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Acceptability of Hypothetical HIV Cure-Related Research Modalities: A Cross-Sectional Study of People Living with HIV in Soweto, South Africa

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Abstract

Various modalities are being explored in HIV cure-related research, but little is documented on their acceptability in Africa, where HIV is most prevalent. To address this, we conducted a cross-sectional study in Soweto, South Africa, assessing stated acceptability of five potential HIV cure-related research modalities and identifying associated factors. Between May and August 2024, we sampled 100 adults living with HIV who provided informed consent. Participants completed questionnaires of socio-demographics and the Theoretical Framework of Acceptability scale measuring general acceptability and seven constructs (affective attitude, burden, ethicality, perceived effectiveness, intervention coherence, self-efficacy, opportunity costs). We summarized data using descriptive statistics. We assessed factors associated with acceptability using univariate and multivariate logistic regression. We found that of 100 participants (44% female, median age 39 years), 66% were willing to accept an intervention that would allow lifelong remission (antiretroviral treatment-free control), 88% were willing if the intervention guaranteed remission for everyone treated, and 87% were willing if the intervention had minimal side effects. Total mean acceptability scores of hypothetical HIV cure-related research modalities were oral or injectable chemotherapeutics (3.8/5), intravenous or injectable antibodies (3.7/5), radiotherapy (3.3/5), transplantation (3.1/5), gene therapy (2.9/5), and across all modalities (3.4/5). Participants rated antibodies and chemotherapeutics with tied top scores for affective attitude (3.8/5) and self-efficacy (4.0/5); chemotherapeutics with top scores for perceived effectiveness (4.0/5), intervention coherence (4.1/5) and having least burden (3.2/5) and opportunity costs (3.3/5); and antibodies with the top score for ethicality (4.2/5). Acceptability was associated with non-binary gender and willingness to take an intervention achieving 2 years remission. In conclusion, people living with HIV have moderately high acceptability for oral or injectable chemotherapeutics and intravenous or injectable antibodies but would need more information about gene therapy, transplantation, and radiotherapy. Antibodies aligned highest with personal values, suggesting support for antibody research and applications.

Keywords: remission, antiretroviral treatment-free HIV control, cure, HIV infections, acceptability, antibodies, genetic therapy, South Africa

Introduction

The goals of current research into HIV cure strategies include functional cure [antiretroviral (ARV) treatment-free HIV control, also called remission, during which HIV persists but is suppressed in blood] or eradication (complete HIV clearance permanently from everywhere in the body). Eradication is more challenging because HIV splices its genes into human genes.[1] Research areas include genotype-selected ARV treatment interruption,[1] adaptive immunotherapy, antibodies, antiproliferatives, CCR5 inhibitors, cytokines, gene therapies, latency-reversing agents, mammalian target of rapamycin inhibitors, selective estrogen receptor modulators, and therapeutic vaccines.[2,3]

Experimental cure-related modalities often differ from the familiar treatment mainstay of chemotherapeutic tablets inhibiting the HIV life cycle. For example, parenteral broadly neutralizing antibodies are either injected or infused as passive immunotherapy or induced via vaccination in the hopes of neutralizing virus.[4] Radioimmunotherapy proposes to combine radioactive isotopes with antibodies against HIV-infected cells.[5] Stem cell transplants replace the

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person's immune system and, owing to their risk profile, are reserved for specific indications. Gene therapies aim to modify the person's cells.[6]

Treatment acceptability is defined as the perception of appropriateness of an intervention based on cognitive and emotional responses.[7] Many studies about acceptability in HIV cure-related research have focused on analytic treatment interruption. For example, in Australia, acceptability of analytic treatment interruptions among people living with HIV was driven by altruism.[8] Moreover, in South Africa, people living with HIV perceived concerns about interrupting treatment, including health risks, HIV-related stigma, fears about transmission to sex partners, and HIV status disclosure.[9]

Our research focused on a different aspect, by quantifying modality-specific acceptability. In the United States, concerns have been noted around gene therapy[10] and transplantation.[11] Ibalizumab, the first infused antibody treatment for HIV, has been studied for safety and tolerability but acceptability is underresearched.[12] Similarly, the acceptability of radioimmunotherapy is understudied, even in oncology where it is used, albeit uncommonly.[13]

There is a need to use a rigorous method to measure acceptability. The Theoretical Framework of Acceptability (TFA) was developed as a structured way to quantify acceptability. Through its constructs, the TFA provides a multidimensional measurement that can help researchers evaluate the factors that influence whether an intervention is likely to be adopted and sustained. In general, acceptability is influenced by the intervention's relevance in addressing the disease, lifestyle suitability, convenience, and effectiveness in managing the disease.[7]

The purpose of investigating hypothetical acceptability is to inform directions in research, development, and programmatic implementation. The acceptability of hypothetical cure-related research modalities where HIV is most prevalent, Africa, is largely undocumented. Our study in Soweto, South Africa, used a quantitative survey based on the TFA to measure acceptability of five hypothetical cure-related research modalities and to identify factors associated with general acceptability across modalities (Fig. 1).

Methods

Study design

This was a cross-sectional assessment from a larger mixed-methods research study with adults living with HIV aged 18 years and older.

Setting

The questionnaires were conducted between May and August 2024 at the Perinatal HIV Research Unit in the peri-urban township of Soweto. Soweto has an estimated population of 3 million people within 63 km^2.[14] Soweto is located in South Africa's most populous municipality, the city of Johannesburg. Johannesburg is in Gauteng province, the smallest land sized but most populous province (15 million people) of South Africa (62 million people). Most of South Africa's population are Black Africans (81%), with 51% females. In Gauteng province, 72% of people are 15–64 years old, 88% live in formal dwellings, 16% attain higher education,[15] and HIV prevalence is 17.6% of 15- to 49-year-olds.[16]

Sample size determination

The sample size was determined using an acceptability rate (expected proportion) of at least 30% in the expression $n = z^2\, p\, (1 - p) / d^2$ where n = sample size, $z = z$ statistic for level of confidence, p = expected proportion, and d = precision.

