‘IT LOOKS LIKE YOU JUST WANT THEM WHEN THINGS GET ROUGH’: CIVIL SOCIETY PERSPECTIVES ON NEGATIVE TRIAL RESULTS AND STAKEHOLDER ENGAGEMENT IN HIV PREVENTION TRIALS

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ABSTRACT
Civil society organizations (CSOs) have significantly impacted on the politics of health research and the field of bioethics. In the global HIV epidemic, CSOs have served a pivotal stakeholder role. The dire need for development of new prevention technologies has raised critical challenges for the ethical engagement of community stakeholders in HIV research. This study explored the perspectives of CSO representatives involved in HIV prevention trials (HPTs) on the impact of premature trial closures on stakeholder engagement. Fourteen respondents from South African and international CSOs representing activist and advocacy groups, community mobilisation initiatives, and human and legal rights groups were purposively sampled based on involvement in HPTs. Interviews were conducted from February-May 2010. Descriptive analysis was undertaken across interviews and key themes were developed inductively. CSO representatives largely described positive outcomes of recent microbicide and HIV vaccine trial terminations, particularly in South Africa, which they attributed to improvements in stakeholder engagement. Ongoing challenges to community engagement included the need for principled justifications for selective stakeholder engagement at strategic time-points, as well as the need for legitimate alternatives to CABs as mechanisms for engagement. Key issues for CSOs in relation to research were also raised.

INTRODUCTION
Despite increased access to HIV treatment globally, new infections continue unabated, with particularly devastating consequences in sub-Saharan Africa, the global epicentre of the epidemic. It has become increasingly evident that ‘we cannot treat our way out of this pandemic.’ Successful treatment programmes will only be possible alongside successful prevention. Nevertheless, access to HIV prevention modalities for much of the world’s population is substantially inadequate, and there is a growing need for increased HIV prevention options.

While clinical trials of new HIV prevention technologies have received a fair amount of research attention, the field has also suffered numerous setbacks. In 2007, two randomised controlled trials (RCTs) in South Africa of biomedical HIV prevention methods, a candidate HIV vaccine (Phambili trial, also tested in its sister trial the STEP Study), and a microbicide candidate (Cellulose

2 Merson et al., op. cit. note 1, p. 485.
3 Merson et al.; Piot et al., op. cit. note 1.
4 Ibid.
Sulphate [CS]⁶ were both stopped prematurely because of trends towards increased HIV infections in the product arm. The unexpected negative results of the Phambili/STEP trial forced a re-evaluation of the HIV vaccine field,⁷ and the closure of the CS trial generated negative media coverage and some controversy.⁸ Despite these obstacles, HIV prevention research remains a priority.⁹ Addressing concerns and securing necessary support for future HIV prevention research is likely to require multi-stakeholder collaboration. Civil society organisations (CSOs) arguably play a key role in facilitating this collaboration. However, they are often a neglected stakeholder in the research process. It is particularly important to understand the impact of negative trial results, and CSO perspectives, in Southern Africa as a primary locale for ongoing HIV prevention trials (HPTs).

In exploring the perspectives of civil society representatives (hereafter, CSOs) involved in HPTs in South Africa, we adopt the UNAIDS-AVAC (2011) ‘all-encompassing’ definition of stakeholders: ‘any individual or collection of individuals who have a stake in a biomedical HIV prevention trial’. Thus ‘stakeholders’ include, amongst others, trial participants, researchers, governments, communities and CSOs.¹⁰

Community participation in research

Community participation has become an ethical imperative in health research.¹¹ Understandings of research have shifted from only knowledge production to a broad, systemic process including preparatory and implementation activities.¹² Calls for community participation in research have emerged against a backdrop of increasing recognition of the right of individuals to participate in decision-making processes which affect them.¹³ Collaboration between stakeholders has become critical to the success of research efforts to improve health, and is especially important in HIV/AIDS.¹⁴

