BMJ Open

Study protocol: A randomised trial of the effectiveness of the Common Elements Treatment Approach (CETA) for improving HIV treatment outcomes among women experiencing intimate partner violence in South Africa

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To cite: Pascoe S, Fox M, Kane J, *et al*. Study protocol: A randomised trial of the effectiveness of the Common Elements Treatment Approach (CETA) for improving HIV treatment outcomes among women experiencing intimate partner violence in South Africa. *BMJ Open* 2022;**12**:e065848. doi:10.1136/bmjopen-2022-065848

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-065848).

Received 20 June 2022
Accepted 08 December 2022

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ABSTRACT

Introduction Intimate partner violence (IPV) is a barrier to consistent HIV treatment in South Africa. Previous trials have established that the Common Elements Treatment Approach (CETA), a cognitive-behavioural-based intervention, is effective in reducing mental and behavioural health problems but has not been trialled for effectiveness in improving HIV outcomes. This paper describes the protocol for a randomised trial that is testing the effectiveness of CETA in improving HIV treatment outcomes among women experiencing IPV in South Africa.

Methods and analysis We are conducting a randomised trial among HIV-infected women on antiretroviral therapy, who have experienced sexual and/or physical IPV, to test the effect of CETA on increasing retention and viral suppression and reducing IPV. Women living with HIV who have an unsuppressed viral load or are at high risk for poor adherence and report experiencing recent IPV, defined as at least once within in the last 12 months, will be recruited from HIV clinics and randomised 1:1 to receive CETA or an active attention control (text message reminders). All participants will be followed for 24 months. Follow-up HIV data will be collected passively using routinely collected medical records. HIV outcomes will be assessed at 12 and 24 months post-baseline. Questionnaires on violence, substance use and mental health will be administered at baseline, post-CETA completion and at 12 months post-baseline. Our primary outcome is retention and viral suppression (<50 copies/mL) by 12 months post-baseline. We will include 400 women which will give us 80% power to detect an absolute 21% difference between arms. Our primary analysis will be an intention-to-treat comparison of intervention and control by risk differences with 95% CIs.

Ethics and dissemination Ethics approval provided by University of the Witwatersrand Human Research Ethics Committee (Medical), Boston University Institutional Review Board and Johns Hopkins School Institutional Review Board. Results will be published in peer-reviewed journals.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study uses an approach to improving HIV treatment outcomes for women who are not virally suppressed or at high risk for poor adherence that has already been shown to improve multiple psychosocial, and mental/behavioural health problems including intimate partner violence (IPV) and unhealthy alcohol use.
⇒ The intervention will be implemented using lay cadres of healthcare providers such as community healthcare workers, allowing the approach, if successful and cost effective, to be more likely scalable.
⇒ If effective, the approach could have a strong impact on reaching United Nations Programme on HIV and AIDS 95-95-95 targets by increasing retention in HIV care.
⇒ One main limitation to the study is that we do not have a pure, no intervention control group, which we believe would be unethical given that our study population is exposed to high levels of IPV; instead, our control population will receive an SMS intervention and safety checks.
⇒ The study population will not include women who do not speak one of three languages and women who do not have a cell phone, and this may change the generalisability of the findings slightly.

Trial registration number NCT04242992.

BACKGROUND

An estimated 7 million people are living with HIV in South Africa and over 4 million are accessing antiretroviral therapy (ART).[1] The national ART programme has made impressive gains in terms of reducing morbidity and increasing life expectancy[2–6] but incidence remains high.[7] South Africa has the largest

HIV care and treatment programme in the world, yet progress towards the United Nations Programme on HIV and AIDS (UNAIDS) 95-95-95 targets—95% of infected patients knowing their status, 95% of those on ART and 95% of those virally suppressed—has stalled, especially in the second and third 95s. Recent estimates suggest that South Africa reached 93%–73%–88% of these targets at the end of 2020,[8] with 59% of those living with HIV suppressed, significantly lower than the UNAIDS target of 86%. Poor HIV treatment outcomes reduce the impact of the massive investment in treatment. Therefore, if effective approaches could be found to keep patients on treatment, adhering and virally suppressed, the impact could be substantial.