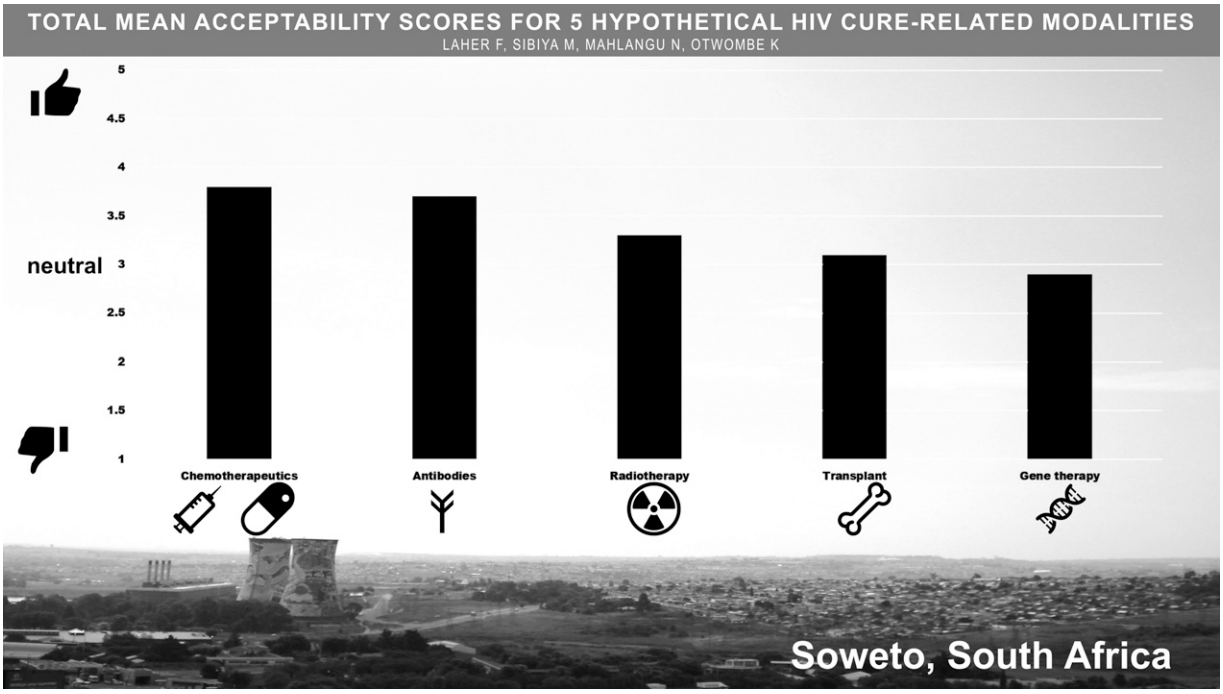

FIG. 1. A graphical abstract showing the total mean acceptability scores for five hypothetical HIV cure-related modalities among 100 people living with HIV in Soweto, South Africa.

Prior studies have shown a mixed range of acceptability rates; thus, 30% was deemed conservative for this precision-driven sample size.[17,18] With 95% confidence interval and a precision of 9% (21%–39%), this study was designed to enroll 100 participants into the survey component.

Recruitment

To mitigate HIV stigma, we recruited participants by snowball sampling in which chain referral began with a community group for people living with HIV as recommended by the site's Community Advisory Board. Although assessing acceptability among individuals who have tried ARV treatment-free control strategies would have facilitated a more comprehensive understanding, such people were rare at the time of recruitment. We could identify and recruit only one such person, and snowball sampling did not identify others.

Eligibility

At the site, after written informed consent, eligibility was assessed, including English-speaking-and-reading individuals aged 18 years or older who stated they were living with HIV (evidence was not required).

Information session

Because of the technical nature of HIV cure-related concepts, we included the same brief information (Table 1) in everyday language to orientate all participants before completing the survey.

Survey

The primary goal of the survey was to assess the acceptability of HIV cure-related research modalities and identify factors associated with acceptability. The survey was pilot tested before implementation. All participants self-completed a questionnaire of close-ended questions. Completed after consent but before enrolment was a section assessing eligibility. Completed after enrolment and the information session were the sections assessing willingness, acceptability, and socio-demographics. The questionnaire assessed willingness to take an intervention resulting in remission by evaluating responses across three categories: duration of remission (1 month, 3 months, 2 years, lifelong), percentage of patients achieving remission (25%, 50%, 100%), and severity of side effects (no/little interference with activities and social life, interference requiring treatment, interference requiring hospitalization, and interference causing permanent disability/death).

The acceptability section followed, based on five hypothetical HIV cure-related research modalities: antibodies, chemotherapeutics, radiotherapy, transplantation, and gene therapy (Table 1). The selection of these five cure-related research modalities was based on published literature rather than their immediate feasibility for implementation.