Communities are amongst the most important social groups to be included in HIV research; yet the way in which community participation is conceptualised depends on how ‘community’ is understood.¹⁵ The meaning of ‘community’ is variable¹⁶ and while definitions of ‘community’ in public health and research have focussed on geographical location,¹⁷ there is increasing agreement that the definition of ‘community’ is multifaceted and much broader than ‘locality’, incorporating social ties, shared interests, values and activities.¹⁸ Given this broad understanding of ‘community’, the array of individuals who legitimately could be considered community members is equally broad. As such, the number of individuals and groups who are relevant stakeholders, and who should be involved in the research in some way, has expanded.¹⁹ Furthermore, in many instances ‘stakeholders’ are often referred to as ‘the community’.²⁰ To capture this broader understanding of ‘community’, references to the ‘community’ in the UNAIDS-AVAC (2007) Good Participatory Practice guidelines, have been updated to ‘stakeholders’ in the 2011 version of these guidelines.²¹

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¹² Delisle et al., op. cit. note 11.


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Community participation is often conceptualised as a continuum of degrees of involvement in, and control over the research process and outcomes. A frequently cited metaphor is a ladder of community participation, ranging from passive non-participation, through tokenistic involvement, to partnership and community initiation and control of research processes. Many advocates of community participation in research consider community ownership of research the optimal level of community engagement. However, this is an ideal, which is rarely achieved. Researchers may recognise the value of incorporating local perspectives into research and of encouraging collaborative processes. However, in most cases researchers maintain control of setting the research agenda, managing the research process, and determining the interpretation and use of the findings.

Civil society participation in research

Civil society refers to ‘the general public’ and consists of networks of individuals engaging in social interactions in both formal and informal organisations and providing and using public services. CSOs emerge as formal co-ordinations of these social interactions. CSOs include non-profit organisations, like non-governmental organisations (NGOs) and community-based organisations (CBOs), ‘that aim to further the interests of the organisations (NGOs) and community-based organisations (CBOs), that aim to further the interests of the communities they serve’, acting as advocates or activists. CSOs provide the vehicle through which groups and individuals might pursue and articulate collective interests.

CSOs, acting in various capacities, have had a significant impact on the politics of all health research and the field of bioethics. CSO engagement in HIV/AIDS treatment research is argued to have influenced almost every aspect of research ethics, largely driving the ethical imperative for community involvement in research. During the 1980s, civil society activists demanded access to HIV treatment research for persons living with HIV as mechanisms for accessing otherwise unavailable treatment. Activists criticised researchers for failing to consider community concerns and for a lack of transparency and accountability in the research process. They demanded involvement in more of the ‘upstream’ research activities, of planning and priority-setting, rather than simply the ‘downstream’ activities of product distribution. Notably, despite scientists’ concerns, allowing activists to become a part of the research priority-setting and design process resulted in research which successfully addressed the needs of the community. Educated CSOs were able to contribute valuable insights to the research team, and the involvement of community representatives has become mandatory in most HIV/AIDS research.

Given that CSOs are often located in, trusted by, and knowledgeable about the communities they serve, they can play a beneficial role as an interface between researchers and the community, helping researchers to identify relevant communities for research, and providing valuable inputs on the social value of research to the community. They can contribute to priority setting, and can play important advocacy roles. They can (and have) put pressure on governments to make interventions available to the public. A key example is the Treatment Action Campaign, who pressured the South African government to provide HIV-positive pregnant women with nevirapine. CSOs may also serve as a distribution channel delivering effective interventions to communities, given their already established networks and outreach activities.

With growing recognition of the implications of the AIDS pandemic for international development, CSOs that previously focussed exclusively on treatment access, have intensified advocacy for greater financial and political support for the scale-up of existing HIV prevention
CSO involvement in HIV prevention trial closures

In 2004, CSOs played a significant role in the premature closure of two planned pre-exposure prophylaxis (PrEP) trials of Tenofovir (an antiretroviral medication) to prevent HIV infection, in Cambodia and Cameroon. Certain CSO representatives accused researchers of ethical violations including selection of vulnerable, under-served groups; inadequate risk-reduction counselling; inadequate access to antiretroviral treatment for sero-convertors; inadequate informed consent processes; questionable likelihood of the trial communities benefiting from the research; and tokenistic community consultation.41

