.

Studies listed in chronological order of start date. This table only includes studies referred to in this Commentary. However, it should be noted that multiple research studies across Wits RHI, including investigator-driven and NIAID-network sponsored, have incorporated elements of GPP as outlined in Figure 1.

the study. A GPP site preparation checklist as well as structured templates for site-specific plans (See Appendix S1 to S3) were developed to address stakeholder education, engagement, communications and issues management, which were regularly reviewed [15,16]. A study-wide communications strategy that aligned with site-specific GPP plans provided useful over-arching guidance for internal and external stakeholder relationship management and rapid response situations [17]. Even when site plans could not be implemented as designed, a framework was nevertheless in place to guide the adaptation of strategies to meet the evolving needs of the study. Oversight of implementation was provided by a full-time GPP manager throughout the trial. It was this upfront investment by the FACTS 001 Coordinating Team, trial sites, and sponsors that would distinguish the study's formal approach to stakeholder engagement from traditional community engagement conducted during previous clinical trials.

As FACTS 001 drew to a close in mid-2014, the process of preparing participants, trial communities and the broader research field for dissemination of study findings began. But this process was heavily influenced by parallel developments in the field. Around the same time, two other HIV prevention biomedical trials in women in Sub-Saharan Africa, one of them which was stopped early, demonstrated lack of efficacy [18,19]. In some cases, blame for these outcomes was placed on the women study participants—accused of not adhering to the study products and then lying about this to trial staff [20,21]. Subsequent inquiry into these indications of sub-optimal adherence seemed to confirm that indeed, there had been major discrepancies between self-reported product use and pharmacokinetic measures of adherence [22]. Nevertheless, the allegations that participants had lied brought to the surface deep-rooted tensions associated with historic power disparities between marginalized, working class populations and an educated elite. These tensions continue to play out between community members, sponsors and implementers of HIV prevention trials in this region and beyond.

It was against this background that the FACTS 001 team began to prepare for study closure, primarily by actively strengthening study-long stakeholder relationships. At each site, community dialogues were convened with local stakeholders to discuss possible outcomes and collectively consider how to communicate a study result to the trial site communities—regardless of the eventual findings. Similar consultations were convened with the study sponsors, national civil society leaders and HIV advocates. The AVAC-led global Communications Working Group provided a further platform for coordinating messaging and outcome scenario-planning efforts with communications officers of global, regional and national research groups. These efforts were aimed at managing expectations and – in the case that results would (and eventually did) show that tenofovir gel did not prevent HIV – pre-emptively preparing to counter any sensationalized or inaccurate media coverage.

While the FACTS 001 study team implemented its GPP strategy across the three phases of study planning, implementation and results dissemination, unfortunately not all aspects of the GPP Guidelines could be applied, due in part to high staff turn-over. This, in turn, resulted in the need for repeat training in GPP planning, execution and reporting. A further challenge emerged in finding ways to formally monitor the

impact of the GPP activities without making reporting too burdensome [23].

Importantly, the implementation of GPP within this trial strengthened the capacity of these South African sites to engage more effectively with communities involved in research, as well as with other clinical trial stakeholders. Staff and CAB members at all nine sites were trained in GPP, and one site received technical support from Wits RHI to establish a new CAB altogether. Developing formal plans, such as an 'issues management plan', enabled even experienced sites to pro-actively prepare for unexpected situations and hone their crisis de-escalation skills. Seven of the eight research institutes involved in implementing the FACTS 001 trial were motivated to adopt at least some of the tools and practices learned during the trial, for use in other clinical studies and research programmes. In this way, FACTS 001 helped to set a new precedent for stakeholder engagement in HIV prevention research across multiple institutions in the country.

By the time FACTS 001 had concluded, GPP tools and training modules had become more readily available for use in trial settings globally [24-27]. Within the field of HIV prevention research specifically, GPP implementation had substantially expanded, and other research fields – from TB [28,29] to emerging infectious diseases [30] – were joining the movement to absorb the 2011 guidelines into their approach. Building on our national-level experience within FACTS 001, Wits RHI was tasked with leading the GPP and closely-related Communications portfolios within the Evidence for Contraceptive Choices and HIV Prevention Options (ECHO) multi-country open-label randomized control trial. This trial is comparing three highly effective, reversible methods of contraception to evaluate differences in risk of HIV infection acquisition among women using these methods [31]. ECHO has benefited from the adoption of existing tools and ability to repurpose activities, such as community dialogues, that proved to be beneficial to FACTS 001. Investigators on ECHO have also incorporated GPP and a number of related recommendations directly into the study protocol and MOP. During the planning phase, stakeholder engagement criteria were added to the site selection process and a GPP expert joined the site selection committee. Once sites had been chosen, they developed GPP plans and began engagement activities, which were documented in a GPP site activation checklist.

For five of the 12 sites, including two sites in South Africa and one each in Kenya, Swaziland and Zambia, ECHO's implementation of GPP has been a novel experience. However, within this cohort, two sites were new to running clinical trials altogether while the other three sites were seasoned in community engagement but new to applying a formal process. In addition to the traditional site-based CABs that include local community leaders and constituency representatives, the study has further established a Global Community Advisory Group (GCAG). Bringing together advocates and other civil society stakeholders that work at the intersection of reproductive health and HIV prevention at national, regional and international levels, this additional engagement mechanism has provided a platform for invested individuals and coalitions that operate outside of specific trial countries to engage directly with the research team. GCAG members review study documents, such as the informed consent forms, participate in quarterly calls with the study leadership, and where feasible,

engage with staff at research sites and local CAB members through site visits. Funding for these activities remains a challenge, with advocates and others volunteering their time to serve as GCAG members.

3.1 | Institutionalizing GPP

As these individual clinical trials embraced GPP, Wits RHI began to expand its efforts to build African expertise in applying GPP principles and adapting its recommendations more widely within the institute. A small band of three to five staff led most of this work, and began training entire multi-disciplinary teams working outside of the scope of clinical research – such as implementation science programmes charged with providing technical support to local public health clinics. With each training, we assessed how each of the 16 topic areas were relevant or could be adapted, and identified opportunities to collaborate between projects and noted gaps in stakeholder relations management. It quickly became evident that many projects had overlapping stakeholders, yet there was little optimal coordination of their engagement activities. At the request of senior leadership, Wits RHI established a committee to streamline community outreach and recruitment activities in 2016. The aim of the institute-wide committee was to identify and leverage synergies between projects and coordinate stakeholder relationship engagement and research participation across geographical areas, facilities and cohorts [32]. With representatives from across the institute's research, technical assistance and service provider portfolios, this unfunded group created a platform to integrate the GPP principles within institutional practices, develop shared resources, and regularly assess stakeholder partnerships and mechanisms for engagement. For example, through a series of compulsory workshops, over 110 community and outreach staff at Wits RHI have been trained on the practical application of GPP principles and tangible ways to strengthen coordination and referrals between research studies on the one hand, and health and social services on the other. The working group has spearheaded efforts to launch an ethics-approved, locally-focused social media campaign, and to coordinate participation in community radio shows that promote community stakeholder education. Job aids are being developed to assist staff in explaining the different research studies to prospective participants, with the aim of empowering them to choose the research or health service that best meets their needs and interests.

These efforts have been bolstered by a USAID-funded and AVAC-led grant, the Coalition to Accelerate and Support Prevention Research (CASPR), which is supporting Wits RHI to extend GPP across the institute with the ultimate aim of establishing a GPP Centre of Excellence (CoE) – a global first. While CoEs are traditionally characterized as “physical or virtual centres of research which concentrate existing capacity and resources to enable researchers to collaborate across disciplines and institutions on long-term projects that are locally relevant and internationally competitive in order to enhance the pursuit of research excellence and capacity development” [33], in the case of GPP – it is precisely these research outputs and capacity development initiatives that are currently lacking and in need of substantive investment if the field as a whole is to effectively put these principles into practice.

Within the context of a growing and global GPP Community of Practice, the aspirational aims of a GPP Centre of Excellence are thus: 1) to build internal cohesion and capacity to implement standardized, yet dynamic GPP tools and strategies across diverse research studies and projects within Wits RHI; 2) document practices and share GPP resources beyond the institute; and 3) nurture the development of GPP specialists across disciplines, deepening their ability to critically analyse and evaluate the true costs, benefits and potential impact of utilizing GPP within HIV prevention and related research. For example, Wits RHI has developed a GPP Leadership Program that trains course participants from around the world on the often overlooked skills of how to negotiate budgets, develop M&E indicators [8,27], gain institutional buy-in, and engage strategically with reluctant stakeholders, among other critical leadership skills for GPP. Learning to navigate these multi-layered and often messy terrains is integral to building the next generation of GPP champions needed to advance implementation beyond the small cohort of enthusiasts currently leading the field.

3.2 | Lessons learned

As Wits RHI continues to invest in institutionalizing GPP, and the dividends begin to materialize, a series of key lessons have emerged. First, throughout the GPP Guidelines, it is stipulated that “trial sponsors [should] ensure sufficient funding and research teams [should] create a budget and allocate funds and staff time” [7] to cover GPP activities. In practice, we have found that this is best achieved via an early commitment to include GPP-dedicated human resources, activities and oversight mechanisms into the initial grant and budget proposal. While donors increasingly request line-item budgets for recruitment and retention activities, CAB engagement and dissemination plans, limiting GPP to these items alone leaves little room for sustaining ongoing relationships or designing innovative approaches. From developing social media campaigns beyond the scope of a specific trial to supporting relevant broad-based initiatives, these activities can prove cost-saving in the long run. Strategies that may appear superlative on the surface can save time and money by building a research-informed and empowered network of stakeholders that can effectively engage without research teams having to “start from scratch” every time a new study enters the research field.

In addition to funding GPP activities within study-specific life cycles, we have found it is the time periods between close-out of one study (and its related contract) and the start of the next, where ongoing communication with stakeholders is still required, and yet often neglected [34]. Even as a large institute and pluri-potent site running multiple clinical trials and research studies, minimizing time lapses between stakeholder activities requires resourcefulness and cost-sharing.

Second, it takes a team to make GPP work. Without the vested buy-in from trial sponsors, lead investigators and the full research team, endeavours left solely to community and outreach staff are often hamstrung. When lead investigators and clinicians participate in consultations and community dialogues, myths can be debunked, clinical procedures can be clarified and ethical issues can be examined as researchers and community members grapple to resolve research design and

Planning / Readiness Phase	<ul style="list-style-type: none"> • Incorporate a commitment to develop and implement GPP, including dedicated human resources, activities and oversight mechanisms into initial grant and budget proposals. Sponsors should request these details upfront. • Include GPP into trial site selection and activation processes by using objective criteria and tools (e.g. GPP site activation checklist). • Get vested buy-in from trial sponsors, lead investigators and the full research team upfront; not just community staff. • Incorporate GPP principles, strategies and activities into formal trial documentation (e.g. protocol, MOP, SOPs). • Budget for protocol-outlined strategy, including stakeholder engagement mechanisms and activities- both virtual and in-person. • Develop a monitoring and evaluation (M&E) plan aligned to the GPP strategy, including indicators to measure community and stakeholder engagement outcomes and optimally impact.
Implementation Phase	<ul style="list-style-type: none"> • Hire, train and maintain staff dedicated to implementing, overseeing and monitoring the GPP strategy and activities. • Train your entire team on GPP principles and why maintaining these values is everyone's responsibility. • Track, monitor and review GPP plans on pre-set schedules (every 6 months optimally and/or before study milestones) • Refine GPP plans as needed. Use performance metrics, not the status quo of community engagement, to make decisions. • Work with implementation partners and allies, cost-share and participate in stakeholder engagement and education activities that address the broader social-structural context of your research and study population. • Establish engagement mechanisms (CAB, events, radio, newsletter, social media, scientific presentations, webinars, etc.) to employ with stakeholders throughout the entire implementation phase (not only during accrual and dissemination)
Close-out, Analysis and Dissemination Phase	<ul style="list-style-type: none"> • Pro-actively work with trial sponsors, governments and others to develop post-trial access plans for exited study participants. • Utilise multiple platforms (dialogues, global stakeholder consultations, communications-based professional networks) to discuss outcome scenarios and prepare with stakeholders for results dissemination and next steps (e.g. policy influence, further research, product licensure). Do this BEFORE the results are known to anyone in the research team. • Minimise stakeholder engagement time lapses by building in cost-sharing and utilising partnerships to support ongoing communication with stakeholders during unfunded periods (e.g. after participant exit during data analysis, or between trials)
Overall Sustainability	<ul style="list-style-type: none"> • Develop generic GPP tools, templates and SOPs that can be adopted across research projects. • Establish multiple knowledge management systems for GPP resource sharing with the ultimate aim of instilling institutional memory. • Convene team discussions to draw connections between living your organisational values and upholding the GPP principles. • Establish GPP-related Key Performance Areas to job descriptions. • Identify and support the development of a cadre of GPP champions within your organisation. • Invest in GPP champions by supporting their participation in training initiatives, such as AVAC's GPP on-line course.

Figure 2. Key Recommendations for Implementing Effective and Sustainable Good Participatory Practice.

implementation challenges together. Not all recommendations are adopted, but the indirect benefits of broaching open and tough conversations builds trust even amidst disagreement.

Even more, rolling out GPP across the Institute has led us to continually re-define the parameters of who is included in this “us” as we strive to uphold the “Nothing about us without us” adage. Wits RHI maintains three independent CABs, including Youth, Prevention and Treatment focused CABs. Until recently, we also convened a distinct CAB for Sex Workers and community members who work closely with them. While these mechanisms support stakeholder autonomy, our research studies recruiting key populations also benefit from and are better equipped to uphold GPP principles of respect, mutual understanding and accountability by employing peer navigators and educators that self-identify with the communities being served – whether adolescents, sex workers or MSM. As we move towards over-arching strategies, shared approaches and efforts to combine engagement activities, we are working to find the right fine balance between meeting the specific needs of distinct populations while maximizing efficiencies with limited resources.

Third, the more ways GPP is integrated into formal trial documentation and procedures, the more likely it is to be successfully implemented. This holds true because trial budgets generally align with what is in the protocol, which in turn is monitored. For instance, in the ECHO Study, the Management Committee regularly reports progress on the study's GPP activities to the donors and to the Data and Safety Monitoring

Board. Likewise, staff are trained to follow the study-specific operating procedures – processes that are no longer optional add-ons, but rather deemed integral to study success.

Related to this, more could be done to strengthen monitoring and evaluation (M&E) of GPP strategies and activities in studies. Currently, most indicators focus on quantifiable outputs, such as CAB meeting attendance or number of workshops convened. Additional metrics could be developed to measure both the quality of community and stakeholder engagement outcomes, and the impact it spurs. This is particularly important, lest one succumb to the notion that meaningful engagement is subjective and difficult to measure. Taking an evidence-based approach, the GPP team at Wits RHI is working to identify lead (input oriented) and lag (outputs) indicators, so that the impact of GPP activities may be better assessed, refined and evaluated. While lag indicators are relatively easy to measure, they can be difficult to improve or influence. Leading indicators, by contrast, are characteristically harder to measure but easy to influence [35]. As a result, standard M&E plans tend to only include lag indicators. However, it is the hard-to-measure lead indicators (e.g. rumours in the community, research literacy levels, clinic accessibility) that often determine and influence lag indicators (e.g. study-specific recruitment and retention rates, or number of people who attend stakeholder engagement activities). While many GPP-related lead indicators can be initially uncovered via “ear to the ground” tactics used by CABs and by outreach staff working directly in communities, we should not underestimate the

use of qualitative research methods to generate empirical data and elucidate underlying patterns in people's experiences of engagement. Possible methods could include formal pre- and post-workshop evaluations, focus group discussions and waiting room observations conducted by trained social scientists.