We adapted the questions from the theory-informed TFA questionnaire, which uses Likert scales to assess acceptability of health care interventions through seven constructs: affective attitude (do you like or dislike these HIV cure methods?); burden (how much effort do you think you would need to take to use these HIV cure methods?); ethicality (how fair and ethical would it be for people living with HIV to get these HIV cure methods?); perceived effectiveness (I think these methods may cure HIV); intervention coherence (it is clear to me how these methods could cure HIV); self-efficacy (how confident would you feel to try an HIV cure with these methods?); and opportunity costs (using these HIV cure methods could interfere with my other priorities). Additionally, there was a question on general acceptability (how acceptable would these HIV cure methods be to you?).[19]

Collected socio-demographics were age, gender identification, highest education, and employment status. We also collected whether participants were currently taking HIV treatment and the year of ARV initiation.

At the end of the questionnaire, participants were thanked and reminded that HIV cures are not widely available yet, so ARV treatment remains the best current option.

Table 1. Information Given to Survey Participants

Information given before survey	
Cure	When we say "cure," we mean ending HIV in a person. A cure is not available right now but is being researched for remission and eradication.
HIV remission	Researchers would try something to keep a person's HIV controlled for a while so that they don't need ARVs during that time. Remission means HIV is still in the body, but it is controlled (suppressed, undetectable in blood) without ARVs. We don't know how long remission can last, so a person may need to test often to see if HIV comes back and may need more remission treatments every time HIV comes back.
HIV eradication	Researchers would try something to get all HIV out of a person. This is more difficult because when we are infected, HIV mixes its own genes into our genes (DNA) in our cells.
Information given during survey	
Antibodies	Immune system proteins given as drips or injections
Chemotherapeutics	Treatment with chemicals given as pills or injections
Radiotherapy	Radiation to kill infected cells
Transplantation	Replacing your cells with special cells from an HIV-immune person's bone marrow
Gene therapy	Gene therapy (changing your genes/DNA)

ARV, antiretroviral.

Variables

The primary outcome was acceptability that was defined as the median of the seven TFA questionnaire items.

Statistical analysis

Questionnaire data in Microsoft Excel underwent quality assurance for inconsistencies and missing values. Outliers were investigated to determine whether they represent true data points or errors.

Sociodemographic and clinical characteristics. Age, gender identification, highest education completed, employment status, current ARV treatment status, and years since ARV initiation were summarized to provide the context for the sample and allow for interpretation of factors associated with acceptability. We calculated descriptive statistics including measures of central tendency (mean and median) and dispersion [standard deviation and interquartile range (IQR)] for continuous variables and frequencies and percentages for categorical variables.

Willingness under hypothetical scenarios. We aimed to describe willingness to take hypothetical intervention under durability, efficacy, and risk scenarios. Willingness was assessed by frequencies based on three scenarios: duration of remission, the percentage of people achieving remission, and the severity of treatment side effects. We compared groups using Fisher's exact test that tested the null hypothesis of no association between gender identification and age-group versus willingness to take the intervention (that had a binary response of Yes or No). In the three-group comparison, we first determined a global *p*-value followed by pairwise comparisons to identify the groups showing statistically significant differences.

Acceptability of treatment modalities. We aimed to describe acceptability by hypothetical modality and factors associated with general acceptability. TFA items were analyzed as described by scoring responses in the scale from 1 to 5 except for reverse scoring two items (namely, burden and opportunity costs).[19] We generated overall acceptability scores using two methods. The first method averaged the mean scores of seven TFA constructs (affective attitude, burden, ethicality, intervention coherence, opportunity costs, perceived effectiveness, and self-efficacy) to obtain a total mean acceptability score for each cure-related research modality, which were then averaged across the five modalities to obtain an overall acceptability score. The second method used the mean score for the General Acceptability item. We thought that these two scores would likely be positively, but not perfectly, correlated because the first method assumes an equal weighting for each TFA construct, which is appropriate because ARVs render HIV non-life-threatening.

In the item scale measures, overall and subscale scores were determined and descriptive statistics estimated overall and by gender, age-group, and duration of treatment. Higher scores suggested a higher likelihood of accepting a cure-related intervention. Reliability of the overall scale and subscales was determined using the Cronbach alpha test with values ≥0.7 considered good. Median values were used to categorize participants into two groups: those with a high likelihood of accepting a cure-related intervention and those without. Univariate and multivariate logistic regression models were used to determine factors associated with a higher probability of accepting a cure-related intervention. Variables with a *p*-value <.1 at the univariate level were considered for inclusion into the multivariate model. The final model was determined using the backward selection procedure: fit was examined by goodness of fit statistics. Statistical analysis was conducted in SAS Enterprise Guide version 7.15 (SAS Institute Inc., Cary, NC, USA).

Ethical considerations

This study was approved by the University of the Witwatersrand Human Research Ethics Committee (Medical). All participants provided written voluntary informed consent.

Results

Socio-demographics

As shown in Table 2, we enrolled 100 participants living with HIV, 44% identified as female, 60% completed high school as their highest level of education, and 76% were unemployed. Median age was 39 (IQR 31–45) years.

HIV

Among the 100 participants living with HIV, 98% were taking ARV treatment. Median time since ARV initiation was 9 years (IQR 6–16) (Table 2).

Willingness to take cure-related interventions

Of the 100 participants, 66% were willing to take an intervention if it would result in lifelong remission, 88% if everyone treated would achieve remission, and 87% if it resulted in little to no side effects.

A greater proportion of females than males were willing to take an intervention if it would result in lifelong remission

Table 2. Descriptive Characteristics of 100 People Living with HIV in Soweto, South Africa

Characteristic	*Total* n = *100*
Socio-demographics	
Age in years, median (interquartile range)	39 (31–45)
Gender identification, *n* (%)	
Female	44 (44%)
Male	40 (40%)
Non-binary	16 (16%)
Highest education completed, *n* (%)	
Primary school	25 (25%)
High school	60 (60%)
Tertiary	15 (15%)
Employment	
Employed, including self employed	24 (24%)
Unemployed	76 (76%)
HIV	
Current ARV treatment, *n* (%)	98 (98%)
Years since ARV initiation, median (interquartile range)	9 (6–16)

(35/44 = 80% vs. 26/40 = 31%, $p = .0030$). A greater proportion of 16 non-binary participants were willing to accept an intervention that lasts for 1 month compared with females (14/16 = 88% vs. 23/42 = 52%, $p = .016$) and compared with males (14/16 = 88% vs. 20/40 = 50%, $p = .014$).