CSO pressure on host governments,42 negative international media coverage and ensuing heated debates about the ethics of the trials, led to the suspension of the Cameroonian trial, which had commenced enrolment, and the Cambodian trial prior to its initiation.43

Since activist-researcher communications occurred indirectly via the media, inconsistent and vague messages were often disseminated.44 This, together with varying levels of understanding of the trials in question, and clinical trials in general, led to misinterpretations and misunderstandings between stakeholders which fuelled mistrust.45 The media reporting amplified misunderstandings, which led to more widespread controversy.46

The closure of both trials for non-scientific reasons, resulted in the loss of an opportunity to establish the efficacy of a promising new prevention modality.47 Aside from the waste of public health funds, the Tenofovir trial closures came at great cost to relationships between stakeholders.48 There was heightened scepticism regarding investment of time and resources into the development of new prevention modalities, and governments became reluctant to support future trials because of potential fallout should something not go according to plan.49 The role of CSOs in driving the premature closing of these trials highlights the value of engaging this important stakeholder group in research.

Ethical guidelines and CSO involvement

The influence of CSOs is noted to have contributed to the development of the UNAIDS-AVAC50 Good Participatory Practice (GPP) guidelines, which focus on meaningful stakeholder engagement. Following the closures of the Tenofovir PrEP trials, UNAIDS convened a global consultation on ‘Creating Effective Partnerships for HIV Prevention Trials’ to identify causes of the controversy and to determine constructive approaches to preventing similar future outcomes.

All major HIV prevention trial guidelines emphasise the meaningful participation of key stakeholders, including civil society groups such as NGOs.51 Some ethical guidelines have specified precise roles CSOs can play in the overall trial process; however, most provide little detail on the ethical goals that can be achieved through the engagement of CSOs specifically.52

Despite their significant influence in the PrEP trial closures, CSOs are often a missing voice in health research.53 This study aimed to investigate the perspectives of CSO representatives regarding the impact of premature trial closures on stakeholder engagement.

40 Merson et al., op. cit. note 1; Piot et al., op. cit. note 1.
41 Ibid.
44 McGrory et al., op. cit. note 43.
45 McGrory et al., op. cit. note 43.
46 McGrory et al., op. cit. note 43.
47 Forbes & Muldaliar, op. cit. note 43; McGrory et al., op. cit. note 43.
48 McGrory et al., op. cit. note 43.
49 McGrory et al., op. cit. note 43.
52 SAMRC, op. cit. note 60; UNAIDS-AVAC 2007, op. cit. note 59; HPTN, op. cit. note 60.
METHODS

Fourteen respondents from South African (n = 8) and international (n = 6) CSOs representing activist groups, community mobilisation initiatives, human and legal rights groups, and prevention advocacy groups, were purposively sampled based on their involvement in HPTs in South Africa. Potential respondents were recommended by the CSO directors or other participants. Potential respondents were approached via email and invited to participate in a semi-structured telephone interview exploring their involvement in HIV prevention trials, their knowledge of negative trials results, especially Phambili (e.g., can you tell us what you know about the Phambili/STEP trials? What was your response to the news that the trial had stopped?), and their perspectives on the impact of these on stakeholder engagement (e.g., What do you think has been the impact of suspending the Phambili/STEP trials? On various stakeholders? And the relationships between stakeholders? especially civil society engagement in HIV prevention research (e.g., how could civil society be better engaged in HIV prevention trials and HIV vaccine trials?). Potential respondents were sent information sheets and informed consent documents for interview participation and audio-recording of the interviews. Respondents were asked to read and sign the consent forms and return these to the researchers prior to their interviews.

Interviews were conducted between February and May 2010, well after the closure of the CS and Phambili/STEP studies, and after the positive Thai (RV144) vaccine trial results,54 but prior to the release of the positive PrEP (iPrEx and HPTN 052)55 and Tenofovir topical microbicide results (CAPRISA 004).56 Trials with negative results refer to those trials of HIV prevention methods which run successfully to completion, but in which the product is found to be ineffective (e.g. Carraguard topical microbicide57) as well those trials for which enrolment or further product administration was suspended because of concerns about futility or increased risk of harm to participants (e.g. Phambili).