Most interventions that have been tested to support patients who have struggled to remain adherent on ART have shown limited results.[9] The majority focus on counselling patients on how to adhere to treatment but do not address the many overt or indirect barriers patients face in consistently taking ART. In South Africa, intimate partner violence (IPV), experienced by up to 50% of women, is one major barrier to adherence.[10 11] Addressing IPV is of critical importance by itself and could have large effects in supporting ART adherence.

IPV negatively affects treatment outcomes including adherence and retention in HIV care and is a major barrier to achieving the 95-95-95 goals. Violence is an endemic problem in South Africa, particularly IPV. The link between IPV and negative HIV treatment outcomes has also been established worldwide[10 12] and in South Africa.[11] A study from South Africa found that among young adults, IPV was associated with a five-fold decrease in ART adherence (OR 5.37; 95% CI 1.37 to 21.1), a four-fold increase in depression (OR 4.25; 95% CI 1.64 to 11.0) and a four-fold increase in substance abuse (OR 4.11; 95% CI 1.42 to 11.9).[13] IPV occurs at high rates among HIV-positive women[14–17] and has been found to directly impact HIV outcomes[18] including CD4 counts and viral loads. These studies suggest that achieving 95-95-95 could be strongly supported by addressing IPV.

There is a lack of effective, evidence-based interventions that address multiple, comorbid underlying barriers to successful HIV care and treatment outcomes. Several reviews suggest behavioural interventions directly targeting adherence alone, such as medication reminders, counselling support and contingency management, can improve ART adherence, although the effects are rarely durable.[19–21] Other studies, which have focused on treating one co-occurring mental health issue, such as depression, that correlates with poor ART adherence and retention, show mixed results.[22–24] To date, interventions have been siloed (to treat one disorder only, most commonly depression), and are interventions that do not account for the normal comorbid presentation of individuals such as IPV, substance use and mental health.[18] Approaches that address the multitude of comorbid underlying problems in a way that is unique to each client are urgently needed to reduce negative HIV outcomes.

The Common Elements Treatment Approach[25–29] (CETA) is a modular, flexible, multi-problem intervention specifically designed for low/middle-income country (LMIC) in which task-sharing is used, and providers often have minimal or no formal mental health training. CETA is built to address a wide range of comorbidly occurring problems (reducing the number of treatments needed to scale for a population). The flexibility within CETA allows a provider to give precision-based individualised care related to the problem and severity. The elements (described below) are chosen and ordered with dosing based on scientific research. CETA has a limited number of elements, uses simple language, has a short manual with practical step-sheets and decision rules giving providers and their supervisors flexible choices in element selection, sequencing and dose. CETA has demonstrated strong effect sizes in clinical trials in Iraq,[29] Thailand,[30] Zambia and Colombia.[31]

Addressing violence and comorbid underlying problems rather than simply trying to incentivise retention and viral suppression has stronger potential to impact HIV treatment outcomes. In this paper, we describe the protocol for an evaluation of the CETA to improve HIV treatment outcomes among women experiencing IPV and who have an unsuppressed viral load or at high risk for poor adherence.

METHODS AND ANALYSIS

Patient and public involvement

While no patient was involved in the development of the research question and outcome measures, design of this study and recruitment to the study, we consulted local clinic staff to better understand the potential impact and reception to the intervention as well as to understand the services the clinic provides to women experiencing IPV and mental health issues and the referral process. Our research team has long-standing relationships with the clinics at which we work. Additionally, a Data Safety Monitoring Board (DSMB) is in place and the study team will meet with them regularly prior to and throughout the trial. Prior to the start of the trial, the DSMB and study investigators determined stopping rules due to the high-risk nature of the study population, but no interim analyses will be performed, only safety monitoring. The DSMB reviews adverse events on a quarterly basis and makes recommendations based on the findings. No independent auditing of the trial is done, but IRBs can monitor the study if needed. Results of the study will be communicated back to participants and other key stakeholders via presentations at the study site.