Compared with participants aged 18–39 years, a greater proportion of those aged 40 years and older were willing to take an intervention that lasts for life (37/48 = 77% vs. 29/52 = 56%, $p = .0344$), has side effects that interfere with activities and social life requiring treatment (28/48 = 58% vs. 14/52 = 27%, $p = .0022$), has side effects requiring hospitalization (18/48 = 38% vs. 3/52 = 6%, $p = .0001$), and has side effects leading to permanent disability or death (10/48 = 21% vs. 3/52 = 6%, $p = .0361$) (Table 3).

TFA reliability

The overall Cronbach alpha value was 0.85, indicating excellent internal consistency of the TFA. For the constructs, Cronbach alpha was 0.65 (affective attitude), 0.75 (burden), 0.71 (perceived effectiveness), 0.78 (ethicality), 0.79 (intervention coherence), 0.76 (opportunity cost), and 0.72 (self-efficacy), indicating that individual TFA constructs were also good measures of acceptability.

Acceptability of hypothetical HIV cure-related research modalities by construct

1. Affective attitude: positive feelings were highest toward oral or injectable chemotherapeutics (mean score 3.8), while negative feelings were highest toward gene therapy (mean score 2.7).
2. Burden: oral or injectable chemotherapeutics (mean score 3.2) had the highest perceived manageability, while transplantation (mean score 2.7) was thought to be most burdensome.
3. Ethicality: alignment with personal values was highest for antibodies (mean score 4.2), but concerns over fairness were strongest toward gene therapy (mean score 3.1).
4. Perceived effectiveness: belief in intervention effectiveness was highest toward oral or injectable chemotherapeutics (mean score 4.0) and lowest toward gene therapy (mean score 3.0).
5. Intervention coherence: perception of understanding was highest toward oral or injectable chemotherapeutics (mean score 4.1) and lowest toward gene therapy (mean score 3.1).
6. Self-efficacy: confidence to try oral or injectable chemotherapeutics was highest (mean score 4.0) and gene therapy was lowest (mean score 2.9).
7. Opportunity costs: oral or injectable chemotherapeutics were perceived to align most with other priorities (mean score 3.3), while radiotherapy was perceived to interfere most with other priorities (mean score 2.7).

For the seven TFA constructs, the total mean score was highest for oral or injectable chemotherapeutics (total mean score 3.8), lowest for gene therapy (total mean score 2.9), and overall was 3.4 for all modalities.

8. General acceptability: Participants scored the general acceptability item highest for oral or injectable chemotherapeutics (mean score 4.2), lowest for gene therapy (mean score 3.0), and overall was 3.5 for all modalities (Table 4).

Factors associated with acceptability

The odds of acceptability were higher in non-binary participants [odds ratio (OR): 1.7 95% confidence interval (CI):

Table 3. Willingness to Take Hypothetical Remission Intervention Among 100 People Living with HIV by Gender Identification and Age

		Gender identification				*Age*		
Willingness to take HIV remission treatment	*Total* n = *100*	*Females* n = *44 (%)*	*Males* n = *40 (%)*	*Non-binary* n = *16 (%)*	p-*Value*	*18–39 years old* n = *52 (%)*	*40 years and older* n = *48 (%)*	p-*Value*
If remission lasts								
1 month	57	23 (52)	20 (50)	14 (88)	**.0258**	27 (52)	30 (63)	.3173
3 months	62	25 (57)	27 (68)	10 (63)	.6225	30 (58)	32 (67)	.4125
2 years	60	28 (64)	26 (65)	6 (38)	.1481	28 (54)	32 (67)	.2236
Lifelong	66	35 (80)	26 (65)	5 (31)	**.0030**	29 (56)	37 (77)	**.0344**
If remission is achieved by								
25% of people	51	24 (55)	19 (48)	8 (50)	.8027	24 (46)	27 (56)	.3257
50% of people	56	25 (57)	20 (50)	11 (69)	.4521	28 (54)	28 (58)	.6905
100% of people	88	38 (87)	36 (90)	14 (88)	.9184	45 (87)	43 (90)	.7622
If remission treatment side effects								
are none to minimal	87	42 (96)	32 (80)	13 (81)	.0605	46 (89)	41 (85)	.7691
interfere with activities and social life, requiring treatment	42	20 (46)	18 (45)	4 (25)	.3312	14 (27)	28 (58)	**.0022**
require hospitalization	21	10 (23)	9 (23)	2 (13)	.7203	3 (6)	18 (38)	**.0001**
disable or cause death	13	6 (14)	6 (15)	1 (6)	.8513	3 (6)	10 (21)	**.0361**

Bold data represents statistical significant *p*-values.