A descriptive analysis58 of CSO perspectives on the impact of negative trial results on stakeholder engagement was undertaken. Key themes were developed inductively through a process of listening to interview recordings and summarising each interview. Emerging issues in relation to research questions were identified and sections of the interview that illustrated these issues were transcribed verbatim.59 These issues provided the basis for the themes, which were developed and refined in team discussions. Transcripts and summaries were coded according to these key themes, which were then grouped in analytically relevant ways. Interviews were conducted until theoretical saturation was achieved.

This study received ethical approval from the Human and Social Sciences Ethics Committee, University of KwaZulu-Natal (Approval number – HSS/0326/09) and the HIV Research Ethics Board, University of Toronto (Reference number – 24517).

RESULTS

The following section presents civil society respondents’ perspectives on the impacts of negative trial results on stakeholder relationships, their perspectives on good stakeholder engagement, and key issues for civil society groups. All CSO representatives interviewed had some experience of HIV prevention in South Africa.

Civil society representatives’ perspectives on the impact of suspended HIV prevention trials

Siloed nature of HIV research

Respondents observed that competition and ‘people operating in silos’ (N002) within HIV research created tensions in stakeholder relationships. Respondents reported some long-standing tension between HIV treatment and HIV prevention advocates, fuelled by competition for funding and resources. This in turn highlighted the necessity to ‘invest in building partnerships between treatment and prevention’ (N002).

Even within HIV prevention research, respondents observed ‘fractures within the field’ (N008) between different prevention modalities:

Someone in the vaccine field stood up at a meeting and said ‘we have a vaccine, it’s going to work. We can get rid of microbicides and you can stop funding these things ‘cause we’re going to show you how to do it’. That was dumb (N009).


Some respondents conceded that there was some effort to create ‘synergies across fields’ (N002) and that ironically, scarce resources and limited funding had forced people to come together to reduce duplication of efforts, especially regarding community engagement.

Others noted that even when the opportunity for sharing exists, ‘it still seems difficult for groups to learn from each other’ (N010).

Despite observations of splits within HIV research, respondents reported that HIV prevention trials generally have resulted in an expanded definition of who makes up the community, from one where the term ‘community’ was traditionally reserved only for host communities, to one where the community is perceived as including other stakeholders, like governments, regional players and CSOs, thereby drawing stakeholders together.

Impact of negative trial results on stakeholders and stakeholder relationships

Premature trial closures, whether due to concerns about increased harm (e.g. Phambili/STEP, CS) or other ethical concerns (e.g. PrEP trials) were argued to highlight the value of good stakeholder engagement: ‘a lack of community engagement can threaten trials as much as the scientific issues’ (N013). Transparent, inclusive stakeholder involvement from the outset was noted to potentially mitigate the mistrust and negative sentiments that negative trials results can ignite:

...so, when things get difficult and you need friends; or you have a hard time like when a trial closes early; you already have people who have a relationship with you, who are aware of your intentions; can be the voice in the community and with the media and with other stakeholders to help get the message out and do some damage control (N013).

Despite the finding of increased risk of HIV infection among a subset of Phambili vaccinees, most respondents believed that owing to ongoing engagement of the media and communities, and successful results dissemination to all involved stakeholders, there was ‘no crisis or controversy around these trials’ (N014). These trial results were argued to have actually ‘brought the field together’ (N004) and strengthened the relationships between stakeholders. It was argued that negative trial results have forced stakeholders to collaborate, and have made overcoming initial feelings of mistrust between stakeholder groups imperative:

A number of trials that have ended early or have had results that have been confusing have forced a different relationship between the groups where they both need each other to move this forward (N010).

A few respondents identified areas for improvement in these trials, such as better engagement of CBOs and local media.