Overview

This is an individually randomised trial comparing the effectiveness of CETA to an mHealth and Safety checks system for improving viral suppression and retention in HIV care among virally unsuppressed women experiencing IPV. The study will be conducted in two or

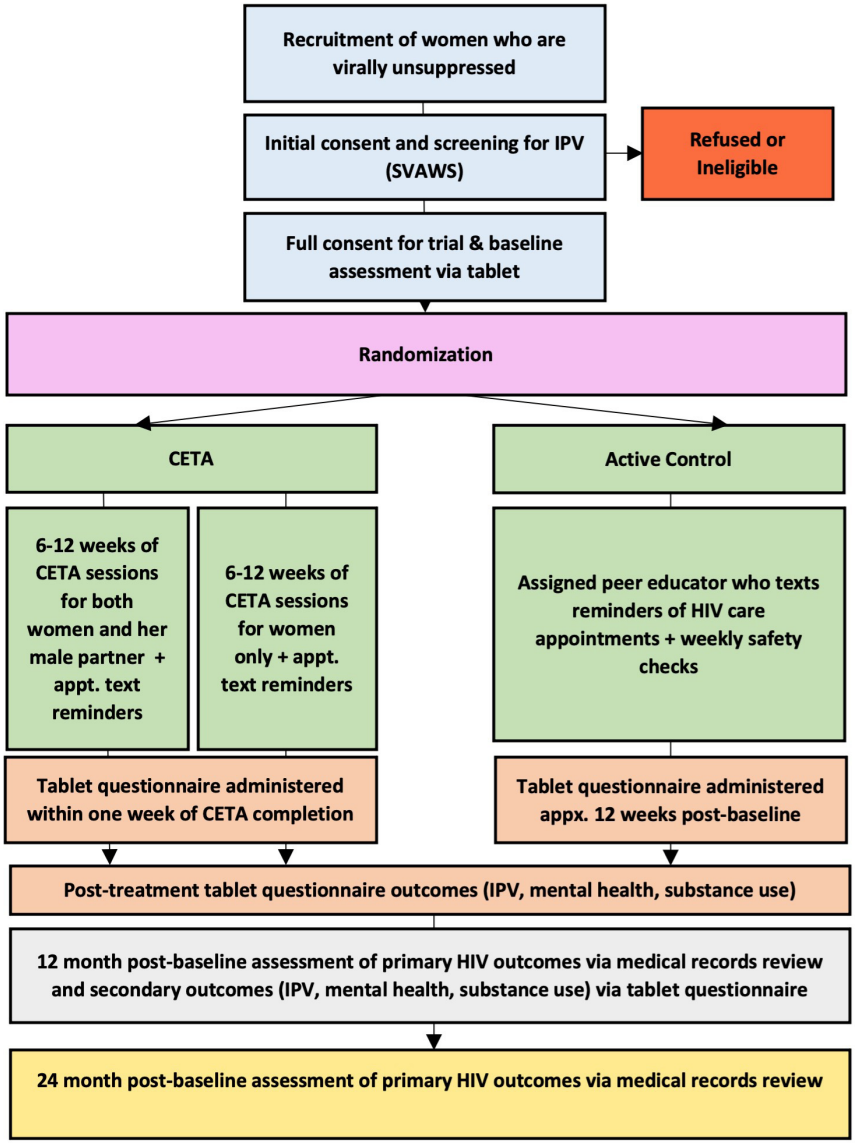

Figure 1 Study flow. CETA, Common Elements Treatment Approach; IPV, intimate partner violence; SVAWS, Severity of Violence Against Women Scale.

more large urban HIV clinics in the Johannesburg area. Currently one is a clinic within secondary and tertiary care and the other is a primary care facility. Study participants will be adult women who are HIV positive, have initiated HIV treatment, whose most recent viral load was unsuppressed or are at high risk for poor adherence, and have experienced IPV. If the woman chooses, we will also enrol their male partners; however, those men will not be included in study outcomes. Participants will be assessed at four time points: baseline, and 3, 12 and 24 months postbaseline. The study flow is shown in figure 1.