Table 4. Mean Acceptability Scores on Scale of 1 (Lowest) to 5 (Highest) (Standard Deviations) of Five Hypothetical HIV Cure Modalities by Theoretical Framework of Acceptability Items

Construct	*Intravenous or injectable antibodies*	*Oral or injectable chemotherapeutics*	*Radiotherapy*	*Transplant*	*Gene therapy*	*Total mean*
Affective attitude (feelings toward intervention)	3.8 (−1.1)	3.8 (−1.1)	3.3 (−1.4)	2.9 (−1.3)	2.7 (−1.3)	**3.3 (0.5)**
Burden (perceived effort of intervention)	3.1 (−1.3)	3.2 (−1.4)	2.7 (−1.5)	2.6 (−1.4)	2.9 (−1.4)	**2.9 (0.2)**
Ethicality (alignment with personal values)	4.2 (−0.9)	4.1 (−1.0)	3.6 (−1.3)	3.4 (−1.3)	3.1 (−1.4)	**3.7 (0.5)**
Perceived effectiveness (belief in successful outcome)	3.8 (−1.2)	4.0 (−1.0)	3.7 (−1.1)	3.3 (−1.2)	3.0 (−1.3)	**3.5 (0.4)**
Intervention coherence (understanding of how intervention works)	3.9 (−0.9)	4.1 (−0.9)	3.7 (−1.0)	3.3 (−1.1)	3.1 (−1.2)	**3.6 (0.4)**
Self-efficacy (confidence to try an intervention)	4.0 (−1.1)	4.0 (−1.0)	3.5 (−1.2)	3.1 (−1.4)	2.9 (−1.4)	**3.5 (0.4)**
Opportunity cost (perception of sacrifices to get intervention)	3.2 (−1.2)	3.3 (−1.3)	2.7 (−1.1)	2.8 (−1.2)	2.7 (−1.2)	**2.9 (0.3)**
Total mean score	**3.7 (0.4)**	**3.8 (0.4)**	**3.3 (0.4)**	**3.1 (0.3)**	**2.9 (0.2)**	**3.4 (0.4)**
General acceptability	4.1 (−0.8)	4.1 (−0.9)	3.4 (−1.2)	3.0 (−1.3)	3.0 (−1.3)	**3.5 (0.6)**

Bold data represents statistical significant *p*-values.

1.04–2.68] and in those willing to take an intervention if remission lasts two years (OR: 1.6 95% CI: 1.06–2.37) versus other durations (Table 5).

Discussion

Our study found that adults living with HIV in Soweto, South Africa, self-reported acceptability of hypothetical HIV cure-related research modalities, with an overall total mean score of 3.4/5. Acceptability varied by modality. Factors associated with higher acceptability included non-binary gender and mid-duration remission.

Our findings reveal lower acceptability among men than women, reflecting broader gender disparities in HIV care. In one meta-analysis, men had lower awareness of HIV status, lower treatment uptake, and lower viral suppression compared with women.[20] Stigma may contribute to these disparities in care.[21] Plausibly, anticipation of stigma may have influenced lower acceptability among men, who may perceive health interventions as threats to their social identity.[22] Some people living with HIV perceive their HIV status as part of their identity, and find treatment to be reassuring, and may not seek a cure.[23] In the United States,[24] more males than females were willing to participate in research trials of latency-reversing agents, gene modification, autologous stem cell transplants, and therapeutic vaccines, while in Ghana,[25] more people older than 40 years, compared with younger ones, were willing to participate in trials with analytic treatment interruption.

Our participants had moderately high acceptability for oral or injectable chemotherapeutics (3.8/5) and intravenous or injectable antibodies (3.7/5) but may need more information about gene therapy (2.9/5), transplantation (3.1/5), and radiotherapy (3.3/5). It seems likely that when we specified a hypothetical modality as oral, injectable, or intravenous, the familiarity, ease of administration, and perceived effectiveness contributed to the hypothetical acceptability of those modalities. This supports findings from a study of 21 countries that oral and injectable medications were the most preferred routes of administration and that African Islamic cultures preferred injectable routes.[26] Indeed prior knowledge is important, because people are more willing to accept gene therapy if it is recommended by their health care providers or other public figures and if they had reference of a person who had success with gene therapy.[10] Other researchers have found that acceptability is influenced by cultural beliefs,[27] and in China, higher education levels were associated with greater acceptance of gene therapy.[28]

To our knowledge, our study is the first to show that antibodies strongly align with personal values in an African setting, with an ethicality mean score of 4.2/5. Our finding of antibody ethicality is interesting in its context of unfamiliarity: generally, antibody treatments are uncommon in medical practice in South Africa, and HIV antibodies are still being researched. Beliefs about antibody products require elucidation, but we find it plausible that the idea of antibodies as natural immune components may resonate with African populations who use natural medicines to help manage HIV.[29] Previously, authors raised ethical considerations of human monoclonal antibody treatments based on its production source, B cells. Natural production, relying on human immune responses, necessitates attention to ethical sourcing of lymphocytes, while synthetic production may bypass human consent requirements if using animal models. B cells may be obtained from peripheral blood, discarded tissues, or, historically, fetal cell lines.[30] In the United States, factors such as race, language, social support, and the presence of comorbidities have been shown to be associated with the decision to accept or decline COVID-19 antibody treatments.[31] Understanding ethicality aids the development and use of antibody treatments by building and maintaining public trust in medical research and health care.

