

# Ethical challenges in developing an educational video to empower potential participants during consent processes in HIV cure research in South Africa

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## Abstract

Obtaining consent for HIV research is complex, particularly in low- and middle-income countries. Low levels of education, complexity of science and research processes, confusion about basic elements of research, and socio-economic conditions that make access to medical care difficult have collectively led to concerns about the adequacy of the consent process. Given the exponential growth of HIV prevention and treatment research in South Africa, HIV researchers are increasingly facing challenges obtaining authentic informed consent from potential participants. It is anticipated that HIV cure research, despite being in its infancy in South Africa, will introduce a new discourse into a population that is often struggling to understand the differences between ‘cure’, ‘preventive and therapeutic vaccines’ and other elements of the research process. Coupled with this, South Africa has a complex history of ‘illegitimate’ or ‘false cures’ for HIV. It is therefore logical to anticipate that HIV cure research may face significant challenges during consent processes.

HIV prevention research in South Africa has demonstrated the importance of early community engagement in educating potential research participants and promoting community acceptance of research. Consequently, in an attempt to extrapolate from this experience of engaging with communities early regarding cure research, a 15-minute educational video entitled ‘*I have a dream: a world without HIV*’ was developed to educate and ultimately empower potential research participants to make informed choices during consent processes in future HIV cure clinical trials. To aid others in the development of educational interventions, this paper discusses the challenges faced in developing this educational video.

Keywords: HIV cure, informed consent, community engagement, ethics

## Background

Obtaining informed consent is essential for the ethical conduct of research. Yet problems persist in its implementation amid concerns that participant consent is not truly informed. Empirical research has raised concerns about the therapeutic misconception (the mistaken belief that a clinical trial will be of clinical benefit to participants with little or no risk), failure of participants to understand key concepts, as well as questions about whether consent is truly voluntary [1–4]. These issues are even more acute in low- and middle-income countries (LMIC), where low levels of formal education and language, and power disparities between researcher and participant, often additionally challenge the ability of potential participants to sufficiently understand and make an informed choice. Socio-economic conditions make accessing medical care problematic. Medical care is often provided as part of participation in a trial, and this can conflate the distinction between care and medical research, exacerbating the therapeutic misconception. Communicable and non-communicable diseases affecting LMICs are in need of research to improve health, but the complex social conditions make informed consent challenging. Such challenging social conditions have been prevalent in HIV research where low levels of literacy or education amongst research participants and power differentials between staff and participants have tested the consent process [5].

HIV cure research will bring added complexity to Africa where there is a history of false cures, such as holy water, prayer or herbal products, and the scientific and lay understanding of cure may differ. Large-scale vaccine trials have recently started in South

Africa, but there is evidence to suggest that a vaccine will be perceived as ‘cure medicine’ [6]. Current preventive vaccine trials may be conflated with future therapeutic vaccine trials and assessing understanding will be essential.

Preliminary interviews with stakeholders in the Western Cape province of South Africa revealed limited awareness and understanding of cure research. Rumours of false cures in the community were reported amid beliefs that HIV is an incurable or ‘end time illness’ [7]. The science of cure research will indeed be complex and low levels of literacy amongst the likely target population, coupled with the diversity of languages spoken in South Africa, will make informed consent challenging. Research towards an HIV cure in South Africa may also face high levels of distrust of scientific research [8], fuelled in part by the history of exploitation and the cultural significance of blood in some communities [9]. It is therefore important that the cure research narrative is set early. This will help resolve any misconceptions and prepare potential research participants for the forthcoming research and empower them to make informed decisions.

As a result of lessons learned from HIV research, there has been recognition of the importance of *community engagement*, the manner of *communication* of information in research and its *understanding*. Prevention research demonstrated the importance of early and sustained community engagement in ensuring scientific rigour, good ethical conduct in research, as well as community acceptance [10]. The development of special media such as video, flip charts, booklets and role plays have been recommended to help inform study participants [11]. The use of a video in informed consent has had some success in increasing knowledge and participation [12], and visual aids have been used as part of the consent process in HIV research [13]. As part of the Carraguard study that had three sites in South Africa, participants watched a 25-minute video in their local language

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and received an illustrated booklet outlining study procedures [8]. Although the Carraguard video was not tested to assess its impact on understanding, other studies in South Africa have demonstrated the usefulness of videos in HIV treatment: a 17-minute video has been shown to improve understanding of treatment and adherence and there are indications that the development of a culturally sensitive video can improve the understanding around taking antiretroviral therapy (ART) [14,15].