Intervention

Our intervention arm will receive CETA. CETA is not a 'new' treatment but rather an *approach* that teaches Cognitive Behavioral Therapy (CBT) elements common to evidence-based treatments. CETA experts will train lay providers using the widely accepted apprenticeship model[32] of 10 days of in-person training, followed by local supervision groups, led by a local supervisor. First, providers (study staff members) are taught to use the evidence-based CBT elements in varying combinations of elements, order and dose to address multiple areas such as violence, substance use, mental or behavioural health problems, and skills deficits that affect HIV care (eg, healthy decision making, adherence). Within the providers, 2–4 are chosen as local supervisors and receive additional training on how to supervise. Following the in-person training, groups of 5–6 providers meet each week with one of the local CETA supervisors for approximately 2 hours to review cases, present problems and decide which treatment elements should be used for each individual. Each local supervisor has weekly calls with CETA trainers for supervision, trouble shooting and further capacity building. This ongoing local supervision and trainer oversight continues throughout the duration of the study to ensure proper oversight and

Table 1 Common Elements Treatment Approach (CETA)

Component	Content	Target
Engagement	Discuss how programme helps, identify obstacles to engagement	Promote client buy in
Safety	Assess client risk or harm to self/others, IPV, abuse; initiate safety planning as needed	Assess/address client safety
Empirically supported cognitive behavioural elements		
Psychoeducation/Introduction	Programme information, normalise symptoms and problems	Psychoeducation; reduce stigma
Substance use reduction	Cognitive behavioral Therapy (CBT) and motivational interviewing (MI) merged to set goals and reduce substance use; identification and strategies for 'drivers' of substance use	Reduce substance use; increase social support
Behavioural activation	Identify and engage in pleasurable activities	Reduce depressive symptoms; activate to engage in helpful programmes (eg, HIV care)
Cognitive coping/ Restructuring	Identify and connect thoughts, feelings and behaviours; replace unhelpful thoughts with helpful ones in order to feel better and behave in a healthier, more productive way	Reduce depressive symptoms, anxiety and trauma-related symptoms; reduce self-blame and stigma; reduce negative thoughts on HIV care; reduce aggressive/violent behaviour; reduce risk taking; improve retention and adherence
Relaxation	Breathing exercises; imagery	Reduce anxiety and stress-related symptoms
Exposure	Talk about trauma memories or face fears using gradual desensitisation	Reduce trauma and anxiety symptoms
Problem solving	Teach a process of steps to solve problems and make healthy decisions	Promote health decision making; skills training for problem solving; improve relationships and communication

IPV, intimate partner violence.

implementation of CETA elements, including safety in both arms. CETA providers work with supervisors to flexibly decide what element(s) (table 1), order and dose are needed depending on presentation.

Female patients randomised to the CETA intervention will meet weekly with a CETA provider for about 1 hour each week, approximately 6–12 times depending on presentation and symptom level. Women enrolled in the study will be invited to include their male partner, but this is not compulsory. If invited, and the male partner chooses to participate, the CETA intervention will be provided to males separately from their partners. There will be no disclosure about reports of IPV from their female partners. Other than tracking the number of sessions the male partner completes, we will not collect outcome data from the men. Our prior CETA research conducted in Zambia has found that male partners engaged extensively in CETA (88% successfully completed CETA).[26] By engaging women and their male partners, CETA led to a significant reduction in experienced IPV both as reported by women (in terms of experiencing IPV) and as reported by men (in terms of perpetrating IPV).[26] Unhealthy alcohol use also reduced significantly in both women and men in that study.[26] Given these previous findings, we thought it important to offer the opportunity to engage with male partners. However, we did not believe it was ethical to exclude women who either did not currently have a male partner or did not want to invite their current male partner to participate. We also believed that not including women without a male partner would limit the reach and generalisability of our findings.