Discussions on developing HIV cure modalities for resource-limited settings in Africa have centered on feasibility, infrastructure, and affordability of antibodies[32] but have neglected African acceptability. Our results suggest antibody treatments are acceptable in an African setting, but limited

Table 5. Factors Associated with General Acceptability of All Hypothetical HIV Cure Modalities

	Univariate		*Multivariate*	
Variable	*RR (95% CI)*	p-*Value*	*RR (95% CI)*	p-*Value*
Age-group 40+ versus 18–39 years old	0.8966 (0.6178–1.3010)	.5654	0.9390 (0.6485–1.3594)	.7387
Gender identification				
Female versus male	1.5341 (0.9820–2.3966)	.0601	1.3808 (0.9048–2.1071)	.1346
Non-binary versus male	1.5625 (0.9135–2.6726)	.1032	**1.6717 (1.0438–2.6774)**	**.0325**
Highest education completed				
Primary versus secondary school	0.9600 (0.5940–1.5516)	.8676		
Tertiary versus secondary school	1.4667 (0.9867–2.1802)	.0583		
Employed versus unemployed	1.0292 (0.6726–1.5748)	.8946		
ARV treatment duration ≥9 years versus 1–8 years	0.8159 (0.5657–1.1768)	.2763		
Willing to take HIV remission treatment if remission lasts				
1 month versus unwilling	1.5975 (1.0502–2.4301)	.0286		
3 months versus unwilling	1.4173 (0.9264–2.1686)	.1080		
2 years versus unwilling	1.5417 (1.0041–2.3671)	.0479	**1.5854 (1.0615–2.3680)**	**.0244**
Lifelong versus unwilling	1.1913 (0.7862–1.8051)	.4091		
Willing to take HIV remission treatment if remission is achieved by				
25% of people versus unwilling	1.3538 (0.9253–1.9808)	.1187		
50% of people versus unwilling	1.2964 (0.8772–1.9160)	.1927		
100% of people versus unwilling	1.0682 (0.5871–1.9434)	.8290		
Willing to take HIV remission treatment if side effects				
are none to minimal versus unwilling	3.8103 (1.0520–13.8009)	.0416	3.4161 (0.9609–12.1449)	.0577
interfere with activities and social life, requiring treatment versus unwilling	0.9063 (0.6190–1.3267)	.6127		
require hospitalization versus unwilling	1.2226 (0.8196–1.8239)	.3247		
disable or cause death	1.3689 (0.9015–2.0786)	.1407		

Bold data represents statistical significant *p*-values.
CI, confidence interval; RR, relative risk.

familiarity with the modality in South Africa, where testing is underway, could have played a role. Antibodies may be associated with viral resistance, cost, and scalability challenges that could reduce acceptability.[33] Currently 1% of existing antibody-based treatment sales are in Africa, with high costs preventing integration into insurance schemes and essential medicine lists. Advances in thermostable formulations, cold chain technology investments, pricing partnerships, and strategic planning with existing health care infrastructure could mitigate cold chain, cost, and infrastructural challenges.[34]

There is clearly a need for information about emerging modalities. Our study suggests limited public knowledge about gene therapy. In the United States, people living with HIV expressed concerns about gene therapy, especially side effect irreversibility.[10] Novelty and invasiveness may also be concerns. Studies in Europe and North America suggest that framing gene therapy using community-preferred words—emphasizing its mimicry of natural bodily functions and potential long-term solutions—can improve understanding.[35] Therefore, developing safe and effective gene therapies for HIV should be concomitant with efforts to inform the public and to form alliances for African markets.

Although stem cell transplantation has cured HIV in isolated cases of people with cancer, it was not very acceptable to the people living with HIV participating in our study who were not known to have cancer. Transplantation is unlikely to become a widespread cure intervention even for people with comorbid cancer, because of its invasiveness, potential for severe side effects, and limited donor availability.[36] In the United States, people living with HIV, researchers, policymakers, and bioethicists perceived risks associated with stem cells from a donor, and opinions differed about whether the risks were acceptable for otherwise healthy individuals.[37] Furthermore, clinical researchers perceived that stem cell transplantation and gene therapy were among the riskiest modalities.[37]

Despite radioimmunotherapy's lack of human trials, our participants reported neutral to slightly positive acceptability toward it. Potential radiation side effects, including immune suppression, remain a concern. Some studies in people living with HIV report decreased CD4 counts months after radiotherapy,[38] while others indicate similar side effect profiles compared with people without HIV.[39]

The percentage of people living with HIV willing to take an intervention varied by other hypothetical factors: remission duration, efficacy, and side effects. Willingness to take an intervention with medium-term duration of remission was associated with overall acceptability. This suggests that individuals who find the concept of an HIV cure generally acceptable may undergo interventions that offer even temporary remission, valuing the prospect of a treatment-free period and reduced burden. Consequently, this justifies developing strategies that offer limited remission to encourage engagement in

care. Our finding aligns with the Health Belief Model, which posits that health behaviors are influenced by perceived susceptibility to illness, perceived severity, perceived benefits and barriers to taking action, self-efficacy, and cues to action.[40] In our context, the general acceptability of a cure-related intervention reflects high perceived benefit, and willingness to take a remission-inducing intervention suggests a willingness to overcome potential barriers to achieve that benefit.

This study had several limitations. First, limited familiarity with the novel HIV cure methods presented in the survey may have influenced responses. Second, the study's setting in a peri-urban township may limit the generalizability of findings to other regions. Third, hypothetical survey responses may not accurately reflect real-world preferences and participation. Fourth, stem cell transplantation, primarily relevant to patients with cancer, was included despite the study's general sample who were not known to have an indication. Fifth, the nonrandom snowball sampling and potential self-selection bias may have led to the overrepresentation of certain subgroups, particularly non-binary participants whose high proportion of positive responses inflates their results and influences inferential outcomes. However, including gender-diverse individuals is informative because of their 13-fold higher risk of HIV acquisition compared with the general adult population.[41] Sixth, another possible limitation was that HIV status was self-reported, meaning we cannot be sure that the sample did not contain people who misrepresented their status.

This study's key strength lies in its rigorous measurement of acceptability, our primary outcome, using the TFA. Additionally, our sample effectively represents populations who would be most affected by an HIV cure, including Africans living with HIV, women, and diverse age-groups. Because most people living with HIV reside in South Africa, it is the country that most needs an HIV cure strategy for profound durable benefit to public health.