To address some of the misconceptions and begin a discussion on cure research, we sought to create a package of educational tools to prepare potential participants for cure research. This included a video, pamphlets and an interactive online platform currently under development. The first of these was a 15-minute video that introduces cure research, addresses misconceptions, introduces basic understanding of the research process, and reinforces treatment and prevention. From conceptualisation to completion, the process took one year. The video *'I have a dream: a world without HIV'* is publicly available on YouTube (<https://www.youtube.com/watch?v=oNfw9n5nBtU>). To aid others in the development of similar educational tools, this paper reflects on some of the ethical challenges in developing such a video.

## Conceptualising cure and managing expectations

At this early stage of cure research, the need to manage expectations is paramount. The research is primarily focused on proof-of-concept studies with no large-scale trials planned as yet. The video had to navigate a complex interplay of aims: inform about forthcoming cure research and give some hope to people living with HIV (PLHIV), while also managing expectations and reinforcing the importance of treatment and prevention.

Conceptualising cure has proven to be challenging, in part due to the different strategies under investigation. Currently, studies working towards a cure are either focused on a sterilising cure or long-term remission [16]. Although both fall under the umbrella of 'cure research' they result in clinically different outcomes. Caution has been urged about the use of the word 'cure' or 'cure research' as potentially creating false and confusing, if not misleading, expectations [17,18]. There has also been the suggestion that this type of research should not be described as research, but rather as an 'experiment'. This more accurately reflects the preliminary stage of the research and can be used to manage expectations, because there is unlikely to be any medical benefit to participants at this early stage [19,20]. Other advocated cure-related terms include 'sustained viral remission' [21], 'HIV remission' [22] and 'curative intervention' [16].

Adding complexity to this problem is the knowledge that the biomedical understanding of a cure differs from the lay understanding, particularly in a traditional African context where disease is often seen as a natural occurrence and treatment perceived as a way to coax the disease to leave the patient alone [23]. The community understanding of cure may therefore not be congruent with the scientific understanding of cure. There may be difficulty in distinguishing between sterilising cure, functional cure and remission because, in many traditional African communities with concepts of disease and cure, remission or absence of symptoms is regarded as cure [24]. In the South African context, 'cures' that may be available in the community may be in the form of herbal remedies or spiritual healing [8]. Early in script development, we were aware of the differing layers of cure: the biomedical understanding of cure, the traditional African understanding of cure in which it is understood as an absence of disease, and the lay and 'quack' cures which are often false claims such as holy water. Undoubtedly, in these early-phase trials, the research is unlikely to be described as 'cure' in the informed

consent documents, as to do so would risk misleading the participants. However, our video is not tied to any particular clinical trial, but rather describes the burgeoning area of cure research and a word that suited this body of work was necessary. A 'cure' within the traditional African context may be more closely aligned with remission: the patient may look and feel 'cured' but the HIV may return. Indeed, suppression of the virus using ART could also fall within this understanding of a cure, adding further complexity.

In light of South Africa's complex history of false cures and the traditional African understanding of cure, we felt ethically obliged to provide scientifically sound information that was nevertheless culturally sensitive. As the first educational intervention on cure research in South Africa, our video would likely frame discussions with the community on cure research. We were faced with two options: we could either wait until the science developed and the concepts that would be used became clearer until producing a video based on empirical investigations of these terms, or develop an educational intervention with input from various stakeholders and community members that would be empirically tested and made widely available to HIV clinics throughout South Africa. However, the former would have represented a missed opportunity to begin early engagement on this complex matter, and HIV research has demonstrated the importance of early and sustained engagement.