Control

Our comparison arm will be an active control which means healthcare providers will follow normal protocols for those exposed to IPV, but in addition will also receive text reminders of HIV care appointments. The widespread use of mobile phones in LMICs has led to numerous studies investigating how text-messaging can promote adherence and retention or not.[33–36] Despite mixed results, it remains a suggested, low-cost method that may help improve retention and adherence, and thus viral suppression.[37 38] This text messaging activity will also be provided in the CETA arm. Text messages will be discussed with the individual and can be 'in code' and will not include HIV or IPV specific information as we have done in similar studies.[26] This allows women to have check-ins as needed without increased risk. Study staff will receive training on simple example messages (eg, 'Please remember to come to the clinic this Wednesday for your

appointment'.), but actual texts can be personalised. Texts may be anonymised to avoid stigma by leaving out references to the clinic (eg, 'We are looking forward to seeing you Wednesday'.). Messages can also be more covert such as 'Remember to walk Wednesday'. Study staff will SMS patients in both arms for appointment reminders.

Safety for both arms

Due to the population being violence affected, we will need to maintain a safety net for everyone in the study. At enrolment, we will meet individually with each woman to assess their IPV situation and severity. For those that indicate current or ongoing violence, a safety plan will be developed with the participant. All participants will receive a resource pamphlet that contains community resources, 24/7 hotlines and emergency numbers. At enrolment, we will explain that we are going to conduct weekly safety checks that include suicidal ideation and violence questions, and we will ask the woman their preference for receiving safety checks to assure safety and confidentiality. For example, women may suggest a neighbour or family member they trust, and we will agree on a 'code' text that they could explain to others should their phone be shared or lost. Women will additionally receive a general text about their availability to respond prior to sending a safety message or call. We will request multiple ways to contact the women, including alternative contact numbers, obtaining their home addressess and inquiring about the ability to message others, to properly manage safety issues as needed. This procedure was used successfully in a previous trial among women experiencing IPV in Zambia.[26]

For weekly safety check-ins, those in the CETA intervention arm will be asked weekly about the IPV situation during weekly sessions or, if the session is missed, via SMS or the telephone based on their indicated preference at enrolment. Participants' safety plans will be updated, as needed, and participants will have continued access to the resource pamphlet. For those in the Control arm, we will send SMS safety check messages containing three suicide questions and one IPV safety question via two-way SMS weekly during the intervention period (3 months) by study assessors. These questions are: (1) 'Are you thinking of killing yourself?'; (2) 'Do you have a plan to kill yourself?'; (3) 'Do you have the means to kill yourself?' and (4) 'Are you at risk of serious injury or death from interpersonal violence?'. Questions can also be coded to ensure that the question is disguised. The IPV SMS question may be altered to avoid risk if there is concern that a partner or other perpetrator of violence might pick up this message. These same questions are asked weekly for all study participants. If the participant responds 'no' to all safety questions, no action is needed from the study staff. If the participant responds 'yes' to any of the safety questions, the study staff, who will be trained in safety planning, will call the participant to ask additional safety questions to assess risk. If the study staff member determines there is even a minimal risk, a telephone safety contract will be completed, and safety planning will be completed via the telephone. This may include creating a full safety plan or updating the safety plan created at enrolment to help keep the participant safe (either for SI or IPV). When needed, household visits are also conducted. All safety planning is overseen by the local supervisors and expert CETA trainers.

Outcomes, randomisation and sample size

We will randomise participants to CETA or control 1:1 using computer generated block randomisation (generated by the study team in Boston) with allocation generated automatically at the time of completing eligibility. Participants and study team members will not be blinded to which arm they are in. Our primary outcome is the proportion of participants who are retained and virally suppressed by 12 months postrandomisation. We will define the primary outcome to be suppression (ie, a viral load <50 copies/mL) any time up to 18 months after enrolment (to account for variation in the timing of the 12 months viral load). We will use routine clinic data collection to determine outcomes. Secondary outcomes will include: (1) viral suppression at 3 and 24 months; (2) attrition at 12 and 24 months; (3) changes in IPV, post-traumatic stress disorder, Center for Epidemiological Studies-Depression Scale (CES-D), alcohol and other substance use from baseline to 3 and 12 months and (4) cost and cost-effectiveness. The routine clinic data have been used extensively in prior research and has been found to be of high quality and fit for research purposes.[39 40] Further, we have used these data approach for several other clinical trials.[41 42] Details on outcomes are provided in table 2.