A final lesson learned relates to sustainability: there are critical roles for technical assistance provision, education and training, and information and resource sharing within and between teams, especially when it comes to building institution-wide GPP platforms that can outlast staff changes and organizational upheavals. Maintaining knowledge management systems and securing institutional memory are often lacking in non-profit organizations. This is a particular danger in the nascent field of GPP, where there is an overall lack of documented evidence [34]. To address this, Wits RHI has set up a resource repository within its internal intranet to strengthen coordination, build efficiencies and embed GPP within the institute. Highlighting specific ways that investing in GPP tools improve donor-monitored performance metrics, providing guidance on how to add GPP-related Key Performance Areas to job descriptions, and regularly discussing how teams can "live" the organizational values and GPP principles are all lending to embedding Wits RHI with a structured and formal approach to stakeholder engagement as outlined in the GPP Guidelines.

4 | CONCLUSION

Over the past decade, there has been tremendous progress in making GPP an integral component of clinical HIV prevention research. A plethora of practical tools and an introductory online training course have been developed [24-27], and the concept of "stakeholder engagement" is increasingly part of the lexicon of clinical research. Our experiences and lessons learned illustrate that a number of challenges remain before the full potential of GPP may be realized. Still, through existing efforts, there are achievable recommendations that research institutes, sponsors and implementation partners committed to GPP can undertake. These are outlined in Figure 2.

Beyond the visible and often cited benefits of GPP, such as improved participant retention and decreased rumours in the community, it is the strengthened relationships and intangible trust that meaningful engagement fosters. From there, shared visions and partnerships for ethical and much-needed research studies can flourish. We have deemed these outcomes based on lived principles as 'collateral benefits', those that accrue from not merely implementing, but also from re-imagining GPP. As HIV prevention clinical trial design becomes ever more complicated, and biomedical research itself expands – with an estimated 25,000 trial participants now enrolled in research studies globally [36] – it has never been more a prudent time to invest in GPP.

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COMPETING INTERESTS

The authors do not have any conflicts of interest to declare.

AUTHORS' CONTRIBUTIONS

DB drafted the first draft of the manuscript, developed the conceptual model with input from co-authors and managed revisions. DB, TE, MM, NM, SP and SDM discussed key ideas and concepts forming the basis of this commentary. FS and SDM reviewed and substantively revised early drafts. All co-authors reviewed and gave input on the final draft, and cleared it for submission.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

- Appendix S1.** FACTS 001 GPP Site Preparation Plan (2011).
- Appendix S2.** Revised Wits RHI's GPP site preparation and activation checklist (2017).
- Appendix S3.** GPP strategic plan template.

RESEARCH ARTICLE

Using theory of change frameworks to develop evaluation strategies for research engagement: results of a pre-pilot study

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Abstract

Introduction: Inadequate community and stakeholder engagement can lead to accusations that research is unethical and can delay or slow research or translation of results to practice. Such experiences have led major funders as well as regulatory and advisory bodies to establish minimal requirements for community and stakeholder engagement in HIV and other clinical research. However, systematic efforts to formally evaluate the contributions and impact of particular practices are lacking.

Methods: A theory of change framework aligned with Good Participatory Practice for TB clinical trials was used to develop a set of measures for use in a minimally burdensome survey of trial implementing sites. The survey was pre-piloted with three TB trial sites in North America, South America and Asia to assess the feasibility of surveying global research sites in a systematic way, and to see if the measures captured informative variation in the use of engagement strategies and desired outcomes. Surveys were conducted at baseline and six months. In-depth interviews were conducted with site staff prior to the baseline survey to understand how sites conceptualized the concepts underlying the framework and the extent to which they viewed their work as aligned with the framework.

Results: Survey measures captured considerable variability in the intensity and variety of engagement strategies, both across sites and within sites over time, and moderate variability in outcomes. Interviews indicated that underlying concepts were often unfamiliar to staff at baseline, but the goals of engagement aligned well with existing values.

Conclusions: Brief, targeted surveys of trial sites to characterize use of broad strategies, specific practices and some outcomes are a feasible option for evaluating good participatory practice. Additional testing is warranted to assess and enhance validity, reliability and predictive value of indicators. Options for collecting outcome measures through additional objective means should be explored.

Keywords: good participatory practice; community engagement; stakeholder engagement; evaluation; theory of change; clinical trials

Additional Supporting Information may be found online in the Supporting Information tab for this article.

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1 | INTRODUCTION

Phenomenal progress has been made in the prevention and treatment of HIV and its comorbidities due in large part to the willingness of hundreds of thousands of people worldwide to volunteer as research participants. This is not to say that engaging participants has been easy. For HIV research, inadequate engagement has led to accusations of unethical behaviour and delayed or slowed research and translation of results to practice [1]. Such controversies reflect historically based concerns about the potential for exploitation of vulnerable populations and persons due to the pervasive social, economic and political realities that travel with the HIV pandemic [2]. These challenges, and their

solutions, are not exclusive to HIV [3-6]. In the case of TB, an important comorbidity of HIV, there is the risk of similar emergent ethical controversies related, for example, to concerns about drug trials that fail to result in the roll-out of successful products because the drugs are prohibitively expensive [7]. The special challenges faced in implementing paediatric multidrug-resistant TB clinical trials have also been noted [8]. These experiences have led major funders as well as regulatory and advisory bodies to establish minimal requirements for community and stakeholder engagement in clinical research on the presumption that such engagement will bolster ethical practice and reduce the risk of trial disruption [9]. While various community engagement strategies have been used in clinical trials, there has been

little formal evaluation of their contribution to achieving ethical and scientific goals beyond case studies and exploratory assessments [9-20].

A model increasingly used for implementing engagement in HIV, TB and other infectious disease clinical trials is the Good Participatory Practice (GPP) model [21-24]. GPP was first developed in 2007 as part of a broader response to controversial biomedical HIV prevention trials and then revised in 2011 [22,25]. In October 2012, the Stakeholder and Community Engagement Workgroup (SCE-WG) of the Critical Path to TB Drug Regimens (CPTR) issued Good Participatory Practice Guidelines for TB Drug Trials (GPP-TB) [21,26]. This provided a unique opportunity to develop an evaluation framework for community engagement strategies for achieving ethical goals in a clinical trial context where such strategies were not already established practice. We undertook this objective by using a theory of change (TOC) approach to develop a framework for evaluating GPP-TB [27,28]. TOC approaches emphasize techniques that are collaborative, participatory, and practical or applied; as such, TOC was well aligned with the explicit values of the Good Participatory Practice model. In contrast with a more general process evaluation approach for community participation [29], TOC frameworks link practices to outcomes and explicitly hypothesize why particular practices are expected to generate specific outcomes. The practices advocated for in GPP models are derived largely from anecdotal evidence, experiential learning and value statements. TOC provided a means for placing this rich history, discussion and consensus into a framework aligned with evaluation standards. Other examples of the use of TOC to develop evaluation strategies are comprehensively described by Breuer and colleagues, who also provide a checklist for reporting use of TOC in public health interventions [30]. A major challenge faced in evaluating GPP is the lack of dedicated funding for this purpose, which means that the work is incremental and not fully aligned with the ideal scenario set out in the Breuer et al. checklist.

We developed a GPP TOC after the release of the GPP-TB guidance, rather than as part of the GPP-TB development process, a factor that others have noted as presenting evaluation challenges [31]. Mitigating this challenge is the fact that development of GPP training programmes is also an ongoing, iterative process. Our efforts to develop a GPP TOC framework have been undertaken with these broader efforts to build GPP capacity globally.

In alignment with the TOC approach, we firstly sought consensus in defining a clear ethical goal of GPP-TB, secondly worked backwards to identify appropriate and reasonable participatory strategies (noted as powerful strategies in the model) hypothesized to achieve the goal and thirdly used an iterative process to refine the framework. We established a project advisory board and brought together board members with other global TB clinical trials stakeholders for a two-day meeting in Decatur, GA, USA in October 2013. The timing and location were chosen to take advantage of the annual meeting of the Community Research Advisors Group (CRAG) of the Centers for Disease Control and Prevention (CDC)-sponsored TB Trials Consortium (TBTC). Following the meeting, the evaluation framework was refined through ongoing discussion with

members of the project advisory board. The full model is briefly outlined in Figure 1; a comprehensive description of the framework is provided elsewhere [32].

With input from the project advisory board, we developed a set of measures mapped to the five participatory strategies and selected outcomes that could be used in a minimally burdensome survey of trial staff at implementing sites. Framework development included iterative discussion of how practices reflective of the powerful strategies could generate outcomes that would cumulatively lead to achieving the ethical goal. In developing the strategy measures we hypothesized that use of a greater variety of practices associated with a powerful strategy may be necessary to increase the effectiveness of the strategy for achieving the GPP-TB goal. We further hypothesized that some practices may be necessary for achieving the GPP-TB goal, independent of the intensity of practices. For example, use of a greater variety of engagement practices may be necessary for some outcomes, while the simple fact of having an established community advisory board or similar mechanism may be sufficient for achieving other outcomes.

Moving from the conceptual exercise of developing the TOC framework to developing appropriate evaluation measures, we explored feasibility of using a low-burden survey as a core data collection mechanism. A priority in the survey design was to generate descriptive empirical data on the strategies and practices in use as well as the absence of use. No such systematic data currently exist. We also wanted to assess the feasibility of incorporating simple outcome indicators in this kind of survey. The work presented here is therefore an incremental step towards a comprehensive measurement approach, which would require the use of mixed methods (e.g. surveys, ethnographic observation, document review) and data from multiple sources beyond clinical trial research sites (e.g. community organizations, local gatekeepers and leaders, trial participants, trial sponsors and funders). In this pre-pilot we were not able to test any hypotheses; this work represents an exploratory first step, including lessons learned and recommendations for implementing systematic multisite evaluations of engagement processes and outcomes.

2 | METHODS

The research was reviewed and approved by FHI 360's Protection of Human Subjects Committee and by ethics review committees at the South America and Asia sites; the North American site's IRB deemed the research exempt. The unit of analysis for this study was the research site. We did not collect identifying information about clients or patients, clinical trial research participants, individual research staff or individual stakeholders. Data collection consisted exclusively of information describing community and stakeholder engagement activities and practices undertaken and research outcomes experienced by each research site. We obtained oral informed consent at the time of the qualitative interviews (an accepted strategy for minimal risk studies that do not collect identifiable information on participants). For the survey, the informed consent language was provided in the email invitation and again at the beginning of the online survey, with responding to the online survey considered consent to participate. All data

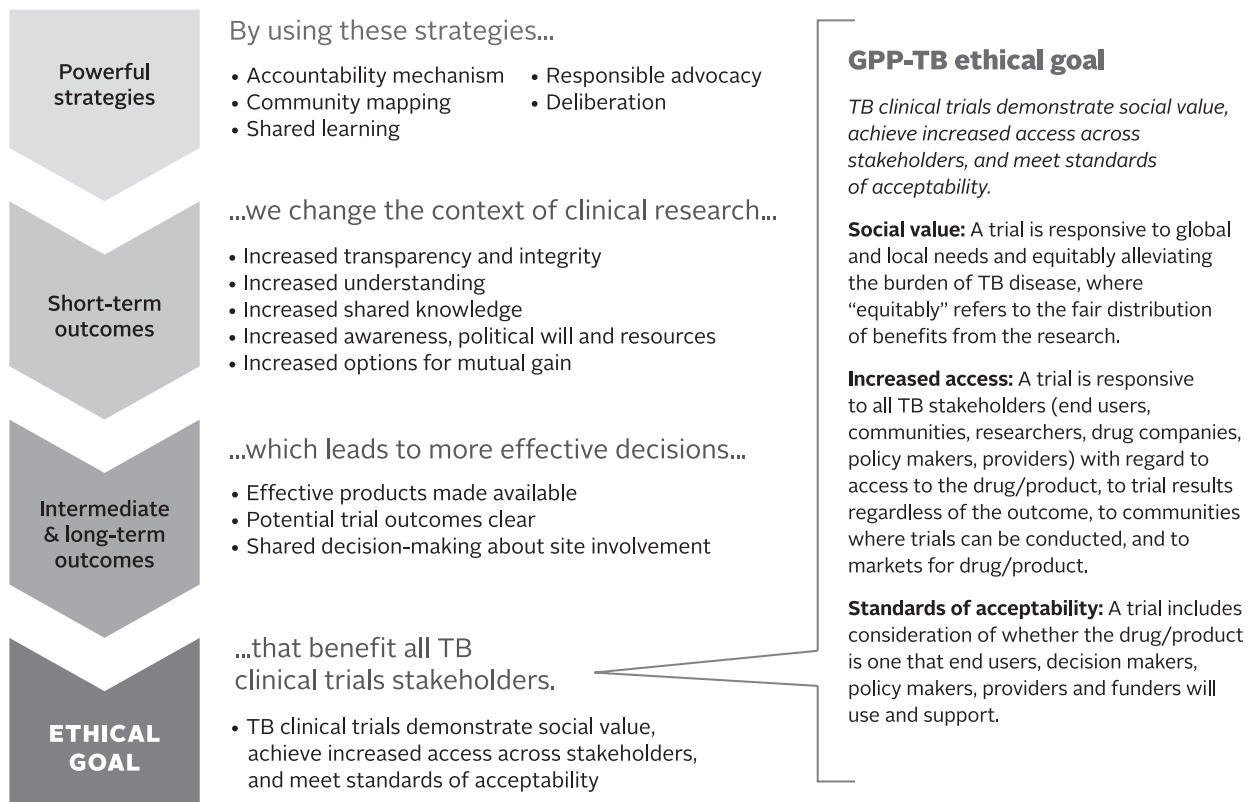


Figure 1. Theory of change framework for evaluating good participatory practice for TB clinical trials. A set of powerful strategies, each comprised of a range of potential practices, are hypothesized to lead to short-term, intermediate and long-term outcomes that cumulatively result in achieving the elements outlined in the Good Participatory Practice-TB ethical goal. To qualify as powerful, a convincing argument or causal hypothesis had to be made for how a proposed strategy would lead to outcomes that in turn would lead to achieving the ethical goal [32].

collection focused on obtaining information about the research sites’ practices and outcomes; no individual-level data were solicited. Individual incentives for participation were not provided, rather, participating sites were provided funding to cover staff support for the various research activities. Data collection took place between May 2015 and April 2016.

2.1 | Measurement

Survey indicators and measures are fully described in Data S1, including reference to the TOC framework components, the rationale for each indicator measure, the range of values associated with indicators, the wording of questions for each measure, how values were calculated from responses and the response items within measures.

2.2.1 | Strategy measures

The measures of the powerful strategies focused on a combination of binary yes/no indicator items and summary scores of the number of specific practices used by a site. The summary scores provided measures of the intensity of practice for a given strategy. One ranked item measure was included for the Deliberation Strategy, to assess the extent to which effort was made to include broad stakeholder perspectives in decision-making. Table 1 provides an overview of the indicator, summary and ranked item measures for each of the five powerful

strategies as well as definitions for each strategy; a more detailed breakdown is provided in Data S1.