Conclusions

This study shows generally positive acceptability of hypothetical HIV cure approaches among people living with HIV in Soweto, South Africa. The average acceptability score varied by modality. Chemotherapeutics and antibodies had higher average scores suggesting more acceptability, while gene therapy was least acceptable. Familiarity with oral and injectable administration and with antiretrovirals as chemotherapeutics likely explains the hypothetical acceptability of chemotherapeutics for cure. Further research would be needed to illuminate the reasons why antibodies were found to be acceptable and aligned with values in Africa. To foster trust in gene therapy, further information about gene therapy would need to be provided to the public.

Our assessment informs the development of future HIV cure-related research modalities that are not only scientifically sound but also socioculturally sensitive to an African context. Incorporating these data may enhance inclusivity, increasing the likelihood of successful implementation and acceptance.

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Authors' Contributions

All authors were involved in conception, analysis, interpretation, and revision of the article; approved the draft; and take final responsibility. F.L. wrote the first draft. M.S. and N.M. were involved in acquisition.

Author Disclosure Statement

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References

1. Einkauf KB, Osborn MR, Gao C, et al. Parallel analysis of transcription, integration, and sequence of single HIV-1 proviruses. Cell 2022;185(2):266–282.e15; doi: 10.1016/j.cell.2021.12.011
2. Barr L, Jefferys R. A landscape analysis of HIV cure-related clinical trials and observational studies in 2018. J Virus Erad 2019;5(4):212–219; doi: 10.1016/S2055-6640(20)30030-3
3. Janssens J, Bruggemans A, Christ F, et al. Towards a functional cure of HIV-1: Insight into the chromatin landscape of the provirus. Front Microbiol 2021;12:636642; doi: 10.3389/fmicb.2021.636642
4. Nel C, Frater J. Enhancing broadly neutralising antibody suppression of HIV by immune modulation and vaccination. Front Immunol 2024;15:1478703; doi: 10.3389/fimmu.2024.1478703
5. Helal M, Dadachova E. Radioimmunotherapy as a novel approach in HIV, bacterial, and fungal infectious diseases. Cancer Biother Radiopharm 2018;33(8):330–335; doi: 10.1089/cbr.2018.2481
6. Solanki D, Murjani K, Singh V. CRISPR-Cas based genome editing for eradication of human viruses. Prog Mol Biol Transl Sci 2024;208:43–58; doi: 10.1016/bs.pmbts.2024.07.012
7. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: An overview of reviews and development of a theoretical framework. BMC Health Serv Res 2017;17(1):88; doi: 10.1186/s12913-017-2031-8
8. Lau JSY, Smith MZ, Allan B, et al. Acceptability, motivation and the prospect of cure for people living with HIV and their healthcare providers in HIV cure-focused treatment interruption studies. AIDS Res Ther 2020;17(1):65; doi: 10.1186/s12981-020-00321-z
9. Mthimkhulu D, Dong KL, Ngcobo MW, et al. 'It is scary to pause treatment': Perspectives on HIV cure-related research and analytical treatment interruptions from women diagnosed during acute HIV in Durban, South Africa. HIV Res Clin Pract 2025;26(1):2455917; doi: 10.1080/25787489.2025.2455917
10. Dubé K, Simoni J, Louella M, et al. Acceptability of cell and gene therapy for curing HIV infection among people living with HIV in the Northwestern United States: A qualitative study. AIDS Res Hum Retroviruses 2019;35(7):649–659; doi: 10.1089/AID.2019.0021
11. Dubé K, Kanazawa J, Taylor J, et al. Ethics of HIV cure research: An unfinished agenda. BMC Med Ethics 2021;22(1):83; doi: 10.1186/s12910-021-00651-1
12. Emu B, Fessel J, Schrader S, et al. Phase 3 study of ibalizumab for multidrug-resistant HIV-1. N Engl J Med 2018;379(7):645–654; doi: 10.1056/NEJMoa1711460
13. Chen Y, Dahal PK, Mosharaf P, et al. Assessing the clinical effectiveness of radioimmunotherapy with combined