CSO–researcher relationship. In terms of their relationship with researchers, ‘advocates feel that . . . there is a huge divide between the scientists and the advocates’ (N011). However it was also reported that there were substantial improvements in the relationship between researchers and advocates from one typically characterised as ‘adversarial’ to one where there is a more valued role for advocates: ‘there has been a gradual but definite improvement in how research groups and advocacy groups work together’ (N010). The early trial closures were noted to have created opportunities for increased collaboration between researchers and advocates which allowed ‘advocates to have more of a voice in the research process’ (N004). Engaging with advocacy groups has been especially valuable to researchers as demonstrated in the Phambili/STEP trials where advocates played an important role in ‘talking to community members and helping community members understand what had happened’ (N004), thereby fostering better community responses to the trial closure.

Media engagement. Respondents argued that the media are integral to successful trial closures. In general, the relationship between media and researchers was reported to be difficult, with the media being implicated in perpetuating misunderstandings and rumours in the early closures of the PrEP and CS trials, as well as in the negative reporting of the MDP 301 microbicide trial results in Zambia: ‘I think, things going wrong for some of those trials... it always kind of ratchets it up, whenever there are those conversations in the media’ (N004). Some argued that this implied that the media had not been well engaged, ‘often negative perceptions about trials emerge because of how these are reported in the media, and indicate a failure on the part of the researchers to properly engage all relevant stakeholders’ (N004). There was some concern that media are only involved when trials are stopped rather than on an ongoing basis, and thus have a negative perception of research. Others contended that some media representatives prefer to write sensationalistic stories and do not want to be engaged: ‘[the media] catch on any news they can get hold of and run with it’ (N007) and ‘a few renegade media journalists... wrote articles that were inflammatory’ (N010).

Some respondents praised media engagement in the Phambili/STEP trials, as reflected in the fairer reporting of these results. Important ‘lessons were learnt after CS on how to communicate effectively with the media’ (N002) and experience gained in ‘handling the potential fall-out’
(N006) from media queries regarding trial closures. Respondents described an improvement in how groups work together around trial closures to create coordinated and consistent messages to the media. A specific example of an initiative for helping to facilitate this dialogue and dissemination of accurate information has been the establishment of the Microbicide and Media Communication Initiative.60

Equivocal impacts on stakeholder relationships. Some respondents described the effects of these trials on researcher-community and researcher-government relationships more ambivalently. It was reported that negative trial results could potentially fuel perceptions that communities were being exploited by researchers:

You have people who have the perceptions that these trials are not meeting ethical standards; that people are being harmed; people’s rights are not being adequately respected; the notion that these trials are happening in Africa and Africans are being used as guinea pigs (N009).

Relationships with government representatives were often-times described as difficult. It was noted that historically in South Africa, some government members held negative views towards certain prevention trials, regardless of their scientific rigor (e.g. the CS results) and these uninformed responses challenged stakeholder relationships. Some contended that the series of trial failures in HIV prevention put policy-makers in a very difficult position to keep supporting research as important, especially when products keep failing’ (N010).

Civil society representatives’ perspectives on good stakeholder engagement

Meaningful engagement

Respondents identified various features of good stakeholder engagement in research, and distinguished this from ‘tokenistic’ efforts ‘to tick the box of community involvement’ (N009), which were generally criticised:

There’s a political dimension to it and they all realise that’s what everyone says, so they might as well do it because they’ll be in trouble if they don’t. . . . a kind of a ‘let me include the community in my research because it’s politically correct’ (N009).

It was noted that good stakeholder engagement required outreach to those parties who may have an interest in HIV prevention research in order to determine the relevant stakeholders. Researchers, identified as holding the financial resources (and social power), were noted to be responsible for this outreach.

Meaningful stakeholder engagement should commence prior to study initiation, and ‘an ideal model of community engagement would involve communities during protocol formulation stages to determine the community’s perceptions of the social value of the research’ (N011). Furthermore,

. . . Communities need to be engaged more over the life of a trial: They should not only be engaged during community meetings when trials are recruiting and then again when results are going to be announced: this does not constitute meaningful community involvement (N011).