Decisions about concepts thus became paramount. 'Remission' was mooted as an alternative to 'cure' and perhaps more accurately reflects the possibility of a return of the disease; however, the word cure has already been introduced in the discourse. Ultimately, after drawing on the experiences of the clinicians in our team, as well as considerable consultation with medical doctors, scientists, nurses, HIV counsellors and PLHIV, it was decided to use both cure and remission. We were mindful that the purpose of the video was not to form part of an informed consent process but rather to introduce new concepts into the HIV research discourse; to start the conversations amongst community members so that they felt empowered to seek more information and have informed discussions during any future informed consent processes.

Although the conceptualisation of cure may differ, cure is firmly embedded within the current HIV discourse. The International AIDS Society has described its cure programme as 'Towards an HIV cure' and this is likely to be taken up by the media. Perhaps by discussing cure we have begun to cement it in the South African discourse. There is, however, a need to distinguish a scientific cure from other forms of purported cures. By confronting the issue, we sought to educate and inform so that there is limited confusion on future possible cures *vis-a-vis* false cures.

Cure is not defined in this video, but the Berlin patient is described as being *cured*. In contradistinction, the period during which the Mississippi Baby appeared to be free of HIV while not on treatment is framed as *remission* and described in the context of cancer treatment whereby patients may look and feel well, but the cancer may return. Admittedly, this leaves the viewer free to ascribe their own understanding to these terms. In a short 15-minute video it was difficult to expand on these differences, but future educational interventions might want to focus specifically on these.

## Potential ethical implications and consequences of the video content

Despite the decision to use the word 'cure', the title of the video does not mention cure, but rather focuses on the ideal of an HIV-free world. Throughout the video, it is reinforced that no cure is currently available. We also sought to remind the audience that cure research is in a very early phase, experimental and with no

guarantee of success. Concerns about content were not limited to use of the word ‘cure’ but soon turned to possible inadvertent consequences of the inclusion and exclusion of specific issues. Topics were selected for discussion in the video after considerable consultation with various HIV stakeholders.

In prevention trials, there was a confusion amongst participants between ‘vaccine’ and ‘cure’, as well as confusion between the experimental nature of the prevention trial and established prevention programs [10]. Similar difficulty in distinguishing between experimental cure research and established treatment can be foreseen. It is essential that any progress in cure research should not undermine success in treatment and prevention made to date. Specifically, our concern lay with possible inadvertent consequences arising from a discussion of treatment interruption. Therefore, discussions about the Mississippi Baby and the cessation of treatment required careful wording in order not to encourage such unsupervised treatment interruption.

The design of future HIV cure trials in South Africa is uncertain, but it is anticipated that participants might be asked to stop taking ART at some point. Participants could risk a viral load rebound and could even potentially develop resistance to their current treatment regimen. The video narrative stresses the dangers of treatment interruption, even for one day, and a clear message that the cessation of ART must only be done in a controlled clinical setting where HIV viral load can be closely monitored is presented.

In the video, cure is also portrayed as part of a package that includes treatment and prevention, which together may end the HIV epidemic. Although the video was intended to focus on cure only, discussions with stakeholders stressed the importance of emphasising both treatment and prevention; this discussion now precedes discussions on cure in the video. There are some notable omissions, such as discussions on abstinence, prevention of mother-to-child transmission (PMTCT), and pre- and post-exposure prophylaxis, and cursory treatment of certain issues, such as the side effects of ART. While these key issues have dominated the HIV conversation for the past few decades, they had to be omitted for the sake of brevity.

The length and complexity of informed consent forms have been continuously identified as problematic and this was kept in mind throughout. There is a need to achieve the appropriate balance between giving enough information so that potential participants are able to balance the risks and benefits, with the need not to exceed an individual’s capacity for understanding during the consent process [5]. We also sought to develop a clear, understandable and short video. Our initial 30-page script entitled ‘What every South African should know about HIV and AIDS’ was eventually reduced to a 5-page script. Supplementary materials are necessary and, in response to this need, the team has developed separate pamphlets on HIV prevention, treatment and cure.