2.2.2 | Outcome measures

Several short-term outcome measures were included in the survey. The simplest measure was the total number of TB clinical trials implemented by the site. A set of three measures (mutual gain, transparency and integrity, shared knowledge) focused on the extent to which a site experienced specific challenges identified by the project advisory board. Scores for each measure were calculated based on whether the site reported that an item was not a challenge (1), somewhat of a challenge (–1) or a major challenge (–2). Mutual gain was calculated as the sum of responses to two challenges: competition with the public health system for human resources (i.e. qualified staff) and whether infrastructure built for TB trials uses standards relevant for the local health system. Transparency and integrity were scored on the response to the challenge of establishing effective communication networks for reporting and monitoring of TB cases identified. Shared knowledge was scored on the response to the challenge of ensuring local stakeholder understanding of TB disease, treatment and prevention. The final short-term outcome measure was included in the Deliberation Strategy section of the survey and was specific to sites reporting that a conflict or tension had arisen in the last 12 months between research principles and/or principles of importance to other stakeholders in the local context. This was a

Table 1. Baseline (BL) and follow-up (FU) responses to survey to assess use of participatory strategies and associated practices at three sites

Participatory strategy & brief definition	Indicators	Examples of practices included in scores	Site A	Site B	Site C
Accountability mechanisms Ensure transparency and ownership of the research process so that stakeholders achieve outcomes of integrity and efficacy through shared information	Is there a community advisory board (CAB) or similar mechanism? (Y/N)		BL = Y FU = N	BL = N FU = N	BL = Y FU = Y
	Summary score for CAB-specific practices (range 6 to 60)	Outreach mechanisms used to recruit members; diversity of stakeholder membership	BL = 19 FU = n/a	BL = n/a FU = n/a	BL = 25 FU = 18
	Summary score for general engagement practices (range 0-43)	Diversity of outreach mechanisms; updates provided in preferred language	BL = 5 FU = 0	BL = 14 FU = 14	BL = 11 FU = 8
Community mapping Establishes a description of the local context (ethnographic mapping), identifies needs (cyclical) and develops an understanding of community to ensure research is mutually beneficial. Also describes the research context and the global public health context as they relate to TB, to understand the opportunities, needs and constraints within which research agendas are developed, funded and implemented	Summary score for community mapping (range 0 to 38)	Staff can readily identify local leaders where participants reside and track global debates relevant to TB	BL = 15 FU = 12	BL = 16 FU = 15	BL = 17 FU = 16
	Summary score for shared learning (range 0 to 51)	Community stakeholders participate in research team meetings; information from conferences shared with stakeholders	BL = 36 FU = 32	BL = 22 FU = 31	BL = 34 FU = 33
Shared learning Provides awareness raising among all stakeholders & encompasses communication and engagement strategies. Measures of success may include mitigation of misconceptions about research, community contributions to research protocols and the language/vocabulary used to describe studies, enhanced stakeholder ownership of trials and/or the research process, transparency and accountability/efficiency/complementarity					

Table 1. (Continued)

Participatory strategy & brief definition	Indicators	Examples of practices included in scores	Site A	Site B	Site C
Responsible advocacy Ensures resources are available to conduct TB clinical trials and ensures access as an element of the ethical goal of GPP-TB. Includes consideration of the role of regulatory bodies and pharmaceutical companies, reduction in barriers and improved access when research is concluded	Summary score for responsible advocacy (range 0 to 5)	Identify stakeholders who are effective TB champions; provide educational briefings to policy makers	BL = 1 FU = 0	BL = 3 FU = 1	BL = 1 FU = 1
Deliberation Ensures options for mutual gain are pursued when trade-offs in GPP-TB principles or benchmarks are needed. Entails formal discussions and negotiation between the various stakeholders who have a legitimate interest in the consequences that a trade-off between considerations might have	Has a conflict between principles arisen? (Y/N) If Y: was there a structured opportunity where concerned stakeholders met? (Y/N) If Y: summary score for deliberation process (range 0 to 6) Ranked score for how site would respond to a future conflict (0 to 5)	Explicit norms for discussion established; authority shared equally by all stakeholders PI would determine appropriate steps (0); research site would seek expert advice (2); conduct rapid assessment to map issues and who affected (5)	BL = N FU = N BL = n/a FU = n/a BL = n/a FU = n/a BL = 0 FU = 0	BL = Y FU = N BL = N FU = n/a BL = 0 FU = 0	BL = N FU = N BL = n/a FU = n/a BL = 2 FU = 0

Higher summary scores indicate more intensive use of practices associated with the strategy. n/a, not applicable.

ranked score item with a value of 2 if use of a structured opportunity led to a successful resolution, 1 if the issue was resolved through other means and 0 if a resolution was not reached.

One intermediate/long-term outcome measure was included. This was a binary yes/no measure indicating whether the most recent clinical trial implemented by the site resulted in the experimental drug tested in the trial being available.

Three summary measures reflective of achieving the GPP-TB ethical goal were included (Access, Social value and Acceptability). The summary measures were derived from responses to 13 potential outcomes for the most recent clinical trial implemented by the site (see Data S1 for a detailed breakdown). Each outcome was scored -1 if it indicated failure to meet the goal and +1 if it indicated success. Items were scored 0 if the site did not check it as a relevant outcome for the trial in question. Most items were reflective of more than one summary measure. Access was calculated as the sum of 11 responses (five negative, six positive) indicative of ability to successfully access study populations and complete the trial, for a successful drug to be accessible by providers and clients following the trial, and to contribute to better health outcomes nationally. Social value was calculated as the sum of five

responses (one negative, four positive) indicative of ability to complete the trial, demonstrate efficacy, generate new TB treatment or prevention guidelines and contribute to better health outcomes nationally. Acceptability was calculated as the sum of five responses (three negative, two positive) indicative of suitability, availability, affordability and successful use of the drug tested in the trial for the local or national context.

2.2 | Site recruitment

We worked with the CRAG to identify three geographically diverse CDC-funded TBTC research sites willing to participate in the pre-pilot. Participating sites were located in North America, South America and Asia. To preserve confidentiality, further details on site location are not provided here; the sites are designated as A, B and C without reference to geographic location. GPP-TB guidelines explicitly state the importance of greater attention to the interests of stakeholders throughout the lifecycle of the research, including site selection, trial planning and site activation. We therefore included a site in the early stages of preparations for the conduct of TBTC-sponsored clinical trials. We engaged research staff at each site in qualitative interviews (via phone, internet or in-person), online

surveys and training related to GPP-TB. Participants at each site included staff engaged in TB trials-related work including staff responsible for stakeholder/community engagement. Leadership at each of the three sites determined which staff were invited to participate in data collection.

2.3 | Data collection and analysis

All data collection was conducted in the local language for each site. For quantitative data collection, we used self-administered internet surveys (Qualtrics, Provo, UT, USA). Each site was asked to identify a point person who was contacted via email to provide the information needed for completion of the surveys. The email invitation included brief instructions and a link to the survey, which took about 30 minutes to complete. Because each survey could require knowledge or expertise shared by more than one person at a site, multiple staff may have helped to complete each survey. It was left up to each site to determine how and by whom each survey was completed.

Because of its recent development, sites had little or no exposure to GPP-TB. We therefore developed a three-part introductory training on GPP-TB (about four hours duration total), conducted via internet (North America and South America) or onsite (Asia) after baseline data collection was completed. The GPP-TB training was open to TBTC site staff, whether they participated in the data collection or not, at the discretion of site leadership. Trainings were conducted in the local language for each site.

Approximately six months after the training, each site completed a follow-up survey using the same measures as at baseline. While this timeframe was too short to fully pilot our ability to track significant impacts of GPP-TB implementation on ethical outcomes, it provided additional insights into variability within and between sites, which is helpful for informing further development of a rigorous evaluation design.

Given the small number of sites, we used simple frequencies to identify the strategies, practices and outcomes identified in the TOC framework. We looked at similarities and differences between the three sites as well as changes from baseline to follow-up within sites. We used reporting functions within Qualtrics and Excel for the descriptive analysis.

The qualitative interviews were conducted via phone with the North and South America sites, and in-person at the Asia site. Interviews were recorded using digital audio recorders combined with note taking; recordings were transcribed verbatim, translated into English (where necessary) and supplemented with the notes. The interviews were conducted individually for the North America (n = 3) and Asia (n = 5) sites and in a small group interview with three site staff along with a separate individual interview (total n = 4) in South America. As with the surveys, it was left up to each site to determine with whom the interviews were conducted. At a minimum, we requested participation of an investigator, community outreach staff or CAB representative, and a study manager. Transcripts were analysed using a structural coding framework that reflected awareness of the core elements of GPP-TB (levels of stakeholders, principles, benchmarks and steps or practices outlined for stakeholder engagement) and

the elements of the TOC framework (strategies, outcomes and ethical goal).

3 | RESULTS

3.1 | Survey findings

3.1.1 | Powerful strategies

We observed variability in the survey measures of powerful strategies as well as room for both increases and decreases in the intensity of use of practices reflective of each strategy (Table 1). For example, under *Accountability*, two sites reported having community advisory boards (CABs) at baseline, one reporting 19 and the other 25 CAB-specific practices out of 60 potential practices. Examples of CAB-specific practices included how CAB members were identified (e.g. recruitment targeted to maximize diversity, community leaders or TB patients asked to recommend members), frequency of CAB meetings and of participation by research team members other than community liaison/outreach staff, and types of resources provided to support CABs (e.g. meeting supplies such as paper and pens, computer/internet access for members, transportation support). The site without a CAB reported the highest number of general engagement practices (n = 14) out of a total of 43 potential practices. Examples of general engagement practices included meetings with community stakeholders, health education events, research literacy training and engagement with stakeholders to discuss mobilization, sensitization or education related to trials. At follow-up, Site A no longer reported having a CAB or using general engagement strategies.

Site B reported the only instance of a conflict requiring *Deliberation* strategies to balance competing principles, at baseline. No structured opportunity was provided for concerned stakeholders to meet and the site reported that the conflict was not successfully resolved. With the exception of Site C at baseline, the three sites reported that the principal investigator (PI) would determine appropriate steps to respond, should a future conflict arise, indicating minimal to no community/stakeholder engagement strategies in place should a controversy escalate.

Sites reported similar intensity of practices related to *Community Mapping* and *Shared Learning* strategies at both baseline and follow-up. There was some variability in *Responsible Advocacy* practices, with Site B reporting the most use of such practices at baseline.

3.1.2 | Outcomes

Responses to the survey questions on outcomes are summarized in Table 2. The three participating sites had a range of experience conducting TB clinical trials. Site A reported conducting seven trials at baseline and eight at follow-up, Site B reported three at baseline and six at follow-up, and Site C (a recently funded TBTC trial site at the time of data collection) reported no trials at baseline or follow-up. We did not ask sites to identify the specific trials that were reported on in the baseline and follow-up surveys, and it is possible that one or both sites may have reported on the same trial in both surveys.

Table 2. Baseline (BL) and follow-up (FU) responses to survey outcome measures at three sites

Type of outcome	Indicators	Examples of items included in scores	Site A	Site B	Site C
Short term	Ranked score for conflict outcome (0 to 2)	Use of a structured opportunity for deliberation led to successful resolution (2); no structured opportunity but resolved through other means (1); unable to reach agreement (0)	BL = n/a FU = n/a	BL = 0 FU = n/a	BL = n/a FU = n/a
	Total number of TB clinical trials implemented		BL = 7 FU = 8	BL = 3 FU = 6	BL = 0 FU = 0
	Mutual gain challenges (−4 to 2)	Competition with the public health system for human resources (i.e. qualified staff); infrastructure built for TB trials uses standards relevant for the local health system	BL = 2 FU = −1	BL = −2 FU = −3	BL = 0 FU = 0
	Transparency and integrity challenges (−2 to 1)	Establishing effective communication networks for reporting monitoring of TB cases identified	BL = 1 FU = −1	BL = −2 FU = −1	BL = 1 FU = −1
	Shared knowledge challenges (−2 to 1)	Ensuring local stakeholder understanding of TB disease, treatment and prevention	BL = 1 FU = −1	BL = 1 FU = −1	BL = 1 FU = .
Intermediate & long term GPP-TB goal	Effective product available as result of most recent trial (Y/N)		BL = Y FU = Y	BL = N FU = Y	n/a
	Access summary score for most recent trial (−5 to 6)	Our site was not able to recruit the target number of participants (−1); the experimental drug tested in the trial is not suitable for use in the local context (−1); the experimental drug tested in the trial is available (1)	BL = 4 FU = 3	BL = −1 FU = 1	n/a
	Social value summary score for most recent trial (−1 to 4)	The trial was closed early (−1); the trial was successfully completed (1); the trial ultimately led to new TB treatment or prevention guidelines (1)	BL = 4 FU = 4	BL = 1 FU = 1	n/a
	Acceptability summary score for most recent trial (−3 to 2)	The experimental drug tested in the trial is not suitable for use in the local context (−1); the experimental drug tested in the trial is available but many providers refuse to use it (−1); the experimental drug tested in the trial is available and successfully used by providers and patients (1)	BL = 2 FU = 2	BL = 0 FU = 0	n/a

., missing value.

3.2 | Qualitative findings

Analysis of the qualitative interviews was informative about how sites conceptualized the concepts underlying the participatory strategies, the extent to which baseline practices were aligned with the TOC framing for each and the extent to which they viewed their work as aligned with the elements of the GPP-TB goal statement. As a reminder, interviews were conducted

before the baseline survey and GPP-TB training for each site. Interviews indicated low familiarity with GPP-TB across all sites and confusion with Good Clinical Practices (GCP) was common.

Regarding *accountability mechanisms*, questions about who would be considered a TB trial stakeholder, and how information would (or would not) be shared with them, elicited responses focused primarily on three dimensions. Firstly, they described the complex relationships within research groups

(investigators, protocol teams, sponsors, laboratories, regulatory groups, etc.). Secondly, they noted the importance of the relationship between patient-participants and clinician-researchers due to the highly burdensome nature of trial requirements (e.g. daily observed therapy, dietary requirements). Thirdly, they discussed the importance of relationship building between researchers and health system providers to facilitate access to patient populations for trial participation. Accountability questions prompted reflections on GCP with little reference to research participants and their communities. Also of note, Site A reported no CAB in the qualitative interview, although reported one in the survey at baseline.

Community mapping as a strategy was described as reliant primarily on local health departments and clinics as sources of data, such as disease trends in subpopulations or areas, and on the personal knowledge of research staff regarding issues impacting the community, such as ease of access to health care or economic stresses impacting patients. One site reported their staff visited clinics to better understand "...how drugs are distributed for patients; patients come to the health station for taking drugs or health workers provide drugs at their home, we want to know about the distance between their house and [the clinic]." Journal clubs, presentations, seminars, trainings and conference attendance were mentioned as mechanisms for research staff to keep up with public health issues related to TB more broadly, but as one site noted, "we do it to some extent, but probably could do more." Another site noted "there is no budget for this, we know it is important."

Discussion of *shared learning* as a strategy focused on working with stakeholders individually or in small groups to share information considered of most value to them, for example, targeted information for patients enrolled in research, TBTC collaborators, health department TB clinic staff, laboratory technicians and nongovernmental organizations addressing TB in the community. Mechanisms for information sharing with the affected community more broadly were generally associated with events like World TB Day and focused on TB generally, with minimal or no attention to a site's research agenda. Limited staffing and budgets were noted as barriers to more systematic information sharing, with most effort going towards working one-on-one to support study participants. While the importance of broader community engagement was noted by each site, the "how and why" of information sharing with community stakeholders was not clearly articulated.