Ongoing dialogue and honest, transparent communication were noted to be critical to fostering good stakeholder relationships. ‘Communicate – let people know how things are going; and, if there is a problem, be honest’ (N009). Establishing mechanisms via which research-related information is communicated to the broader community were identified as critical:

A mistake is if you keep your cards close to your chest and don’t really talk to people and don’t engage the community and don’t engage local stakeholders, and then something goes wrong and then you go knocking on people’s doors it’s a very different situation. It looks like you just want them when things get rough – so engage them throughout the whole process. . . . talk to them and don’t delay community engagement and stakeholder engagement and communication (N013).

Engagement and communication with various stakeholders should not be reserved for times of crises.

Meaningful engagement was also described as taking serious account of the opinions of the various stakeholders and allowing them to play a role in research-related decision-making. Making decisions ‘without consultation with the trial community in which you’re working means trials probably aren’t going to work’ (N013). This enables stakeholders to accept decisions taken as part of research, even if not favourable to them. It was also argued that community involvement should be viewed as far more than simply a means of obtaining passive community endorsement of a study.

While it was claimed that communities and stakeholders should have a say in decision-making, there was acknowledgement that there are certain decisions which require specific experience or technical expertise, and thus in which community-stakeholder involvement is inappropriate, for example: ‘People should have a say in decision making but you will have a futile trial that closes early if you turn over key decision-making to people who do not

understand how science works and why trials are designed in particular ways’ (N014) and ‘to expect somebody after six months on a community advisory board to be equipped to make key decisions about how these things are going to get designed and implemented is naive’ (N014).

I think they must be consulted and they must be asked; but I’m a little bit sceptical of this, ‘let’s just involve communities for the sake of it’. They don’t have the skills; they’ve got other things to do, they’re busy; and I really do think there are other priorities for them other than to spend hours in consultation with prevention researchers (N009).

Respectful engagement also means recognising that research may not be a priority issue for some stakeholders, and their other commitments should be respected.

It was also acknowledged that there are realistic limitations to engaging multiple stakeholders, as this could create a challenge for reaching consensus on key issues:

If you have people at the table not because they are going to contribute in work but because they just want to be there, then you are going to expand the amount of work that needs to get done and the complexity of it but not necessarily improve the outcome. And that’s what we’re struggling with . . . Every time you add another group or another person to the mix for a particular meeting, it’s not additive because you also include pre-existing relationships (N014).

Beyond the CAB model

Respondents noted that CABs are good structures for community engagement and work as intermediaries between researchers and communities, helping to facilitate education and information dissemination. However, there were a number of critical concerns about CABs as the sole means of community engagement. ‘One evolution of community engagement is that people don’t feel that that is enough; just having a group in place does not necessarily mean that you are doing appropriate community engagement’ (N013). These concerns included: insufficient monitoring of whether CABs engage with the community they claim to represent: ‘in terms of the research site hand-picking’ – ‘where the community doesn’t necessarily feel a strong connection to the people sitting on the CAB’ (N013).

There are a lot of difficulties with CABs in and of themselves – are they hand-selected? Are they elected? Are they selected by the research institution? Do they have autonomy from the research endeavour? Are there conflicts of interest, or perceived conflicts of interest? Are they trained to review protocols and capacitated to ask critical questions that they are supposed to be there to ask? Or are they just ‘rubber-stamping’ things? (N013)

Other concerns included research literacy enabling critical evaluation of study protocols, and how to strike the balance between site support of CABs and their independence:

I’ve seen many CABs, not all CABs being empowered enough to engage actively in the research. I also think the CAB’s being constituted by the research community and being sustained by the research community introduces some bias to what they do (N002).

As a feature of meaningful community engagement, CABs should be more than ‘tokenistic endorsement’ (N010). One suggestion for CAB strengthening was to involve CSOs in CAB training or CAB representation:

I would rather see CABs where there’s an external independent organisation that builds their respective capacity and so, they can indeed be independent in their assessments and information and perspective about the trials (N002).