radionuclide/monoclonal antibody conjugates in cancer treatment: Insights from randomised clinical trials. Cancers (Basel) 2025;17(9):1413; doi: 10.3390/cancers17091413
14. Statistics South Africa. Statistical Release Mid-year population estimates 2017 [Internet]. Available from: http://www.statssa.gov.za/publications/P0302/P03022017.pdf [Last accessed: Decemebr 1, 2024].
15. Statistics South Africa. Statistics South Africa Census 2022 [Internet]. Available from: http://census.statssa.gov.za/ [Last accessed: Decemebr 1, 2024].
16. Human Sciences Research Council. Fifth South African National HIV Prevalence, Incidence, Behaviour and Communication Survey (SABSSM V) 2024. Available from: https://hsrc.ac.za/uploads/pageContent/9234/SABSSMV_Impact_Assessment_Summary_ZA_ADS_cleared_PDFA4.pdf [Last accessed: Decemebr 1, 2024].
17. Delhove J, Osenk I, Prichard I, et al. Public acceptability of gene therapy and gene editing for human use: A systematic review. Hum Gene Ther 2020;31(1–2):20–46; doi: 10.1089/hum.2019.197
18. Evans MDR, Kelley J, Zanjani ED. The ethics of gene therapy and abortion: Public opinion. Fetal Diagn Ther 2005; 20(3):223–234; doi: 10.1159/000083910
19. Sekhon M, Cartwright M, Francis JJ. Development of a theory-informed questionnaire to assess the acceptability of healthcare interventions. BMC Health Serv Res 2022;22(1): 279; doi: 10.1186/s12913-022-07577-3
20. Nardell MF, Adeoti O, Peters C, et al. Men missing from the HIV care continuum in sub-Saharan Africa: A meta-analysis and meta-synthesis. J Int AIDS Soc 2022;25(3): e25889; doi: 10.1002/jia2.25889
21. Ettiègne-Traoré V, Tuho MZ, Mohamed F, et al. Differences between HIV-Infected men and women in antiretroviral therapy outcomes—six African countries, 2004–2012. MMWR Morb Mortal Wkly Rep 2013;62(47):945.
22. Mursa R, Patterson C, Halcomb E. Men's help-seeking and engagement with general practice: An integrative review. J Adv Nurs 2022;78(7):1938–1953; doi: 10.1111/jan.15240
23. Laher F, Mahlangu N, Sibiya M. Beliefs about HIV cure: A qualitative study of people living with HIV in Soweto, South Africa. South Afr J HIV Med 2025;26(1):1644; doi: 10.4102/sajhivmed.v26i1.1644
24. Dubé K, Evans D, Sylla L, et al. Willingness to participate and take risks in HIV cure research: Survey results from 400 people living with HIV in the US. J Virus Erad 2017; 3(1):40–50.e21; doi: 10.1016/S2055-6640(20)30295-8
25. Bonney EY, Lamptey H, Aboagye JO, et al.; H-CRIS Massive Action Team. Unwillingness of patients in Ghana to interrupt antiretroviral therapy for HIV cure research. J Virus Erad 2021;7(1):100027; doi: 10.1016/j.jve.2020.100027
26. Murdan S, Wei L, van Riet-Nales DA, et al. Association between culture and the preference for, and perceptions of, 11 routes of medicine administration: A survey in 21 countries and regions. Explor Res Clin Soc Pharm 2023;12: 100378; doi: 10.1016/j.rcsop.2023.100378
27. Woollard L, Gorman R, Rosenfelt DJ. Improving patient informed consent for haemophilia gene therapy: The case for change. Ther Adv Rare Dis 2021;2:26330040211047244; doi: 10.1177/26330040211047244
28. Li Y, Zhang X, Xiang Z, et al. Public attitudes about the use of gene therapy in mainland China. JAMA Netw Open 2023;6(8): e2328352–e2328352; doi: 10.1001/jamanetworkopen.2023.28352
29. Richard K, Poli ANR, Andrae-Marobela K, et al. Medicinal plant and traditional knowledge-guided strategies to combat HIV persistence. Curr HIV/AIDS Rep 2024;22(1):5; doi: 10.1007/s11904-024-00712-1
30. Glassy MC, Gupta R. Technical and ethical limitations in making human monoclonal antibodies (an overview). Methods Mol Biol 2014;1060:9–36; doi: 10.1007/978-1-62703-586-6_2
31. Bierle DM, Ganesh R, Wilker CG, et al. Influence of social and cultural factors on the decision to consent for monoclonal antibody treatment among high-risk patients with mild-moderate COVID-19. J Prim Care Community Health 2021; 12:21501327211019282; doi: 10.1177/21501327211019282
32. Gieber L, Muturi-Kioi V, Malhotra S, et al. Clinical and regulatory challenges and opportunities for monoclonal antibodies in low-and middle-income countries: Lessons from COVID-19 and beyond. Pharmaceut Med 2023;37(3): 203–214; doi: 10.1007/s40290-023-00473-z
33. Mahomed S, Pillay K, Hassan-Moosa R, et al. Clinical trials of broadly neutralizing monoclonal antibodies in people living with HIV–a review. AIDS Res Ther 2025;22(1):44; doi: 10.1186/s12981-025-00734-8
34. Malhotra S, Cameron AI, Gotham D, et al. Novel approaches to enable equitable access to monoclonal antibodies in low- and middle-income countries. PLOS Glob Public Health 2024;4(7):e0003418; doi: 10.1371/journal.pgph.0003418
35. Hart DP, Branchford BR, Hendry S, et al. Optimizing language for effective communication of gene therapy concepts with hemophilia patients: A qualitative study. Orphanet J Rare Dis 2021;16(1):189; doi: 10.1186/s13023-020-01555-w
36. Passaes CP, Sáez-Cirión A. HIV cure research: Advances and prospects. Virology 2014;454–455:340–352; doi: 10.1016/j.virol.2014.02.021
37. Dubé K, Taylor J, Sylla L, et al. 'Well, it's the risk of the unknown. . . right?': A qualitative study of perceived risks and benefits of HIV cure research in the United States. PLoS One 2017;12(1):e0170112; doi: 10.1371/journal.pone.0170112
38. Housri N, Yarchoan R, Kaushal A. Radiotherapy for patients with the human immunodeficiency virus: Are special precautions necessary? Cancer 2010;116(2):273–283; doi: 10.1002/cncr.24878
39. Höcht S, Wiegel T, Kroesen AJ, et al. Low acute toxicity of radiotherapy and radiochemotherapy in patients with cancer of the anal canal and HIV-infection. Acta Oncol 1997; 36(8):799–802; doi: 10.3109/02841869709001360
40. Orji R, Vassileva J, Mandryk R. Towards an effective health interventions design: An extension of the health belief model. Online J Public Health Inform 2012;4(3):e61050; doi: 10.5210/ojphi.v4i3.4321
41. UNAIDS. Human Rights Fact Sheet Series. 2021. Available from: https://www.unaids.org/sites/default/files/media_asset/04-hiv-human-rights-factsheet-transgender-gender-diverse_en.pdf [Last accessed: April 15, 2025].

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