Use of *responsible advocacy* as a strategy was limited. One site focused around World TB Day activities, with participation and support by research staff but not leadership for the events. All sites described advocacy primarily to gain support from TB treatment programmes for referral of patients to clinical trials. One site described a recent medical research controversy precipitated by a very critical newspaper article (not TB related), noting "This article has caused a lot of damage for the research community in our country" but also:

...in part, this [controversy] is the researchers' wrong doing as [education] is only done in response to a negative media publication or communication instead of being consistent and trying to use the communication/media to work on our side so the researchers are taken serious and not how it is described in the media.

To understand how *deliberation* was or might be used at the sites, we asked first if the site had faced any research-related dilemmas that required finding a balance between competing principles or values. If yes, we asked for a description of the dilemma and its resolution. If not, we asked sites to think about a situation where such a dilemma might arise and how their site would likely resolve it. We then asked how typical the approach was, whether there were dilemmas that might require a different approach and what options might be used in the case of stalemate or deadlock on a resolution. Types of dilemmas centred on balancing the needs of participants with study requirements, for example, issues of stigma, addressing patient fears about research, delays in starting treatment due to study requirements for preliminary testing and whether treatment for another illness could be modified so that a patient could qualify for a TB trial. In all cases, hypothesized or real, sites emphasized the importance of a "team effort" for resolving dilemmas, which could potentially include community stakeholders, patients and their family members, and research staff. However, when asked how the site would deal with a stalemate, all sites indicated that the PI would have the final say in how the dilemma would be resolved.

In discussions about the elements of the *GPP-TB goal statement*, social value centred on local responsiveness and getting a good match between a research study and patient population needs. One site noted, "There have been a couple of trials that we haven't participated in directly, because they just didn't seem to be very relevant to the population of our TB patients...so the main emphasis is on, is it going to be clinically relevant for our practice here? But of course we hope to be able to make some contributions to improving the global TB care." Another site noted multiple benefits of research, including "improved community awareness and shortening the TB treatment period; a second benefit is TBTC sites have been restructured and equipment has been provided with funding support from the donor, [and] capability of health workers also improved."

When asked how much consideration sites gave to whether a trial drug was something providers in their location would prescribe, one site noted the combined considerations of cost and funding: "We don't know if it will be accessible to the community and we have to trust the [pharmaceutical company] to take this into consideration...Unfortunately this is also a political issue in our country." Post-trial access to effective drugs was viewed as very important by all sites, although viewpoints varied regarding the relative influence or role of regulatory agencies, providers and pharmaceutical companies in assuring such access; the potential role of advocates or civil society did not come up. Sites did not feel strongly empowered to influence funders and regulatory agencies, but rather saw their role as more passive and subject to the direction from others, for example, "We can [try to] persuade policy makers but we won't achieve success every time" and "We can only suggest, we can start the conversation with the entities that make these decisions but we cannot put pressure on them, it will not guarantee the approval."

There was general agreement that all stakeholders, including patients, should have access to the research results, although sites were sensitive to confidentiality issues related to how patients were re-contacted to share results.

4 | DISCUSSION

Evaluation efforts have not kept pace with the expanding calls for greater use of GPP and other participatory engagement models in HIV, TB and other challenging clinical research contexts [3,4,33-36]. Limited empirical data exist on the contribution of GPP to clinical trials or even descriptive data on what clinical trial sites are doing when they implement GPP. Outcome evaluation of GPP as a global endeavour is a complex problem that has not received any attention. The study presented here is a first and basic, but essential, step towards building an outcome evaluation framework for GPP and related participatory models for clinical trials. The study demonstrated the feasibility of collecting informative data aligned with elements of a TOC evaluation framework and using a minimally burdensome online survey in multiple languages. The measures captured considerable variability in the intensity and variety of engagement strategies, both across and within sites over time. Sites were forthcoming regarding selected outcomes reflective of the GPP-TB goal statement.

In developing the measures, we were keenly aware of the need to generate a descriptive baseline of strategies and practices to gain meaningful insight into what works and under what conditions. The strategies and practices in our TOC framework reflect the purposeful framing and selection of a broad universe of engagement strategies and practices that the developers of the TOC framework believe will lead to the desired outcomes and goal of GPP-TB. Trial sites may be using many of these existing practices without reference to any of the GPP guidance documents, including sites that are new to clinical trials research if they already have a culture of engaged community practice in other work. Conversely, even experienced trial sites with knowledge of GPP may not be using some, or any of the strategies included in our TOC framework.

Generating a baseline description of engagement practices in use and not in use by trial sites is a necessary step in ultimately being able to evaluate the contribution of intentional strategies and practices to long-term desired outcomes. In this regard, it is helpful to think of GPP as a widely used intervention to improve ethical, social and scientific outcomes of clinical trials that is not fully standardized and has not been evaluated for effectiveness. Establishing a baseline description of what is and is not being done in the name of GPP is a basic requirement to move the field of practice forward on something stronger than anecdotal evidence. The strategy measures developed for this study, while not comprehensive for all engagement models, are likely to have broader applicability than the evaluation context of GPP-TB. For example, our intentional inclusion of non-CAB engagement practices as part of the *Accountability* strategy reflects calls by others of the need for broader mechanisms of community and stakeholder engagement [35]. There is also clear benefit to be gained from exploring how the GPP-TB TOC framework measures align with others being developed within the broader field of community-based participatory research [37].

The small number of sites included in this pre-pilot makes it difficult to identify meaningful patterns in the data, and such an analysis was not one of the objectives of this study. That said, one interesting point is the fact that Site B used several *Responsible Advocacy* practices in the same time period that they were unsuccessfully struggling to address a conflict in need of *Deliberation*, and had been unable to recruit the target

number of participants for the most recent TB trial conducted at the site. Regarding *Accountability Mechanisms*, the site had no CAB but reported more general engagement practices than the other sites, and, in the six months following the baseline survey, they reported three additional trials being conducted. The ability to parse such patterns with data from only three sites is promising for more rigorous analysis with more robust data, and for generating potentially testable hypotheses, for example, in line with a Realist Evaluation approach to determining what works, for whom and under what conditions [38,39].

The qualitative data added rich detail about the way research staff who were largely unfamiliar with GPP-TB perceived the strategies, practices and outcomes outlined in the TOC framework. At times, site staff did not understand the questions and asked for clarification, said they could not answer the question, or responded with information derived from GCP guidelines or local regulatory requirements. The fallback to GCP is not surprising, given the emphasis on training and compliance with GCP for trial sites. But it underscores the importance of building a shared lexicon around the basic concepts and principles of engagement, to ensure that all stakeholders inclusive of trial staff do not talk past each other. It is encouraging to note that endorsement of the core elements of the GPP-TB goal statement was evident across all three sites.

Lessons learned from this pre-pilot point to several challenges for implementing a more comprehensive evaluation of GPP-TB (or other engagement models) aligned with a TOC framework. First, this was a small pre-pilot study with three sites with limited generalizability; a more comprehensive global survey process would require more extensive work to build support among clinical trialists and demonstrate the value of the resulting data for their practice as researchers. Second, the survey responses were self-reported data, and may be subject to the various forms of misreporting generally associated with self-reported data. For example, Site A reported having a CAB in the baseline survey but indicated no CAB present at their site during the qualitative interviews conducted around the same time. This may have been due to differing interpretations of what a CAB is, including whether the CAB needs to be specific to a research site or could reference an advisory board whose members are drawn from multiple communities participating in trials sponsored by a network such as the CDC TBTC. Additional testing is needed to ensure the measures used are valid and robust, especially when translated into multiple languages. Third, a limited set of outcomes reflective of the TOC framework were measured and all were subject to self-report bias. Outcome measures could potentially be collected through more objective means, such as online clinical trial registries, peer-review publications, treatment guidelines and recommendations, and epidemiological reports on disease trends. Fourth, additional measures such as stakeholder understanding of potential trial outcomes, the extent of shared knowledge and perceptions of transparency and integrity require data collection with stakeholders beyond the research team to understand how they perceive and experience the changes hypothesized to result from the use of the strategies and practices. Such measurement presents additional challenges for recruiting participants and data collection in settings where stakeholders are likely to be geographically dispersed, linguistically diverse, with a range of literacy, and potentially limited ability to respond to an online survey.

5 | CONCLUSIONS

Community and stakeholder engagement in clinical trials for HIV, its comorbidities and other socially complex diseases is recognized as of value both ethically and practically. But systematic efforts to evaluate what works, for whom and under what conditions in the context of TB and other clinical trials are lacking. Results from this exploratory pre-pilot indicate the feasibility of generating a description of the variety and intensity of engagement practices being used by research sites globally. Capturing such variability is a necessary step for assessing how particular strategies and practices correlate with desired outcomes (such as timely recruitment, retention and uptake of results) and, potentially, how well they predict such outcomes when observed at multiple sites over time. This type of global survey would be a valuable addition to building a theory-driven, mixed methods evaluation approach to better understand and enhance engagement as a critical component of global clinical research.

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AUTHORS' CONTRIBUTIONS

KM, NE, MF and CH contributed to conception and design of the study and interpretation of the data. KM and NE contributed to data collection and analysis. KM wrote the manuscript and NE, MF and CH contributed to critical revisions. All authors contributed to the writing of the manuscript and reviewed and approved the final version.

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DISCLAIMER

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Data S1. Survey indicators and measures, including reference to the Theory of Change framework components, the rationale for each indicator measure, the range of values associated with indicators, the wording of questions for each measure, how values were calculated from responses, and the response items within measures.

COMMENTARY

Power to participants: a call for person-centred HIV prevention services and research

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Abstract

Introduction: While biomedical HIV prevention offers promise for preventing new HIV infections, access to and uptake of these technologies remain unacceptably low in some settings. New models for delivery of HIV prevention are clearly needed. This commentary highlights the potential of person-centred programming and research for increasing the cultural relevance, applicability and use of efficacious HIV prevention strategies. It calls for a shift in perspective within HIV prevention programmes and research, whereby people are recognized for their agency rather than assumed to be passive beneficiaries or research participants.

Discussion: Person-centred HIV prevention reorientates power dynamics so that individuals (rather than interventions) are at the centre of the response. Respecting personal choice and agency – and understanding how these are shaped by the context in which people exercise these choices – are critical dimensions of the person-centred approach. Community-based participatory research should be employed to inform and evaluate person-centred HIV prevention. We argue that community-based participatory research is an orientation rather than a method, meaning that it can be integrated within a range of research methods including randomized controlled trials. But embracing community-based participatory approaches in HIV prevention research requires a systemic shift in how this type of research is reported in high impact journals and in how research impact is conceived. Community-based organizations have a critical role to play in both person-centred HIV prevention and research.

Conclusions: HIV prevention is situated at the intersection of unprecedented opportunity and crisis. Person-centred approaches to HIV prevention and research shift power dynamics, and have the potential to ensure a more sustainable response with each individual actively participating in their own care and meaningfully contributing to the production of knowledge on HIV prevention. This approach taps into the resourcefulness, resilience and knowledge of the person and their communities, to strengthen research and programmes, making them more relevant, appropriate and effective.

Keywords: person-centred; HIV; prevention; participatory research; community-based organisations

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1 | INTRODUCTION

Biomedical HIV prevention research has made a major breakthrough, making the end of HIV possible, at least in theory. It has been established that antiretroviral treatment (ART) is an efficacious HIV prevention tool [1] for people living with HIV who have undetectable viral loads. Moreover, the use of pre-exposure prophylaxis (PrEP) by people not living with HIV pre-emptively inhibits HIV acquisition [2]. The combination of HIV prevention interventions and strategies has led to an overall worldwide decline in new HIV infections: In 2016 there were approximately 1.6 million new HIV infections among people over 15 years, a reduction of 10.6% compared to 2010 [3].

But this decline is far from the prevention target that most governments pledged to achieve when they signed the 2011 Political Declaration on HIV and AIDS. The target was a 50% reduction in new infections acquired through sexual

transmission or injecting drug use between 2010 and 2015 [4]. Social and structural factors continue to compromise access to and use of evidence-based biomedical HIV prevention strategies among populations most affected by HIV [5-7]. Indeed, approximately 45% of all new seroconversions globally are among sex workers, gay, bisexual and other men who have sex with men and people who inject drugs [3]. These rates have either remained steady or increased over the years.

New models of delivery of HIV prevention are clearly needed to ensure that nobody is left behind. In this commentary we highlight the potential of person-centred programming and research for increasing the cultural relevance, applicability, efficacy and uptake of HIV prevention strategies [8,9]. We suggest key areas for consideration to help shape HIV prevention services and research. We do not provide a specific set of guidelines because person-centred HIV prevention services and research are context-specific and highly dependent on individuals' preferences, concerns and needs [10]. Rather, we

call for a shift in perspective within HIV prevention programmes and research, whereby people are recognized for their agency rather than their vulnerabilities.

2 | DISCUSSION

2.1 | Applying a person-centred lens to HIV prevention

There is an increasing recognition that HIV prevention must be reorientated so that it places people (rather than interventions or disease) at the centre of our response [10,11]. Person-centred HIV prevention is a principled approach [12], which builds on the Greater Involvement of People living with HIV (GIPA) principles and the Positive Health, Dignity and Prevention Framework [13] to offer an inclusive model for HIV prevention services, which can otherwise sometimes overlook their users' complex needs. However, person-centred HIV prevention also corresponds to evidence on HIV epidemiology, health service research [9] and a public health perspective, which recognizes that people living with HIV and those at risk of acquiring the virus are deeply affected by socio-economic, legal and cultural environments, which in turn affects their enrolment and continued engagement in HIV prevention, treatment and care [6,7,14]. In addition to acknowledging that socio-environmental factors shape people's decisions and health outcomes, person-centred services aim recognize and respond to people's needs and competencies [15].

At the core of person-centred HIV prevention is the acknowledgement that people are best placed to decide which prevention methods are right for them [4]. Person-centred HIV prevention also recognizes that a person's health needs change over the course of their life [10]. A person's needs are also shaped by a range of factors that are personal (age, gender, gender identity, profession, etc.), contextual (location, community, physical security, economic status, etc.) and structural (stigma, racism, violence, criminalization, political and legal participation). By investing in long-term relationships with people and their communities we can sustain their involvement and make space for demand-driven services and community action to hold policy makers to account to end AIDS. Respecting personal choice and agency – and understanding how these are shaped by the context in which people exercise these choices – are critical dimensions of the person-centred approach. The evidence base on person-centred HIV prevention is in very nascent stages, particularly in low- and middle-income countries which bear the brunt of the HIV epidemic. However, the broader literature on healthcare suggests that person-centred services hold promise for people's health outcomes. For example, a recent systematic review examining the efficacy of person-centred care as an intervention in controlled trials found that 8 out of 11 included studies showed person-centred care to be successful [9].

While person-centredness [16] is not a new concept, adapting the delivery of HIV programming to individual needs is a departure from intervention and risk-focused approaches. It should be noted that differentiated services have begun to shift focus to more responsive and customized offerings. However, they categorize (and sometimes assume) people's needs based on treatment status or age [17]. Differentiated services are an important step in the right direction to addressing

people's diverse needs but they are still intervention focused, and categorize people based on their level of risk. While a differentiated service is oriented around the needs of epidemiologically relevant subgroups of people [17], a person-centred service aims to respond to an individual person's needs, which may vary over the course of their life [10].