Key issues for CSOs

Civil society representatives reported that CSOs, especially locally-based groups, risk neglect in the research process: ‘you still don’t see too much engagement between local PIs and CSOs’ (N002). However, it was argued CSOs have a key contribution to make. Respondents also acknowledged that CSOs themselves also need to better integrate HIV prevention research into their agendas, and need broad research literacy to enable them to converse with researchers, as well as educate participating communities:

research literacy is absolutely important and the job is on civil society groups to do it; because when it’s done by the researchers, it looks like social marketing and all you want to do is make sure people accept your research, rather than coming from a neutral perspective (N010).

Specific roles for CSOs

As ‘the voice and representative of the community’ (N001), CSOs have a key role to play in ensuring that local needs and priorities are reflected in the research agenda. It was argued that CSOs should be involved in shaping research priorities to focus on specific areas of identified need, advocating for accelerated exploration of new prevention modalities and making ‘sure all the players are talking about the most important things’ (N005). It was noted that:

advocacy organisations could be more of a driving force in the research agenda instead of following – the power in the setting of the science agenda resides
elsewhere. Advocates are seen as the necessary noise that should come after the agenda has been drawn, instead of being the ones drawing some of the agenda because they are so much in touch with communities (N012).

Respondents also noted that there is a need for an HIV prevention advocacy movement in South Africa and that CSOs could play a valuable role here.

CSOs were noted to be engaged in advocacy for scientifically valid trials: ‘I see my role, certainly as an advocate, to advocate that the only way to do this is through good science’ (N009) and, ‘that prevention should be based on the best evidence available’ (N009). It was also argued that advocacy should adopt a more critical role by ‘taking the field to task about what they committed to and where they’ve gone’ (N010), being critical of researchers, of prevention research, pointing out the flaws in the field, and holding government and policy makers accountable.

As advocates for the populations they serve, CSO involvement in research is ‘important for ensuring that people who are vulnerable do not get exploited’ (N014). A central role of CSOs in research was argued to be that of ‘watchdogs’, overseeing and monitoring the field and trial processes and ensuring scrupulousness in research conduct. CSOs could ensure that, in the conduct of research, human rights and ethical standards are upheld, that communities benefit from the research in which they participate, and that consent is voluntary and fully informed. Furthermore, CSOs were noted to be well placed to make inputs into ethical frameworks to ensure that these address the issues of conducting research with the communities they advocate for. CSOs were noted to be key in advocating for ethical standards – including standards of care and prevention in research, meaningful informed consent, and access to research benefits.

**DISCUSSION**

Certain early HIV prevention trial closures have challenged stakeholder relationships. Reactions from community stakeholders and trial participants in the aftermath of the STEP trial included questioning of the informed consent process, and criticism of delays in unblinding of participants. However, in this study exploring CSO perspectives it was observed that Phambili/STEP negative trial results were viewed as opportunities to strengthen stakeholder relationships. These mixed results suggest differences in perspective among and within various stakeholder groups. In general the present findings suggest that negative trial results and early trial closures have necessitated a more collaborative relationship between stakeholders in HIV prevention research and have highlighted stakeholder engagement as a cross-cutting issue. However, in reflecting on the field of community engagement in general, respondents identified some tensions, and divergent perspectives.

Most ethical guidelines require that stakeholder representatives, including CSOs, should be included in an early and sustained manner in the overall cycle of clinical trials. The 2007 Good Participatory Practice guidelines (now superseded by a later edition) made specific recommendations for how CSOs could be involved. In concordance with these guidelines, respondents thought that CSOs have a specific and particular role to play in HIV prevention research, but that investment in their capacity is required for them to fulfill these roles. The 2011 Good Participatory Practice guidelines include CSOs as a critical stakeholder, and outline a role for CSOs in ensuring access to care and prevention services for trial participants, and designing an access strategy for an effective product) but do not specifically delineate the ethical rationale for CSO involvement. In this study respondents identified several ethical rationales for CSO involvement in HIV prevention trials, including enhancing the social value of research by ensuring priority problems are addressed, and in ensuring that successful interventions are implemented. It was also suggested that CSOs could strengthen review and oversight standards by holding researchers accountable for the ethical and scientifically valid conduct of research.