We estimate that only 40% of those who are unsuppressed (or at high risk of poor adherence) will be retained in care and virally suppressed 12 months post-baseline in the control arm.[43] We believe a 20 percentage point increase in the proportion suppressed and retained between the CETA and control arms would be clinically meaningful. With 80% power and a two-sided α=0.05, using a χ^2 test for independent proportions our sample size required is 91 per arm (182 total).[26] We increased the sample size to 400 total with a minimum of 75 women in the CETA arm who include partners (up to 100) to allow for assessment of mediation outcomes and other secondary outcomes. We are ensuring reaching our targeted enrolment by increasing the number of study sites if enrolment is less than optimal.

Screening and enrolment

Recruitment will be from large urban HIV clinics in the Johannesburg area and a primary healthcare clinic. The first is a large public-sector HIV treatment site located at a larger an urban secondary-level public sector teaching hospital. Clients receiving care from the clinic are primarily from the Johannesburg area and includes a diverse group of nationalities and low-income clients. An additional study site has also been selected for recruitment. The

Table 2 Primary and secondary outcomes

Outcome	Description
Retained and virally suppressed at 12 months	Viral load testing is routinely done at the clinic at 6 and 12 months post-ART initiation and every 12 months thereafter. Due to the variability in when viral load testing is done, we will define the primary outcome to be suppression (ie, a viral load <50 copies/mL) any time up to 18 months. As our primary outcome includes retention, we are not able to contact patients who miss routine viral loads as this would affect attrition. Instead, we will use routine clinic data collection to determine outcomes. Missing viral loads will be a negative outcome. A combined retention/viral suppression outcome is looked at to better understand the impact of the intervention on both negative outcomes. This is because looking at suppression without considering retention rates only considers the clients retained in care and misses the large proportion of patients who drop out of HIV care
Viral suppression at 3 and 24 months	CETA may have some effects on suppression and retention over the first year of treatment mediated through the increased contact with patients that CETA entails. It is not clear for how long after the CETA intervention effects will be sustained. Thus, we will look at suppression at 24 months, long after CETA is complete. As our population should be monitored for suppression more frequently than every 12 months, we will also examine suppression within 3 months
Attrition at 12 and 24 months	Attrition (the opposite of retention) will be defined as being more than 90 days late for a study visit
IPV, mental/behavioural health, alcohol and other substance use	We will measure the effectiveness of CETA in reducing IPV and stress-related problems commonly associated with IPV and HIV, mental health (trauma, depression, anxiety, post-traumatic stress) and alcohol and substance use. We will also assess whether a change in these factors mediates the effectiveness of CETA on the primary outcome
Cost and cost-effectiveness	We will estimate the incremental cost-effectiveness of CETA vs active control in achieving the primary study outcome, retained in care and virally suppressed by 12 months, from the provider perspective. If found to be effective, a budget impact analysis will be conducted to estimate the affordability of routine implementation of the intervention at scale

ART, antiretroviral therapy; CETA, Common Elements Treatment Approach; IPV, intimate partner violence.

second is a large primary healthcare community health centre located in the west of the Soweto township to the South West of Johannesburg. This clinic offers a range of healthcare services including HIV prevention, care and treatment services. Clients at this secondary site are again predominantly low-income clients and live or stay in the sub-district wards that form the catchment area for this clinic. Initial recruitment will be done by non-study clinic staff who will read a recruitment script to women whom they believe to be virally unsuppressed, and if willing, will refer them to study staff. It is common for clinic staff to know patients that are struggling with high viral load and poor adherence. Patients who agree to be referred to a member of our study team will receive a brief consent form for screening to determine eligibility. The short consent form will explain what questions participants will be asked, including questions related to IPV, as part of the screening process. If consented, the screener form will then be given, which includes the 27-item physical/sexual violence subscale of the Severity of Violence Against Women Scale[44] (SVAWS) to assess IPV exposure. The SVAWS physical/sexual violence subscale will be completed using a self-administered audio computer-assisted self-interviewing (ACASI) tablet-based questionnaire. The system allows responders to both hear questions audially while wearing headphones and read text on the screen in the language of their choice. They are able to navigate and answer sensitive questions privately and discreetly. The use of ACASI in LMIC has been found to elicit more accurate reporting of sensitive behaviours.[45]

For those meeting all inclusion criteria (see table 3), study staff will obtain full informed consent. Consent will cover all remaining study activities (full assessments, randomisation, intervention, data collection, etc). The consent form will include permission to access their clinic records and allow linking study questionnaires to the participant's treatment records.