Evidence on person-centred HIV prevention programming is scarce but emerging studies suggest it may help reach the most marginalized populations who may have intersecting vulnerabilities and are not being reached through public health systems. For example, Women Initiating New Goals of Safety (WINGS) is an individualized screening, brief intervention and referral to treatment model for addressing intimate partner violence and HIV risks among women who use drugs or engage in heavy drinking [18]. Following a harm reduction approach and Social Cognitive Theory, WINGS aims to employ a 'non-judgmental stance to meet women where they are with respect to their intimate relationships and to enable them to set and enact their own goals to improve relationship safety based on whether they wish to stay with or leave their partners' [18]. The model includes individual tailoring to women's needs and boundaries, identifying individual motivation for behaviour change and the manual requires facilitators to build on individual women's strengths. Based on the information provided, facilitators identify existing ways in which women who use drugs have developed personalized coping strategies, solved problems and exhibited courage and determination [18]. Recent randomized controlled trials suggest that the programme is effective in reducing various forms of gender-based violence experienced by women who use drugs in the United States [19] and Kyrgyzstan [20], which is likely to have follow-on effects on HIV prevention [21]. In India, a preliminary pilot suggested that the intervention is feasible when delivered by other women who use drugs, and a pre-post evaluation indicated reductions in intimate partner and other violence victimization [22]. Together with HIV/AIDS Alliance India, we are currently planning a randomized trial to examine whether this person-centred intervention brings added benefits to regular harm reduction for women who use opioids in India.

There is an urgent need for more evidence on which person-centred approaches work for whom and in what contexts, and for evidence-informed implementation guidance. The following sections of this paper highlight the need for person-centred HIV prevention research to meaningfully engage with communities and call for a shift in how community participation in HIV prevention research is reported.

2.2 | Implications for person-centred HIV prevention research

2.2.1 | Community-based participatory research and re-orientating the locus of power in research

Person-centred research is determined based on the *focus of enquiry*: it is defined as research examining person-centredness [23]. We posit that community participatory action research is an adequate *orientation* for developing or evaluating HIV prevention interventions that aim to be person-centred.

Community-based participatory research involves planning, executing and disseminating research "with the people whose

life-world and meaningful actions are under study” [24]. The main difference between participatory and non-participatory research is the locus of power and ownership of the research process [24]. Participatory research places its participants at the centre of the knowledge production process. This perspective recognizes that the validity and applicability of research findings are highly dependent on meaningful involvement of community expertise. A growing evidence base on participatory research sets a strong foundation for guiding people on various practical aspects of meaningful engagement of communities in HIV prevention research. Drawing on practical experience, researchers have reported on the benefits and challenges of co-designing interventions, building capacity so that community partners understand the utility of evidence for advocacy and setting funding priorities, and using participatory research to comprehend the cultural acceptability and applicability of HIV prevention tools [25-28]. UNAIDS and AVAC published Good Participatory Practice guidelines for biomedical HIV prevention trials, which recommend community participation to strengthen the ethical and scientific quality of biomedical HIV prevention trials [29]. However, to our knowledge, there is no similar consolidated set of guidelines for community participation in non-biomedical HIV prevention research.

Building further from the aforementioned participatory practices, if a study is concerned with also being *person-centred*, then the focus of enquiry must expand from a disease (or vulnerability to the disease) to the whole person and their lived experience [15,30]. As part of this, person-centred research explicitly examines people’s integration within their environment, their relationships with other actors in their lives, their aspirations and their rights [9]. In practical terms, this means that while all person-centred research is participatory, not all participatory research is person-centred. For example, it is possible for a study concerned with biomedical HIV prevention to follow good participatory practice guidelines but focus only on clinical outcomes determined based on a person’s HIV risk [29]. In contrast, a person-centred study would also examine the wider aspects of people’s everyday lives that might have the potential to strengthen HIV prevention [30,31]. HIV prevention studies mainly measure HIV prevention outcomes such as condom use, reduction in viral loads and PrEP use. However, from a person-centred perspective, outcomes measured should reflect what matters to service users, even if this entails a departure from what is normally considered as relevant to public health, for example, sexual pleasure outcomes [32]. Critical to person-centred research is anti-reductionism and a commitment to understanding people’s strengths, potential and resilience [15].

Person-centred research is grounded in the belief that the evidence on HIV prevention must adequately respond to the broad needs and aspirations of people who take part in the research and who we hope to uptake the HIV prevention technologies and interventions. For example, a mixed-methods longitudinal study of adolescents living with and affected by HIV in South Africa, has used a participatory approach to examine what might improve young people’s uptake of health services. Through the “dream clinic” exercise [33], a qualitative method which was co-developed with adolescents, young people designed and drew their ideal health facilities. The resulting “dream clinic” illustrations were analysed together with

young people. Findings indicated a wide range of aspirations that young people have for their health services, including clean water supplies and food through soup kitchens, tuck shops and/or gardens. Young people also expressed their desire for easily accessible healthcare, with well paved roads, proximity to their homes and schools and linkages to social services. Their dream clinics included healthcare providers who treated them respectfully. This person-centred and participatory research study produced practicable recommendations for innovations in development and healthcare, and informed the objectives of South Africa’s 2017 National and Adolescent and Youth Health Policy.

2.2.2 | **Researchers should be accountable to communities they aim to serve**

Participatory research has often been categorized as a qualitative research method – portrayed in contrast to positivist quantitative science [34]. We position person-centred research as an orientation rather than a method, meaning that it is compatible with and can be employed in quantitative HIV prevention research [35]. Even randomized controlled trials, which are considered the golden standard of evidence, can be conceptualized, designed and implemented through community-based participatory partnerships [36]. For example, within a community based participatory partnership, Rhodes and colleagues [37], tested an HIV prevention intervention with and for immigrant Latino men who have sex with men in the United States. Essential to this process was capacity building among community partners to understand the utility of high-quality evidence for policy change and for guiding funding priorities [37]. Unfortunately, there are few HIV prevention studies that report employing both a quasi-experimental or experimental design and community-based participatory approaches [34]. Reasons for this remain unknown because, as noted above, applying community-based participatory approaches to robust quantitative studies is possible. Evidence from broader HIV-related research supports the notion that participatory research methodologies can be applied to quantitative studies. For example, Mavhu and colleagues have used mixed methods participatory research to highlight the dominant issues in the lives of young people living with HIV in Zimbabwe, using it to enhance existing adherence and sexual and reproductive health programming with psychosocial support [38]. Person-centred HIV prevention is possible only if the production of knowledge is co-owned between researchers and the community. In line with this, we reiterate that community-based participatory research can and should be applied across the spectrum of research methods.

Embracing community-based participatory approaches in HIV prevention research requires a systemic shift in how this type of research is reported in high-impact journals. High impact peer-reviewed publications featuring emerging evidence on HIV prevention, including this journal, require that authors adhere to gold standard reporting guidelines for effectiveness and epidemiology studies. But the relevant reporting guidelines for randomized controlled trials [39,40] and observational studies [41] do not include requirements to report on community involvement in the research. Quantitative HIV prevention studies may employ community-based

participatory approaches more frequently than is reported. However, without proper documentation readers are not able to understand or evaluate to what extent this has occurred, and are not capacitated to replicate approaches to community-based participatory research [42]. Leading multidisciplinary HIV and AIDS journals such as this one are uniquely positioned to catalyse a culture change in how quantitative HIV prevention research is conceived and reported.

Further, for those of us providing HIV prevention services and strategies, the outcome of community-based participatory research cannot be stand-alone research outputs. Rather, the research process should be fully embedded in and intertwined with all other elements of HIV prevention. For us, HIV prevention research is a tool for optimizing service delivery. In order to inform person-centred HIV prevention, the research must also be participatory, whereby people are not merely participants but rather essential technical advisors, partners in the research design and implementation, co-owners of data and key stakeholders for dissemination [12].

Networks of key populations and people living with HIV, community groups, women's rights groups and community activists can play instrumental roles in posing difficult ethical questions, identifying relevant community partners and helping ensure that the research is conducted in a way that maintains accountability to communities. Community-based participatory research in the context of HIV is challenging. Debates around these challenges are important and, in our view, reinforce the importance of engaging with community-based organizations in HIV prevention research. For example, researchers have expressed tensions between the basic tenets of ethics to protect participants versus the basic principles of community-based participatory research which recognizes people's autonomy and authority over their own lives [43]. Questions have also been raised around who represents the community [34]? Community-based organizations working on the frontlines of HIV prevention and human rights have an essential role to play in defining ethical guidelines for this type of research. Without the possibility to engage all members of an affected population, community organizations can provide critical linkages, offer guidance for meaningful engagement, and be a vital source of real-time data about the issues the population is facing.

3 | CONCLUSIONS

HIV prevention is situated at an intersection of unprecedented opportunity and crisis, with prevention targets not being met for marginalized populations [3,4]. While biomedical HIV prevention offers promise for reducing the spread of HIV, access to and uptake of these technologies remain unacceptably low in many settings. Key populations disproportionately affected by HIV continue to experience severe structural barriers to HIV prevention, including stigma and criminalization [6,44]. Few issues in the HIV response are more urgent than to apply a more person-centred approach to prevention for these communities. Ultimately key populations have a wealth of experience in manoeuvring their lives and they know exactly what is appropriate and effective in their circumstance. Person-centred HIV prevention services should listen and respond to these perspectives.

In order to achieve this, a reorientation of power dynamics in research is essential. We posit that community-based participatory approaches to research are highly relevant to shaping person-centred HIV prevention. Here, community-based participatory research is employed as an orientation to scientific enquiry, which can be applied to both qualitative and quantitative research methods. Community-based organizations have a critical role to play in strengthening community-academic partnerships and ensuring that research is done ethically in a way that is accountable to communities.

Person-centred approaches to HIV prevention services and research shift power dynamics, and have the potential to ensure a more sustainable response with each individual actively participating in their own care. This approach taps into the resourcefulness, resilience and knowledge of the person and their communities, to strengthen research and programmes, making them more relevant, appropriate and effective.

Key recommendations for person-centred HIV prevention and research

Recommendations for programme implementers

- 1 Recognize that there is no one-size-fits-all solution and be willing to implement flexibly
- 2 Treat people as experts, not patients
- 3 Recognize that people are resourceful, learn about the strategies they use to improve HIV prevention and capitalize on this

Recommendations for researchers

- 1 Use participatory approaches to designing, implementing and reporting on research so that communities' preferences are taken into account. This applies to both qualitative and quantitative studies.
- 2 Investigate research questions that highlight people's strengths and aspirations rather than just risks and vulnerabilities
- 3 When writing a paper, report on community engagement; when reviewing a paper, ask authors to report on it; when editing a journal or special issue, make it a requirement for empirical papers to report on community engagement (or lack thereof).

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AUTHORS' CONTRIBUTIONS

CR, ER, MP and SS conceptualized the commentary. MP, CR and SS provided content on person-centred HIV prevention programming. MP and ER provided content on implications for research. MP drafted the manuscript, and all authors contributed to revisions.

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VIEW POINT

Building effective multilevel HIV prevention partnerships with Black men who have sex with men: experience from HPTN 073, a pre-exposure prophylaxis study in three US cities

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Keywords: African American; homosexual; community engagement; PrEP research

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The sub-population at greatest risk for HIV infection in the United States is Black men who have sex with men (BMSM), and there is an urgent need for effective HIV prevention interventions among them [1]. Despite advances in biomedical and behavioural interventions, healthcare systems continue to fail to slow the epidemic among BMSM. This is particularly the case among young men [2], who have an estimated lifetime risk of HIV infection of up to 50% [3]. It has been well demonstrated that tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) as pre-exposure prophylaxis (PrEP) are effective in protecting those at risk of HIV acquisition from sex or injection drug [4,5], but prescriptions to BMSM have sorely lagged behind other affected populations, including gay and bisexual White men [5,6].

Myriad structural characteristics, including poor health, poverty, stigma, high rates of incarceration, inadequate housing, lack of health insurance, decreased educational attainment and unemployment, impede recruitment and retention of BMSM in studies [6,7]. This constellation of factors is likely responsible for both high HIV prevalence and low uptake of PrEP (and other interventions) [8]. Clearly, effective interventions to increase PrEP uptake among BMSM are urgently needed; yet, in public health and medicine, we continue to miss the mark [5].

Just one demonstration project cannot overcome this full range of barriers. However, in the HIV Prevention Trials Network (HPTN) 073 study discussed in this view point article, we focused on what we perceived to be primary factors precluding adequate study of HIV prevention interventions among

BMSM: lack of indigenous scientific leadership evident throughout the HIV prevention research field; and low BMSM enrolment in nearly all PrEP studies, including the initial iPrEX trial itself [2,9]. The key to our approach was purposefully increasing representation of Black researchers in leadership roles [10]. HPTN 073 was unique in its being led by researchers of the community under study and its thoughtful connectivity and engagement with this community at all points of study design, implementation, analysis and dissemination. This approach was grounded in the foundational work of Andrasik *et al.* [11], who identified three key themes as barriers to engage BMSM in HIV prevention research: authentic/true partnerships with community-based organizations; a real investment in the Black gay community; and the follow-up to truly inform and educate the community after the study is completed.

HPTN 073 was an open-label antiretroviral PrEP demonstration project. Eligible BMSM aged 18 years and older in three US cities were offered daily oral co-formulated FTC/TDF, with primary outcomes being PrEP uptake/initiation and adherence [12]. The majority of the HPTN 073 leadership team, including the protocol chair and co-chair, behavioural scientist, intervention developer and key staff members, worked together on a previous BMSM study (HPTN 061) [7,13,14] and had many years of significant linkages to BMSM communities and organizations across the US. In addition, along with key staff at all sites, they were also members of the BMSM community.

The behavioural intervention developed for this study was client-centred care coordination (C4), which incorporated

theoretical and public health approaches from comprehensive risk counselling and self-determination theory [15] tailored specifically for BMSM supporting participants' evaluation of their risk for HIV and personal ability to accept and adhere to PrEP if they elected to take it [16,17]. The study sites included Washington, District of Columbia; Los Angeles, California; and Chapel Hill, North Carolina.

HPTN 073 included standardized and rigorously evaluated site development activities to assist study teams in assessing and enhancing their readiness to work with BMSM, including a comprehensive cultural competency component designed by the HPTN Black Caucus [presence/place at the table (PAT)], specifically manualized for the study. Intrinsic to this approach was the concept that the study itself was not objectifying disconnected community members, but rather partnering members of the community with esteemed academic experts. This allowed participants to realize from the outset that the results of this study were intended to impact the lives of men in their communities in real time. This comprehensive approach embraced all facets of study, allowing brisk recruitment, strong retention and collection of high-quality data. In addition, emerging from this demonstration project are new scalable approaches for engaging historically under-represented researchers in leadership roles in the future.

HPTN 073 sites successfully recruited and screened 344 people and ultimately enrolled 226 BMSM between February 2013 and September 2014, retaining 92% of participants for the 12-month follow-up]. The findings from the HPTN 073 study suggest that behavioural and biomedical interventions can be used in combination to support BMSM acceptance of, adherence to and benefit from oral PrEP [16,17].

It is already known that PrEP works when taken and that removing barriers helps uptake. This study went further showing the critical importance of meaningful engagement between the community and researchers who embody the priorities of the participants. BMSM leaders of the study ensured that all facets of HPTN 073 were rigorously performed to support the needs of the BMSM themselves, and not just to prepare an article read only by researchers. The depth of community support, from recruitment to evaluation and analysis, were consistent in all sites. Study participants and community members identified the significance of having BMSM leadership. By supporting staff's awareness of and ability to engage in active listening, critical examination of barriers to service delivery and attention to understanding multilevel needs of BMSM, the HPTN 073 staff created supportive environments in which men could develop HIV prevention approaches, including PrEP tailored to their needs.