Despite earlier calls for CSOs to be involved in more of the ‘upstream’ research activities like driving the research agenda or shaping research priorities, some civil society representatives reported that CSOs, particularly at the local level, are more likely to be engaged when there is a need to recruit participants, or disseminate findings. While the strength of CSOs is in managing adverse outcomes of trials, as demonstrated in their involvement in...
the Phambili/STEP trial closure, they cannot be expected to fulfil this role unless they are engaged in an ongoing way.

In reflecting on how to optimise engagement with participating communities, respondents argued that relevant stakeholders must be involved in making meaningful decisions about trial aspects for which they have expertise. Without a principled justification for involving stakeholders, engagement may be perceived as tokenistic or politically correct, or that communities are being treated as mere means to an end. It might also be perceived that engagement efforts are only for the benefit of researchers who want cooperation of the community and in order that the research process is seen as legitimate. The need for a legitimate community representative body beyond a CAB was noted. CABs could be perceived as potentially biased to the research organisation because they are supported and educated by trial sites. One refinement was noted to be including CSO representatives on advisory bodies in order to make community representative structures more independent. Similar recommendations for supplementing CABs are made in the new Good Participatory Practice guidelines, and which illustrate the particular ethical ends. Going too broad can create complexities and may actually impede good stakeholder engagement. Without a principled justification for involving particular stakeholders at particular time-points to participate does little to clarify who exactly researchers should engage with, at what time-points, and to what extent. Going too broad can create complexities and may actually impede good stakeholder engagement. Further, it is not in line with the principle of respect for communities to require stakeholders to contribute to all levels of the research process when they may not have the capacity to do so, nor is it respectful to assume that HIV prevention research is a priority for all stakeholders.

This study highlighted critical features of good stakeholder engagement, and specifically pointed to the value of engaging CSOs throughout the trajectory of HPTs. However, data from this study suggests that involving all stakeholders at every level of the research process may be difficult to justify and may be pragmatically difficult. Requiring the ‘community’ to be redefined as all research stakeholders does little to clarify who exactly researchers should engage with, at what time-points, and to what extent. Going too broad can create complexities and may actually impede good stakeholder engagement. Further, it is not in line with the principle of respect for communities to require stakeholders to contribute to all levels of the research process when they may not have the capacity to do so, nor is it respectful to assume that HIV prevention research is a priority for all stakeholders.

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In this study, CSO representatives reflected that negative trial results underscore the actual and perceived value of early and sustained engagement with groups such as themselves. Their observations about negative trial results are a reminder that stakeholder engagement is best viewed and implemented as a steady investment, rather than crisis-driven.

CSO representatives reported that meaningful stakeholder engagement in HIV prevention research requires ongoing outreach, clear communication and involvement of relevant groups in research decision-making. Although agreeing that engagement must be expanded beyond host communities, they reported tensions around stakeholder engagement efforts becoming too broad and unfocussed. Broad calls to involve all relevant stakeholder groups at all important stages of clinical trials suggest more thinking is required to refine recommendations to engage particular stakeholders at particular time-points to particular ethical ends.

CSO representatives emphasised the particular contribution they can make to the trial process, including agenda development and ongoing oversight. The specific roles that CSOs (and other stakeholders) might play at each stage of the research process should be more clearly articulated in order to make the rationale for their involvement clearer and their participation more meaningful. This research suggests that stakeholders themselves can help to identify their distinctive contributions that are more or less impactful at specific times in the sequence of trials. Such work may optimise stakeholder engagement efforts to realise ethical value in what is an expensive and resource-intensive endeavor, yet most essential to the future of HIV prevention research.

71 Morgan, op. cit. note 13.
Conflicts of Interest
This study was funded in part by grants from the Social Sciences and Humanities Research Council International Opportunities Fund, the Canadian Institutes of Health Research/Canadian HIV Vaccine Initiative, and the Canada Research Chairs program. The funders had no role in the research. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

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