Baseline and follow-up data collection

There will be four data collection points: baseline, which occurs immediately following screening and informed consent, and 3, 12 and 24 months postbaseline. Electronic medical records will be obtained at all time points to assess our primary outcome. We will assess violence, mental health and substance use at three data collection points: baseline, post-CETA completion (approximately 3 months postbaseline) and again at 12 months postbaseline (figure 1). This will be completed using an ACASI as with the screener and is expected to take approximately 30–45 min. The ACASI will include the following instruments: (1) SVAWS: 46 items assessing frequency of recent IPV; the measure includes a 27-item subscale on physical/sexual violence, which is part of screening as described above (this subscale will not be repeated at baseline as it was completed during screening), as well as a 19-item

Table 3 Inclusion exclusion criteria

Patient inclusion criteria will be	Exclusion criteria will be
Adult HIV-positive women ≥18 years old	Unwilling to complete the informed consent process
Initiated HIV treatmen	Currently psychotic or on unstable psychiatric regimen
Most recent viral load >50 copies/mL, have defaulted from treatment or had a missed or late (>14 days) visit in the last year	Suicide attempt/ideation with intent and plan, and/or self-harm in the past month
Has experienced IPV in the past 12 months	Enrolled in any other intervention study
Has their own phone and can receive text messages	
Literate and able to speak and read one of: English, Zulu, SeSotho	
If including a partner, the woman has disclosed HIV status to the partner that will be invited to participate	

subscale on threatened violence[44]; (2) CES-D: 20 items assessing frequency of depression symptoms over the past week (never, 1–2 days, 3–4 days, 5–7 days)[46]; (3) Harvard Trauma Questionnaire (HTQ): 17 items assessing lifetime traumatic events, 39 items assessing post-traumatic stress symptoms in past week (not at all, a little, quite a bit, extremely)[47] and (4) Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST): a comprehensive assessment of substance use for a range of substance types.[48]

At the baseline visit, we will collect the following information: (1) enrolment Information (eg, national ID (to link records), clinic ID, enrolment date, etc); (2) contact information (eg, phone number, address where they stay, who they share their household with); (3) demographic information (eg, date of birth, sex, socioeconomic data, etc) and (4) HIV-related information (only for women): (eg, initiation date, ART regimen, pharmacy data, lab results, etc). We will use the following data from medical records at baseline and up to 24 months postbaseline to assess primary and secondary outcomes: (1) all visit dates and scheduled visit dates, and reasons; (2) all confirmation HIV tests, CD4, viral load results and dates; (3) date of ART initiation and ART regimen; (4) pharmacy refill records and (5) resource usage: drugs, lab tests, supplies, etc. Resource usage above the level of the individual patient will be obtained from records maintained by the study sites, including routine clinic registers, financial records and management reports. Unit cost data will be obtained national tender documents (eg, drug costs), published government salary scales, state price lists (eg, laboratory tests) and other relevant financial and procurement records pertaining to the study.

Data management

All study data will be kept in a password-protected database with identifiers removed. Data collected will be electronically transferred from the field devices into the study database at the Health Economics and Epidemiology Research Office (HE^{2}RO) offices daily. Data on the devices will then be permanently deleted. Intervention data will include: (1) dates, times and SMS messages sent for both arms; (2) attendance at CETA sessions; (3) weekly checks of symptom severity (eg, substance use, mental health); (4) clinical notes recorded after each session by the peer educator and (5) responses to the weekly safety questions and any additional notes on safety. To assess symptom severity, a client monitoring form is used during the weekly CETA sessions to track any changes in symptom severity among CETA participants.