The researchers used a culturally tailored PrEP programme for BMSM with intentional indigenous scientific leadership and ongoing codified efforts to ensure adequate training and cultural competency; this led to numerous positive outcomes [12]. The role of knowledge in the form of BMSM leadership is a key factor in supporting future research efforts. Those in control of access to, and interpretation of knowledge and research processes can and do shape what is validated and what is not. As Tunde Wey writes, "It is about who gets to create us and what those representations mean for our lives... The world has a way of turning on the careless words of fools." (2018, March 11, SF Chronicle) [18].

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The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

All authors have contributed substantially to the conception and design of the manuscript or acquisition, analysis or interpretation of the data for this work. Each author has participated in the drafting or revision of the content. Additionally, DPW was the chair of the HPTN 073 study and SDF was the co-chair of the study. LW was the lead behavioural scientist and LEN was the lead implementation scientist for the study. JPL provided scientific leadership in all phases of community engagement for the study. MM, LHW and SS were the site investigators for the study in their respective cities. KHM, DPW, SDF, LW, LEN, MM, LHW and SS provided scientific leadership in the conceptualization, development and implementation of the study. GB and YQC provided statistical analysis for the study. LME supervised data management for the study. KHM served as a protocol team member and provided scientific, medical- and health-related expertise for the study. IK provided research, data analysis and interpretation for the study and was also a co-PI for her respective site. CCW served as the chair of the HPTN Black Caucus. CHO and CH served as HPTN Black Caucus Vice Chairs and provided socio-cultural expertise for the study. All authors contributed to the writing of the manuscript. All authors have read and approved the final manuscript.

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COMMENTARY

Qualitative research on community experiences in large HIV research trials: what have we learned?

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Abstract

Introduction: Very few pragmatic and community-level effectiveness trials integrate the use of qualitative research over all stages of the trial, to inform trial design, implementation optimization, results interpretation and post-trial policy recommendations. This is despite the growing demand for mixed methods research from funding agencies and awareness of the vital importance of qualitative and mixed methods research for understanding trial successes and challenges.

Discussion: We offer examples from work we have been involved in to illustrate how qualitative research conducted within trials can reveal vital contextual factors that influence implementation and outcomes, can enable an informed adaptation of trials as they are being conducted and can lead to the formulation of theory regarding the social and behavioural pathways of intervention, while also enabling community engagement in trial design and implementation. These examples are based on published findings from qualitative studies embedded within two ongoing large-scale studies demonstrating the population-level impacts of universal HIV testing and treatment strategies in southern and eastern Africa, and a qualitative study conducted alongside a clinical trial testing the adaptation, acceptability and experience of short-cycle therapy in children and adolescents living with HIV.

Conclusions: We advocate for the integration of qualitative with clinical and survey research methods in pragmatic clinical and community-level trials and implementation studies, and for increasing visibility of qualitative and mixed methods research in medical journals. Qualitative research from trials ideally should be published along with clinical outcome data, either integrated into the “main” trial papers or published concurrently in the same journal issue. Integration of qualitative research within trials can help not only to understand the *why* behind success or failure of interventions in different contexts, but also inform the adaptation of interventions that can facilitate their success, and lead to new alternative strategies and to policy changes that may be vital for achieving public health goals, including the end of AIDS.

Keywords: qualitative research; community; randomized controlled trials; publishing; social sciences

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1 | INTRODUCTION

In 2009, Simon Lewin and colleagues published a review on the use of qualitative methods *alongside* research trials of complex healthcare interventions [1]. They observed that of the 100 trials reviewed (every fifth trial of the 492 trials listed in the register of the Cochrane Effective Practice and Organisation of Care Review group for 2001 to 2003), 30 had included qualitative work or had research based on qualitative methods associated with them. A number of these trials had made use of qualitative data before and during the trial, but only two had, at that time, integrated the use of qualitative research in all stages of the trial. Reasons given for not using mixed methods included lack of supportive funding and appropriate qualitative expertise as part of the main research team. In recent years, the use of mixed methods in trials has become more accepted by funders [2-5] and social scientists

more likely to be a *part* of the trial team (not working *alongside* the trial) [6-8].

That said, qualitative methods are often still viewed as contributing to particular aspects of the trial such as informing recruitment of target groups or intervention adherence strategies, measuring and supporting community engagement [9-11] or contributing to explaining trial results [12-15]. In this commentary, we summarize the key benefits of inclusion of qualitative and mixed methods in trials. We examine the use of qualitative methods for contributing over all stages of the trial, including trial design, optimizing implementation, interpreting results and shaping post-trial policy recommendations. We advocate for equitable collaborative working across disciplines and in approaches to publication and all forms of dissemination.

We take several examples, based on published sources, from work we have been involved in, to illustrate how

integration of qualitative research within randomized controlled trials and implementation studies can reveal vital contextual factors that can influence implementation and outcomes (including both positive and negative unintended consequences), can enable an informed adaptation of trials as they are being conducted and also lead to the formulation of new hypotheses regarding the social and behavioural pathways of intervention action (i.e. theory building). We share examples of qualitative research studies embedded within two large community-based trials testing the population-level effects of universal HIV testing and treatment (UTT) (which aims to extend HIV counselling and testing to an entire population and antiretroviral therapy (ART) to all those person living with HIV) in southern and eastern Africa [16], and of a clinical trial of an intervention to test the adaptation, acceptability and experience of short-cycle therapy [17] in children and adolescents living with HIV.

2 | DISCUSSION

2.1 | A UTT intervention trial in Kenya and Uganda

Our first example is taken from the Sustainable East African Research in Community Health (SEARCH) (NCT# 01864603) study, an ongoing community cluster randomized controlled trial (NCT#01864603) in 32 communities of approximately 10,000 persons each located in three regions in Kenya and Uganda. SEARCH aims to evaluate the health, economic and educational impacts of a community-based strategy for immediate and streamlined ART for all HIV-positive persons. A longitudinal qualitative research study embedded within the trial aims to reveal social, behavioural and implementation processes that influence the UTT strategy and its outcomes: why the strategy works or fails in communities, and how it operates in diverse settings. The qualitative findings also have been periodically “fed back” to trial leadership and regional teams to explain how the intervention has evolved, and to inform optimization. The SEARCH trial design is adaptive, and newer methods for inference and estimation of “treatment effect” are used [18], which permitted refinements to the intervention design and implementation over time. Thus, inclusion of a longitudinal qualitative study within SEARCH was particularly valuable. Methods include annual in-depth interviews with cohorts of community members, community leaders and healthcare providers, participant observation at community health campaigns (CHCs) and focus group discussions with CHC attendees. Data collection began in February 2014 and is ongoing.

The SEARCH strategy involved multiple interventions to achieve the UNAIDS 90-90-90 targets. To reach the first “90%,” the study conducted multi-disease testing and services at CHCs combined with home-based testing for those who did not participate in campaigns [19]. The strategy began with community ethnographic mapping (used to define characteristics for pair-matching) as well as consultative community meetings to ascertain community preferences for certain intervention elements (non-HIV services, which varied by community, included hypertension and diabetes screening, malaria rapid diagnostic testing, medical male circumcision, cervical cancer screening and other services). To ensure at least 90% of those diagnosed were linked to care, the study used rapid linkage at testing,

appointment reminders, improved provider access through telephones and face-to-face meetings, and missed appointment tracking. To ensure that 90% of those in care have undetectable viral loads, SEARCH used a “streamlined care” approach designed to lengthen intervals between visits for stable patients, offer shorter waiting times and ensure a friendly environment in clinics [20]. SEARCH demonstrated the effectiveness of its model for high HIV “cascade coverage,” and increased population viral suppression from 45% to 81%, exceeding the “90-90-90” targets within two years in intervention communities [21]. Initially, testing uptake in the study for men was lower than that of women (62% vs. 74%). Early qualitative research findings on the structural and cultural factors that hindered men’s participation in testing campaigns [22] helped to explain these observations. The team found that men’s livelihoods and mobility meant they were often away from rural homesteads and could not easily access testing campaigns or HIV care during work hours. Gender norms that ran counter to men’s care-seeking, and valorized their risk-taking, were also said to inhibit their interest in CHCs; many men preferred to “test by proxy,” inferring their own HIV status from their wife’s. Qualitative interviews and focus groups revealed that health campaigns and clinics were seen as “female spaces” that men hesitated to enter, despite incentives and other features targeting men. SEARCH responded to these early observations by adapting its approach to mobilizing men for testing. The location and timing of CHCs were adjusted to better meet men’s needs, with more campaigns conducted near workplaces and on weekends (including “moonlight CHCs” at Lake Victoria beach landing sites). The resources allocated for home-based testing (disproportionately preferred by men) at client-selected locations were increased, while campaigns were redesigned to include more incentives, sports activities and other features targeting men to increase their demand for testing. These included football matches, boat races and live bands at campaigns. Men’s “spaces” and services were set up at campaigns, including a “men’s tent” offering counselling on male sexuality, urgent care services and linkage to male circumcision. Local formal and informal male community leaders were hired to assist with mobilizing other men.

These efforts yielded positive results vis-à-vis community-wide participation in testing, and also in qualitative findings showed that they precipitated new opportunities and anxieties related to the disclosure of HIV-positive status among those either newly diagnosed or confronted anew with a need to disclose as a result of the intervention. An analysis of experiences related to disclosure of HIV status in narratives of people living with HIV (PLHIV) from SEARCH published by Maeri and colleagues [23] revealed that HIV-related stigma in communities during the study’s baseline year was perceived to be high by community members. Many individuals resisted disclosure because of anticipated stigma, and there were stark gender inequities in the negative consequences of disclosure, with women more likely than men to experience violence or abandonment by partners as a result of their disclosure of HIV-positive status. That analysis called for efforts to strengthen capacity in health systems for gender-sensitive provider-assisted disclosure to address the differing support needs of men and women.

2.2 | A trial testing a health system intervention to accelerate ART initiation in Uganda

At the same time, qualitative research in SEARCH using data collected in the first two years of the study provided early signs that norms, beliefs and attitudes related to HIV testing, status disclosure and engaging in HIV treatment were changing. Combining these with data collected from another large randomized controlled trial, the Streamlined ART Initiation Strategy (START-ART) trial in Uganda (NCT#01810289), an analysis published in this journal by Camlin and colleagues [24] posited an unforeseen pathway of intervention action in strategies that seek to harness the potential of ART to bring about improvements in individual health outcomes for PLHIV and large-scale reductions in HIV incidence. In that article, authors propose that the advent of widespread testing campaigns and efforts to accelerate antiretroviral “treatment for all” in eastern African communities has precipitated a rapidly expanding shift in how people living with HIV infection view themselves and act in the community to promote better health for other PLHIV. HIV-related stigma acts to reinforce hierarchies of power and to systemically exclude those less enfranchised from society and render them “invisible.” But narratives from PLHIV in communities and in clinics revealed that whether or not they were remunerated, and whether they encountered other PLHIV in clinics or in communities, PLHIV in Kenya and Uganda have been taking on new roles and self-conceptualizations that are transforming their “spoiled” or stigmatized identity into a new valorized social identity, finding a moral “redemption” via their public advocacy of HIV testing and treatment. These trials did not foresee or plan for it; but as the benefits of ART embolden more and more PLHIV to openly engage in care, many “advocates for ART” are emerging in communities, actively engaged in encouraging others to test, to enrol in HIV treatment, to adhere to ART regimens and to stay engaged in care. PLHIV are not only creating a renewed, destigmatized subjecthood, but are leading opinions and playing a pivotal role in shaping new social norms and attitudes related to HIV testing and treatment in eastern Africa. These findings have led to a deeper understanding of the community impact of the UTT strategy and presented opportunities to engage and support the unanticipated positive social change.

2.3 | A UTT intervention trial in Zambia and South Africa

Our next example also illustrates the value of qualitative research for informing trial teams about study communities in the early stages of a trial and for shaping subsequent research. Social science research is integrated into the design of HPTN 017 (Population Effects of Antiretroviral Treatment to Reduce HIV Transmission [PopART]) cluster randomized trial [25] to demonstrate the effects of a UTT strategy, as is the case with SEARCH. In 2013, during the initial selection of the 21 communities in Zambia and South Africa for HPTN 071, rapid qualitative research (termed a Broad Brush Survey [26]) was conducted to gather data on each community, prior to the implementation of the trial intervention. While the results of this work are drawn on in a number of publications [27-30], this example focuses on the work published by Bond

and colleagues in 2016 [31]. For the rapid assessment, a small team of social science researchers spent about two weeks staying in each study community to undertake data collection, using group discussions, key informant interviews and observations. The work was organized in a sequence to ensure the team acquired a good overview of the setting before holding in-depth interviews and discussions about the “HIV landscape” of the community, including access to HIV prevention and care services. Those data were used to document the social, demographic and economic profile of each site for use by the trial implementation team, and also to conduct analysis of the contextual heterogeneity across sites. The authors analysed the variability in response to HIV interventions early in the trial using first year process indicator data from the trial (2014 to 2015) from four Zambian intervention communities (“Arm A”) along with the qualitative assessment findings [31]. The latter data were organized according to four meta-indicators spanning physical features, social organization, social networks and “community identity” narratives, to facilitate comparison between communities. These indicators were developed by a research group aiming to classify the “capability” of response to change across diverse settings in Rome, Turin, London, Zambia and South Africa [32]. Applying the meta-indicator frame to the HPTN 071 rapid assessment data, Bond and colleagues concluded that combining the two sets of data provided valuable insights regarding which differences between communities were likely to matter for HIV intervention uptake. For example, “social organization” differences that mattered included mobility (primarily for work), young men’s work patterns, population variability across different housing types and the presence of HIV stakeholders. These were factors that could be tracked for change over the duration of the trial and be used to help interpret variability in the trial outcomes [29].

2.4 | A multi-country trial to develop a treatment intervention for young people living with HIV

The last example is from the BREATHER (PENTA 16) clinical trial. Working across 11 countries (including one centre in Uganda), this trial compared virological control of short-cycle therapy (five days on: two days off) with continuous EFV-based ART in 199 children and young people (aged 8 to 24) (70 from Uganda) living with HIV with viral load <50 c/mL to examine adaptation, acceptability and experience of short-cycle therapy to inform intervention development [17,33]. The social science component was not fully funded within the trial funding, and a parallel grant from a different funder was secured by the social scientists to support the qualitative research in Uganda. The qualitative study consisted of repeat in-depth interviews with a sample of participants from both arms of the trial, and discussion groups at the end to discuss emerging trial results. The qualitative data showed that while there was a strong preference for the option of short-cycle therapy, to allow weekends off from treatment, young people from both arms reported frequent medication side effects and occasional missed doses that they had rarely shared with clinical staff [34]. The final discussion group allowed participants to voice concerns about the risks of short-cycle therapy for young people who struggled to adhere to treatment [35]. These findings informed the way

in which the final trial findings were reported and could provide valuable input for further research. It should be noted that while some of the qualitative study findings were integrated into the “main” trial paper the paper [17] detailing the qualitative findings (which was submitted at the same time as the main trial findings paper) was not accepted for publication. The qualitative findings paper was published later in a different journal [34].