## Culturally appropriate video

In order to increase authenticity, healthcare professionals working in public health facilities were used as actors. Dr Maseke is played by a black female Nigerian doctor, dispelling the myth that all people of authority in South Africa are white or indeed male. There were concerns about featuring a foreign doctor, but this scenario reflects the reality of the public health care sector in South Africa. Nomsa is played by an HIV adherence monitor and Andiswa is played by a clinical trial recruiter. Prof Cotton plays himself (a pre-eminent paediatric HIV researcher), as do Dr Riaad Moosa (a prominent doctor and comedian), Zackie Achmat (a prominent activist) and Archbishop Desmond Tutu (a South African icon,

Nobel Peace Prize laureate, social rights activist and active HIV campaigner).

Since screening the video, the decision to include two women as the HIV-positive actors, in lieu of a male and female actor, has been questioned because it may fuel misconceptions that women are carriers of the disease. In South Africa, women are generally in charge of the care of a child, and thus the caregiver needed to be female; equally, the issues that Nomsa discusses, such as rape and female condoms, also necessitated a female actor. In South Africa, HIV affects a disproportionate number of young black women and this video speaks to these women. It is possible that men may not readily identify with these characters, but this once again underscores the fact that this video is not intended to be the only message on HIV cure research, but the first in what is hoped to be a series of educational interventions on cure research targeted at different populations, using a variety of different media.

Due to the importance of traditional medicine in South Africa, it was also decided to discuss the interplay it may have with ART. The video also contains a short interaction between two actors regarding consultations with traditional healthcare practitioners (THPs). THPs are widely used in South Africa, but some traditional medicines have been shown to interact with conventional medication, such as ART. This has caused tension between biomedicine and traditional medicine, but the reality is that many PLHIV may also take traditional medicines to alleviate the side effects of ART. We chose to recognise this interplay between traditional medicine and biomedicine and acknowledge its cultural significance. We attempted to do this in a manner which emphasises the importance of discussing proposed alternative treatments, such as herbals and other traditional medications, with clinic staff before patients take them, rather than to dissuade patients from consulting with THPs.

## Translation and understanding

Finally, as with informed consent, the communication of the information is just as important as the content. Since English is widely understood in South Africa, it was chosen as the language of communication in the video. However, it is one of 11 official languages in South Africa, and since it is only the fifth most widely spoken home language in the country, assumptions about proficiency should be guarded [25]. Informed consent should preferably be discussed and obtained in a participant’s home language, but indigenous languages have not all developed the medical or scientific vocabulary to allow for translation of new scientific terms.

Initially, professional translators added subtitles in isiXhosa, Afrikaans and Zulu, based on the script. Translation of study material generally benefits from the involvement of those who have worked with the community, helping to ensure it is pitched at the correct level and includes appropriate metaphors and concepts [5]. Native speakers thus reviewed these drafts and, while differences arose, most could be resolved by the clinically trained, native Zulu and Afrikaans speaking team members. However, having no native isiXhosa speaker on the project did result in difficulty, in particular with translating the term ‘remission’. It was eventually decided to use the same term used by study nurses, but it is likely that others may adopt different terms. Consulting with African language centres in the future may address some of these issues, but differences in translation are likely to be unavoidable.

## Moving forward

Cure research is an extremely exciting development for PLHIV in South Africa, but discussions to date have largely remained within

the domain of the academic environment. This conversation must start to engage the community, both to familiarise potential participants with cure research and also to involve them in developing cure strategies and trials. To achieve this, potential research participants should be comfortable with ‘cure speak’ and we have a responsibility to make the science accessible to them.

Engagement in early-phase cure research is complex because the science is novel and, in many instances, innovative. This places an obligation on researchers to invest time and resources in science translation. Engagement that bridges the divide between scientific and participant communities can address some of these challenges. Furthermore, evaluation of consent tools is important and the publication of the evaluation of this video is imminent. Finally, an interactive online educational platform on HIV cure that is currently under development will complement this video and allow patients and potential research participants to raise questions related to the video’s content and receive answers. This compendium of tools to facilitate community engagement will hopefully prepare future research participants for HIV-related trials – prevention and cure alike.

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