3 | CONCLUSIONS

With increased attention to translating biomedical research advances into clinical practice, policy and population-level impact (requiring widespread social and behavioural change), there is a demand for incorporation of qualitative methods in pragmatic clinical and community-level trials and implementation science studies [4]. The structure of this methods “mixture” can draw upon existing taxonomies of mixed methods designs [36,37], but we suggest that the integration of qualitative methods within trials, particularly when applied using constructivist grounded theoretical approaches (e.g. as articulated by Charmaz [38]), can allow researchers to not only pursue a set of research questions defined *a priori*, but also generate new avenues of inquiry and opportunities for theory building in response to unexpected empirical findings. Especially in complex trials, interventions are often not implemented as planned, secular trends affect outcomes, and outcomes and their generalizability cannot be interpreted intelligibly without an in-depth understanding of context. The increasing use of novel adaptive trial designs and hybrid implementation-effectiveness trial designs is propitious for integration of longitudinal qualitative research, because these designs facilitate use of qualitative findings to inform optimization of interventions as they are being implemented; moreover, these designs value measurement of heterogeneous “implementation” and “contexts,” aiming to elucidate rather than obscure these factors. The integration of qualitative research within trials can help not only to understand the *why* behind success or failure of interventions in different contexts, but also inform the adaptation of interventions that can facilitate their success, and lead to new alternative strategies and to policy changes that may be vital for achieving public health goals.

We advocate specifically for the pairing of qualitative with clinical and survey research methods in trials and implementation studies, and for the publication of qualitative research from trials with clinical outcome data, either fully integrated into the “main” trial papers or published concurrently in the same journal issue. The option of two complementary papers (of equal weight) is probably the most viable, given word limits may preclude adequate coverage of all results in one paper.

The findings from qualitative research within trials offer valuable information on the ways people behave and communicate, and the complex social worlds with which research is conducted – information that is essential to the understanding of trials’ results [6]. However, we continue to find that papers based on qualitative methods from trials are afforded lower priority by many medical journals, despite recent efforts to urge editors to reconsider policies towards the publication of such research [39]. Social scientists continue to push the

boundaries of disciplinary biases in biomedical HIV research and the medical literature, but the advocacy of clinical researchers is essential to achieve widespread awareness that biomedical research is strengthened through the inclusion of social sciences in the centre of its sphere of inquiry.

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COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHORS’ CONTRIBUTIONS

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RESEARCH ARTICLE

Village community mobilization is associated with reduced HIV incidence in young South African women participating in the HPTN 068 study cohort

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Abstract

Introduction: Adolescent girls and young women (AGYW) in South Africa bear a disproportionate burden of HIV. Community mobilization (CM), defined as community members taking collective action to achieve a common goal related to health, equity and rights, has been associated with increased HIV testing and condom use and has been called a 'critical enabler' for addressing the HIV epidemic. However, limited research has examined whether CM is associated with HIV incidence among AGYW.

Methods: We examine the association of CM with incident HIV among AGYW (ages 13 to 21) enrolled in the HPTN 068 cohort in the Agincourt Health and socio-Demographic Surveillance System, South Africa. This analysis includes 2292 participants residing in 26 villages where cross-sectional, population-based surveys were conducted to measure CM among 18- to 35-year-old residents in 2012 and 2014. HPTN 068 participants completed up to five annual visits that included an HIV test (2011 to 2016). Household-level data were collected from AGYW parents/guardians and census data is updated annually. Mean village-level CM scores were created using a validated community mobilization measure with seven components (social cohesion, social control, critical consciousness, shared concerns, organizations and networks, leadership and collective action). We used pooled generalized estimating equation regression with a Poisson distribution to estimate risk ratios (RR) for the association of village-level CM score and CM components with incident HIV infection, accounting for village-level clustering and adjusting for key covariates.

Results: There were 194 incident infections over the follow-up period. For every additional standard deviation of village-level CM there was 12% lower HIV incidence (RR: 0.88, 95% CI: 0.79, 0.98) after adjusting for individual, household and community characteristics. CM components associated with lower HIV incidence included critical consciousness (RR: 0.88; CI: 0.79, 0.97) and leadership (RR: 0.87; CI: 0.79, 0.95); while not statistically significant, social cohesion (RR: 0.91; CI: 0.81, 1.01), shared concerns (RR: 0.90; CI: 0.81, 1.00), and organizations and networks (RR: 0.91; CI: 0.79, 1.03) may also play a protective role.

Conclusions: These results suggest that having strong community social resources will reduce AGYW's risk of HIV acquisition. Work to mobilize communities, focusing on building social cohesion, shared concerns, critical consciousness, and effective and accountable leadership, can fortify prevention programming for AGYW.

Keywords: community mobilization; critical consciousness; HIV incidence; adolescents; social capital; South Africa

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1 | INTRODUCTION

It is estimated that there are over 8500 new HIV infections per week among adolescent girls and young women (AGYW) ages 15 to 24 years in sub-Saharan Africa [1]. Within the region, South Africa has the largest epidemic; 5.6% of AGYW ages 15 to 19 are living with HIV, increasing to over 17.4% by ages 20 to 24 [2]. The steep rise in HIV incidence during this time is shaped by a critical period of human development marked by profound physical, cognitive, and social changes

and developmental tasks (e.g. establishing identity, independence) that characterize the transition from adolescence to young adulthood [3-6]. Within this complex transition period, the sociocultural environment is likely to play a large role in shaping behaviours and risk [6,7]. In fact, adolescence has been labelled a period of "heightened sensitivity to sociocultural signals in the environment" [8] when the influence of peers and their school and community environments may play a greater role in determining HIV risk than at other stages of their lives [9,10].

There is growing evidence that the social environment, inclusive of the physical surround and cultural context in which social relationships occur and people interact [11], shape health and health behaviours [12-16]. For example, studies of community well-being or a sense of community connectedness, social capital and social cohesion have demonstrated protective effects on early sexual debut and rates of sexually transmitted infections in the US [17-21]. Studies in multiple contexts have also found that women who perceive their environments to be cohesive or who engage in community groups have better sexual health outcomes [22-26]. There is also evidence that in the critical adolescent years, increasing social connection to and engagement within the community is associated with protective behaviour [27,28]. Prosocial involvement or participation in the community, including participation in school groups, athletics or sports clubs, religious groups, or arts and cultural groups, can provide young people with a sense of meaning, value, or belonging, and has been associated with lower levels of substance use, risky sexual behaviour and violence [29-37].

To shape and harness community well-being to support young people in preventing HIV infection, it is critical to improve our understanding of the many facets of community 'social health' that may play a role in HIV. Currently, there is disagreement around which aspects merit focus and a lack of consensus on how to monitor and measure these components. In recent years, there has been a growing international focus on community mobilization (CM) for health, which UNAIDS has called a critical enabler for HIV programmes, or "an activity that is necessary to support the effectiveness and efficiency of basic programme activities" [38]. To further efforts to engage and mobilize communities and understand which aspects of the social environment can facilitate improved health for young people, our team developed a conceptual framework and measure of community mobilization – a collection of community characteristics and processes that we hypothesize are collectively needed to improve health outcomes or behaviours [39,40]. These mobilizing components include: (1) a shared issue or concern that is the target of change; (2) community sensitization or building of critical consciousness; (3) an organizational structure with links to groups/networks; (4) leadership (individual and/or institutional); (5) collective activities/actions; and (6) community cohesion [39]. We also measured a seventh component: social control, or the mutual expectation of community members to intervene for shared interests [41,42]. We previously developed and validated the Community Mobilization Measure (CMM) [40], and applied our measure in a population-representative survey across 26 villages where longitudinal research with AGYW was underway. In this manuscript, we examine whether living in a community with higher levels of mobilization is associated with HIV incidence among AGYW and assess which community mobilization components are associated with reduced HIV incidence. As a result, this manuscript expands the focus of this special issue on community engagement theory and practice in research to a broader view of community mobilization for health, offering findings that can inform future directions for both complementary areas of study.

2 | METHODS

2.1 | Setting and procedures

HPTN 068 took place in the high HIV-prevalence district of Ehlanzeni, South Africa [2] within the rural Agincourt Health and socio-Demographic Surveillance System (HDSS) site, where the Medical Research Council/Wits University Rural Public Health and Health Transitions Research Unit (Agincourt) conducts an annual census [43]. HPTN 068 (NCT01233531) was a randomized trial of cash transfers conditional on school attendance among 2533 AGYW ages 13 to 20 residing in the Agincourt HDSS study area enrolled in grades 8 to 11 at local government (public) schools at the time of study enrolment (March 2011 to December 2012). Following informed consent procedures, cohort participants were randomized 1:1 to conditional cash transfer or to the control condition. In both arms participants completed an audio computer-assisted self-interview and HIV counselling and testing (HCT) at baseline and at up to three follow-up visits during the 068 trial and an additional posttrial visit; follow-up visits occurred approximately annually. Parents or guardians completed a computer-assisted personal interview to gather household-level data at baseline and each follow-up visit during the 068 trial period. A detailed description of the 068 trial and cohort is published elsewhere [44,45].

Simultaneous to the HPTN 068 trial, a community mobilization programme and research initiative was underway at the Agincourt HDSS site, with implementation of a CM intervention in 11 of 22 randomly selected villages in the area [46]. The CM intervention, conducted in partnership with Sonke Gender Justice and carried out by a trained team of mobilizers and community volunteers, sought to address intersections around HIV risk and gender norms that contribute to gender-based violence and power inequities, encouraging community members to examine how to make changes in both their own lives and in their communities through workshops and varied community activities. The intervention was evaluated using cross-sectional surveys conducted prior to ($n = 1181$) and following ($n = 1403$) the two-year intervention (2012 to 2014). Survey participants included randomly sampled adults, ages 18 to 35 years, with approximately 55 people in each community (or village) at both time points. The sampling frames for the surveys were the 2011 and the 2013 Agincourt HDSS annual census, respectively. Eligibility criteria for participation included: consent to participate in the survey, residence in the home, being 18 to 35 years of age, and having lived in the study village for the majority of the past 12 months. A detailed description of the survey sampling and procedures is previously published [46], as are trial results [47,48]. This manuscript utilizes the CM domain measures to understand aspects of the social environment that shape HIV risk among AGYW.

Institutional Review Board approval for HPTN 068, for the community surveys, and for merging the data sources for these analyses was obtained from the University of North Carolina at Chapel Hill (UNC) and the University of the Witwatersrand Human Research Ethics Committee. The University of California-San Francisco also approved the community

surveys and protocols for merging data. The data sources merged for this analysis is displayed in Figure 1.

2.2 | Measures

We collected quantitative measures of CM domains in both the 2012 and 2014 community surveys. The community mobilization measure (CMM) is composed of seven domains (Figure 2). Questions regarding a shared concern about HIV/AIDS are designed to capture whether members of the community (1) define HIV as an important, problematic and mutable issue; (2) discuss and are aware of the impacts of HIV in their village; and (3) believe they can work together to improve outcomes. The shared concern scale is the only topic-specific scale, the other subscales refer to general community qualities, not specific to HIV. The scale for critical consciousness is designed to capture whether members of the community are undergoing processes of critical reflection and dialogue about their circumstances and ways to address injustices. Questions about leadership capture leadership capacity, diversity, responsiveness, accessibility and support of collective decision-making. Questions regarding organizations and networks are designed to capture the existence and influence of community-based organizations, groups and networks that can serve as a resource in mobilizing – both for exchange and diffusion of ideas and as a structure that can be utilized for community organizing. Questions regarding collective action are designed to capture the presence, breadth and quantity of collective activities in the villages aimed at social change. Questions about social cohesion and social control capture the level of working trust and mutual expectation to intervene for the common good, as originally theorized by Sampson and colleagues [41,42]. Based on formative work, responses included 3-point Likert scales, with responses including “agree a lot, somewhat agree, do not agree at all” for all domains except social control, which included responses of “very likely, somewhat likely, unlikely,” and organizations and networks which assessed whether organizations existed and if they were “very important, a little important, or not important” in the community. We aggregated individual responses on the surveys into mean community mobilization scores and domain scores for each village, with higher scores indicating increasing amounts

of each domain (e.g. more mobilization). The measures, their performance (reliability coefficients [49]) on the 2012 survey and example items are described in Figure 2 and reported on extensively in a previous publication [40].

HIV status in the AGYW 068 cohort was determined by conducting parallel HIV rapid tests in the field using the Determine HIV-1/2 test (Alere Medical Co, Matsudo-shi, Chiba, Japan) and Uni-gold Recombigen HIV test (Trinity Biotech, Bray, County Wicklow, Ireland). If both HIV rapid tests were non-reactive, no further testing was done at that study visit. If one or both tests were reactive or positive, confirmatory HIV testing was conducted using a western blot assay. Quality control of HIV diagnosis was performed at the HPTN Laboratory Center to confirm baseline HIV status and incident HIV infections.

Covariates of interest at the individual level included age at study entry and 068 study arm as well as a number of time varying covariates including study visit, current educational status (in school or graduated vs. not attending or dropped out), and family household assets (operationalized as the total number of durable goods from a list of 27 items each household owned). At the community level, covariates came from the census data. We explored mean years of education in the community, the proportion of the community composed of permanent residents, and the mean socio-economic status (SES) derived from a list of household assets, access to water, housing material and owned livestock, with higher scores indicating more assets. We noted instability in regression coefficient results when using the original community characteristics variables due to multicollinearity. We therefore used the -pca- command in STATA with a varimax rotation (orthogonal transformation) to repartition the total variance of the three correlated variables into linearly uncorrelated principal components, which were included as control variables in the analyses described below. While component scores are less interpretable than original variables, this approach allows us to remove potential confounding of community SES, education, and residency. Communities with higher scores on the combined measure were more highly educated, wealthier and had fewer permanent residents (were more mobile). We also included village intervention randomization assignment from the community mobilization study (2012 to 2014) as a covariate

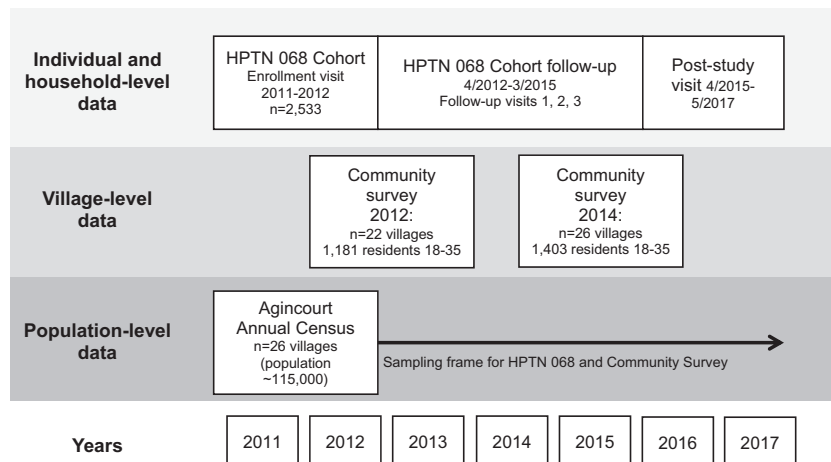


Figure 1. Study schematic of three contributing data sources and data collection timelines in Agincourt, South Africa.

	Shared concern: HIV	Critical consciousness	Leadership	Organization & Networks	Collective activities	Social Cohesion	Social Control
Quantity & format	10 items Likert	11 items Likert	14 items Likert	10 items binary + Likert	6 items (quantified and categorized)	6 items Likert	8 items Likert
Example Item	People in your village are concerned about HIV.	People in this village not only talk about problems but also try to solve them.	Leaders in your village encourage participation in decision making.	Are there groups with which you can volunteer to help your community?	How many times has your community worked together to fix a problem in your village?	People in this village are willing to help their neighbors.	Your neighbors would intervene if the neighborhood water tank was broken?
Scale Performance*	ρ : 0.85 CI: 0.84, 0.86	ρ : 0.93 CI: 0.92, 0.94	ρ : 0.92 CI: 0.91, 0.93	ρ : 0.81 CI: 0.78, 0.84	ρ : 0.84 CI: 0.81, 0.86	ρ : 0.81 CI: 0.79, 0.83	ρ : 0.89 CI: 0.87, 0.90

* Reliability coefficients represented by Raykov's ρ , conceptually similar to Cronbach's coefficient alpha, but relaxes the assumption of equal factor loadings of scale items onto the scale's underlying latent factor.[49] CI: 95% Confidence Interval

Figure 2. Community mobilization domains and measures.

a priori, though prior analyses have indicated that scores did not differ between the intervention and control communities (i.e. the intervention did not impact CM scores) [47].

2.3 | Analysis

To assess how a community's level of mobilization is related to HIV incidence among AGYW, accounting for individual, household and community-level factors, we merged data from the O68 participant and household surveys, the two community surveys, and the census data. The merging process was conducted such that each HPTN visit was assigned the most recent village data, including CM scores. As a result, the data structure ensures community (exposure) data precedes HIV outcome data and preserves temporality. For this analysis, we have restricted our study population to young women who were HIV-negative at entry (78 with prevalent HIV infection at baseline were excluded), and to those who lived in villages included in the community surveys ($n = 159$ excluded due to no community data). Finally, we excluded four participants who became HIV infected prior to having community survey data, in order to ensure temporal ordering ($n = 4$).

We used pooled generalized estimating equation (GEE) regression with a Poisson distribution to estimate the risk ratios (RR) of incident HIV infection among AGYW, adjusting for relevant confounders and addressing village-level clustering via robust Huber–White cluster-adjusted standard errors. Community mobilization scores were standardized using the pooled standard deviation for the 2012 and 2014 surveys (to ensure comparability) and included in multivariate analyses such that the risk ratio represents the difference in HIV incidence associated with a one standard deviation increase in each community measure/score. Bivariate Poisson regression was used to determine the association between the independent variables and HIV incidence. Covariates were included in the adjusted analysis if they were significant at the 0.1 level in the bivariate analysis or were selected *a priori* based on the literature.

3 | RESULTS

In total, 2292 AGYW living across 26 communities were included in this analysis. At enrolment, participants had a

mean age of 15.5 years and 100% were in school, with just over 26% reporting being sexually active and 3% reporting engaging in transactional sex. (Table 1) By the end of the follow-up period, 88% were either graduated from high school (matric) or still in school (12% had dropped out/never graduated) and 58% reported ever having sex with 24% reporting engaging in transactional sex in the past 12 months. There were 194 incident infections over the follow-up period. Community demographics did not change substantively over time. Community mobilization domain scores varied slightly over time with differences that were not statistically significant. (Table 1).

Association of the overall village community mobilization score with incident HIV infection, adjusting for individual and community-level covariates is presented in Table 2. Community mobilization village score was protective against HIV incidence in both unadjusted (RR: 0.77; CI: 0.65, 0.91) and adjusted (RR: 0.88; CI: 0.79, 0.98) analyses, such that for every additional standard deviation in village-level CM there was a 12% lower HIV incidence after adjusting for age, study visit, education, household assets, O68 and CM randomization arms and community characteristics.

We also explored the association between individual CM domains and incident HIV infection, in order to determine whether particular domains might be driving the association with HIV incidence among AGYW in the cohort (Table 3). While all CM domains with the exception of social control demonstrated a protective association, only critical consciousness (RR: 0.88; CI: 0.79, 0.97) and leadership (RR: 0.87; CI: 0.79, 0.95) reached statistical significance. Social cohesion (RR: 0.91; CI: 0.81, 1.01), shared concerns (RR: 0.90; CI: 0.81, 1.00), and the organizations and networks domain (RR: 0.91; CI: 0.79, 1.03) demonstrated similar magnitude of protective effects but did not reach statistical significance.

4 | DISCUSSION

We set out to understand the role of community mobilization in incident HIV among adolescent girls and young women living in rural communities in northeastern South Africa. We found that community mobilization, which is in essence a collection of different facets of community social resources, is

Table 1. Baseline characteristics of HIV-negative adolescents girls and young women enrolled in HPTN 068 (n = 2292) and their communities (n = 26)

	Baseline (n = 2292) n (%)	By end of follow-up (n = 2225) n (%)
Participant characteristics		
Mean age at entry into 068 (SD)	15.5 (1.6)	–
In school or graduated	2229 (100)	1961 (88.1)
Any sexual intercourse	613 (26.8)	1299 (58.4)
Have a sexual partner ≥5 years older in past 12 months ^a	119 (5.2)	330 (14.8)
Engage in transactional sex in past 12 months ^a	72 (3.1)	548 (24.6)
Condomless sex in last three months ^a	189 (8.3)	699 (31.4)
HIV status		
HIV negative	2292 (100)	2031 (91.3)
HIV positive	0	194 (8.7)
Drink alcohol once a month or more	117 (5.10)	432 (19.4)
Mean number of household assets, (SD) (asked about 27 durable goods)	14.03 (0.06)	15.56 (0.07)
Community characteristics^b		
	Unweighted mean (SD) 2012	Unweighted mean (SD) 2014
Mean years of education	6.08 (0.61)	6.79 (0.49)
% permanent residents	62.36 (4.23)	59.81 (3.81)
Mean SES asset score	0.09 (0.54)	0.09 (0.52)
Community mobilization^c		
	Weighted mean (SD) 2012	Weighted mean (SD) 2014
Total community mobilization score	2.22 (0.12)	2.15 (0.11)
Social cohesion	2.34 (0.15)	2.48 (0.16)
Social control	1.96 (0.17)	1.31 (0.13)
Critical consciousness	2.46 (0.15)	2.49 (0.17)
Shared concerns (around HIV)	2.13 (0.10)	2.23 (0.18)
Leadership	2.10 (0.19)	2.19 (0.22)
Organizations and networks	0.98 (0.19)	0.84 (0.17)
Collective action	1.60 (0.28)	1.16 (0.08)

^aAmong sexually active participants.

^bData from Agincourt Health and socio-Demographic Surveillance System census.

^cData from community surveys.

associated with lower HIV incidence among AGYW longitudinally. To our knowledge, this is one of the first quantitative explorations of whether community-level (in this case village-level) social characteristics are protective against HIV in AGYW. We also noted which components of community mobilization contribute to the protective association, finding strong evidence for critical consciousness and leadership and suggestive evidence that social cohesion, shared concerns around HIV, and organizations and networks may also be protective against HIV infection. Overall findings indicate that AGYW experience reduced HIV infection in villages where residents feel connected, dialogue and address their circumstances, consider HIV an important community issue and have leadership that is present and accountable.

While community mobilization has been neither previously associated with reduced HIV incidence among adolescents nor empirically measured at a community level in a sub-Saharan African context, studies in the United States have demonstrated health benefits of social capital, which is a

related construct. Social capital characterizes the social resources and organization inherent in a group, including trust, norms and networks that facilitates coordination and benefits group members [29,50]. Social capital is most often operationalized as participation or civic engagement in community organizations and at times measured by community bondedness – making it similar to the cohesion and organizations and networks measures, included in our CMM. Research on social capital has demonstrated protective associations with sexually transmitted infections among youth in ecological (state and community-level) studies [18,51]. Further, research conducted in the United States has noted protective associations of perceived social cohesion (most often measured as trust and closeness in a community) or social control (most often measured as expectations of reciprocity) with prevalence of sexually transmitted infections among youth [17,19,51] and early sexual debut [20,21,52]. There has been less exploration of these constructs in sub-Saharan Africa, with little previous research on community social

Table 2. Unadjusted and adjusted risk ratios (RR) of HIV among adolescent girls and young women enrolled in HPTN 068 (N = 2292)

Characteristics	Unadjusted RR (95% CI)	Adjusted ^a aRR (95% CI)
Individual level		
Age at baseline	1.24 (1.15, 1.33)***	1.19 (1.13, 1.26)***
Study visit (first follow-up visit is reference)		
Second follow-up	1.27 (0.74, 2.19)	1.32 (0.76, 2.27)
Third follow-up	1.67 (0.95, 2.95)	1.59 (0.95, 2.65)
Post-intervention visit	4.85 (3.24, 7.25)***	3.38 (2.18, 5.24)***
Currently enrolled in school or graduated high school	0.17 (0.11, 0.28)***	0.50 (0.33, 0.77)**
Mean number of household assets	1.02 (0.99, 1.04)	1.00 (0.98, 1.03)
HPTN 068 intervention arm – cash transfer versus control	1.04 (0.77, 1.41)	1.09 (0.76, 1.55)
Community level		
Community mobilization	0.77 (0.65, 0.91)**	0.88 (0.79, 0.98)*
Community characteristics ^b	1.24 (1.15, 1.34)***	1.10 (1.02, 1.19)*
Community mobilization arm intervention village versus control	0.98 (0.74, 1.30)	0.91 (0.73, 1.14)

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

^aModel adjusted for all other covariates in the table.

^bCommunity characteristics is a collated measure of three community-level variables (mean years of education, mean socio-economic status asset score, and proportion of the community who are permanent residents).

Table 3. Adjusted risk ratios (RR) of HIV incidence among adolescent girls and young women as a function of village mean community mobilization domain scores

CM domain	Adjusted ^a aRR (95% CI)
Social cohesion	0.91 (0.81, 1.01)
Social control	1.05 (0.96, 1.15)
Critical consciousness	0.88 (0.79, 0.97)*
Shared concerns (around HIV)	0.90 (0.81, 1.00)
Leadership	0.87 (0.79, 0.95)**
Organizations and networks	0.91 (0.79, 1.03)
Collective action	0.96 (0.82, 1.13)

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

^aAdjusting for age at baseline, time, education, household assets, 068 intervention arm, community mobilization intervention arm, and community characteristics.

resources measured at the community level and its impact on adolescent health. Studies of social capital and social cohesion at the individual-level among adult women in Africa have yielded mixed results – some protective for HIV [26,53] and some not [25].

To our knowledge, this is the first study to consider which aspects of community social resources are protective against HIV infections in young people, which is needed to guide future intervention work. We found strong evidence that critical consciousness and leadership are protective and additional suggestive evidence (not reaching statistical significance) that social cohesion, shared concerns around HIV, and organizations and networks may also be protective. These findings are consistent with the literature on establishing critical consciousness as a means to improve health and well-being [54-56], and the extensive literature (cited above) on how

cohesive communities and social trust can play a large role in fortifying community health. Furthermore, the HIV Competent Community initiatives [57] have provided insights into the role of critical consciousness as a means for communities to identify and resolve problems, with building of shared understandings and identities and collaborative partnerships playing a complementary role [54,58,59]. Notably, we did not find an association with collective action, though between-village variability in the later survey was likely insufficient to detect an association.

We also found a strong protective association between higher village leadership scores and reduced HIV incidence. Investigations of what is needed for successful health promotion have proposed that skilled, accountable, flexible and inclusive leadership and leadership networks (including coalition building) are essential in fostering structural change and strong health programming in the United States [60-62] and abroad [63], with poor or authoritarian leaders negatively impacting HIV community capacity [64]. This study is, however, among the first to associate a quantitative measure of community-rated quality of leadership (including items on community leaders' capacity, diversity, responsiveness, accountability, accessibility, and support of collective decision-making) with reduced HIV infections.

Finally, our results imply that having more local availability and higher levels of community engagement with organizations and networks (e.g. women's groups, cultural groups, school or youth groups, sports organizations and other groups seeking to support the community), might play a protective role. There are multiple pathways that a community with more engaged residents could be protective for youth, including building more opportunities for youth to get involved and participate themselves in community groups as well as instilling norms of engagement. Indeed, adolescent involvement in sports, clubs, and other organizations (either in school or

extracurricular groups) can provide young people with a sense of meaning or belonging [37] and has been associated with better health outcomes, including improved sexual health [30,33,35,36]. Youth engagement in activities would also bring increased social contact with other youth, and therefore could also imply more protective sexual networks with less time to venture outside of those safer networks (for example with older partners who are more likely to be infected) [65]. It is also possible that this domain is synergistic with leadership, in that communities with more accountable and inclusive leadership may also have more opportunities for organizations and networks to thrive, both of which contribute to (and are fortified by) having a more engaged citizenry.

While this study is among the first explorations of how community social factors may influence HIV infection among AGYW, we cannot comment on how these same community characteristics shape HIV incidence among adolescent boys and young men, who may benefit differently from community social resources. We have assessed each of the community mobilization domains separately and in a combined measure, but cannot yet comment on the interplay of these components in terms of temporal relationships between domains or complementarity and synergy in impacting AGYW outcomes, though this will be the topic of future study. Finally, though the CM measures in this study have undergone extensive validation, any measure of complex latent constructs will be imperfect.

Increased understanding of what it is about living in a more mobilized community that is protective will help lay the foundation for programming to address and enhance protective community social characteristics and provide an environment that enables risk reduction and optimizes HIV prevention for the broadest population [66,67]. Unfortunately, a great deal of HIV-related programming remains focused on individual behaviour change and does not aim for structural change or engage in community mobilization, which may often lie beyond the comfort zone of health and research funding mechanisms and beyond their programme time horizons. There is a burgeoning movement for community engagement in large research initiatives, often conducted in service to biomedical trials to inform and involve communities through public education, outreach, and community advisory boards, but can also include broader participatory goals [68,69]. These efforts, based on Good Participatory Practice [70], also need to be distinguished from what we refer to as community mobilization. While the evolving field of community engagement can lead to improved community involvement in research and potentially to improved utilization of outcomes, which is laudable and important, this focus is unlikely to bring about sustained improvements in HIV outcomes without a purposeful emphasis on broad community capacity building. Community mobilization, in our view, is not about recruitment or motivating people to participate in research, but has at its core the building of community social resources to address inequities, disparities, and injustices and for communities to build their own responses to health, in this case HIV. Its purpose is not to facilitate research or to empower a few, but to build a collective community response [71]. Nonetheless, understanding the community social resources, and to what extent communities may be mobilized, can serve as an

important tool to inform good participatory practice, both as an indicator for heightened vigilance or more considerable resource provision in less mobilized communities and as a marker to expect intensified community involvement in highly mobilized communities. Though extensive CM programming may be beyond the purview of most biomedical trials, ways to factor in community building and fortification of social resources should be sought whenever such programming is feasible in order to ensure the broadest impact possible.

5 | CONCLUSIONS

In the context of the persistent HIV epidemic among AGYW, insufficient attention has been paid to the community context and how communities might be strengthened to support prevention for young people. Our findings are among the first in sub-Saharan Africa to draw a direct link from community social context in the form of mobilization domains to AGYW's HIV acquisition. Work to mobilize communities, focusing on fostering social cohesion, promoting shared concerns around critical health issues, generating dialogue and capacity building for critical consciousness, and encouraging engaged and accountable leadership, including availability and partnerships with networks and organizations, can fortify prevention programming for AGYW. Seeking to strengthen these community traits should not be an afterthought, but a conscious piece of HIV prevention and care programming for young people.

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COMPETING INTERESTS

We declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

SAL, AP, TBN, JA and KK conceived this study. AP, KK, CM, SMT, FXGO, RT, RGW and AS were responsible for HPTN 068 design and implementation; SAL, AP, CM, DP, SMT, RGW, RT, AS, FXGO and KK were responsible for community mobilization study design and implementation; AML and DEG were responsible for data merging and management. AML led the analysis with assistance from TBN, SAL, JA and DEG. SAL and AML wrote the paper. All authors read and approved the final manuscript.

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