Electronic data files will be stored on secure, protected drives at the HE^{2}RO in Johannesburg and at the US sites, with access limited to relevant study staff. All participants will be assigned an identification number used to identify individual participants in the study databases and for all data analysis. An electronic linking file will be created to link this information to a patient ID number. We will also link data from women with any data from their participating male partner through their study IDs.

Data analysis

All primary analyses will be by intention-to-treat. The unit of analysis will be the woman. Our primary analysis will be a comparison of risk differences with 95% CIs. If we identify differences in baseline covariates, we will conduct an adjusted linear regression to get an adjusted risk difference. We will analyse direct effects of CETA on continuous secondary outcomes (eg, IPV, mental health and substance use) using linear mixed models. For our continuous secondary outcomes (SVAWS, CES-D, HTQ and ASSIST), a total sum score will be constructed for each survey. The distributions of the scores will be inspected for normality and if needed will be converted to standardised z-scores. Fixed effects will include treatment arm, duration of follow-up, and arm by time interactions. Random effects will include participant ID to account for repeat measures. We will calculate robust standard errors. The models will estimate the difference in mean symptom change from baseline to each postbaseline assessment between the treatment groups. The difference in mean change will be standardised to calculate Cohen's d effect size. As in previous CETA trials, we will consider clinically meaningful effect size[49 50] to be small (d=0.2), medium (d=0.5) and large (d=0.8) based on guidelines suggested

by Cohen.[51] This will facilitate comparisons to CETA trials in other populations and comparisons to other interventions among a similar population (women with HIV and have experienced IPV). Additionally, we will analyse the effectiveness of CETA in a subgroup of women who have a male partner that successfully completed CETA to better understand the impact male partner involvement may have.

A per-protocol analysis will be conducted that includes only participants who successfully completed CETA (ie, the participant was considered to have completed all necessary CETA sessions deemed required by the counsellor and clinical supervisors).

A standard cost-effectiveness analysis will be done from the provider perspective with the study primary outcome at 12 months used as the measure of effectiveness and compared with the control arm.[52] Cost estimation will follow the reference case for estimating the cost of global health interventions, where appropriate.[53]

Limitations

The main limitation of the study is that we lack a pure control group as asking safety questions related to IPV and suicide is an intervention beyond treatment-as-usual. We considered a three-arm trial so that we could have a true control group; however, it is unethical to not provide safety check-ins to participants experiencing IPV. The other main limitation is that we will not be collecting any data on the men. We have also limited the study population to women who own a cell phone (for safety reasons) and to those who speak one of the three main languages spoken in the area, which may limit generalisability. No patients or the public were involved in design, conduct or reporting of the research.

ETHICS AND DISSEMINATION

The study protocol has been approved by the University of the Witwatersrand Human Research Ethics Committee (Medical), the Boston University Insitiutional Review Board (H-39746) and the Johns Hopkins School of Public Health Institutional Review Board (12546). The study was approved as non-human subjects by the Columbia University Institutional Review Board (AAAS9661). Written informed consent will be obtained from all study participants prior to enrolment by study staff. Protocol changes are approved by the IRBs and critical changes are reported to the trial registry. Results will be published in peer-reviewed journals and presented at international conferences. Participants will be reimbursed for completing the baseline and follow-up surveys and for travel costs for CETA. The authors declare no competing interests and there are no contractual agreements limiting access to the data. Authorship is decided by contributions to the work and no professional writers will be involved.

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Funding Research reported in this publication is supported by the National Institute of Mental Health of the National Institutes of Health under award number R01MH121998. LCL is supported by the National Institute of Mental Health of the National Institutes of Health under grant number K01MH119923. JK's contribution is supported in part by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) under grant number K01AA026523. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

1 Kaplan SR, Oosthuizen C, Stinson K, *et al*. Contemporary disengagement from antiretroviral therapy in Khayelitsha, South Africa: a cohort study. *PLoS Med* 2017;14:e1002407.
2 Fox MP, Shearer K, Maskew M, *et al*. Treatment outcomes after 7 years of public-sector HIV treatment. *AIDS* 2012;26:1823–8.
3 Johnson LF, Mossong J, Dorrington RE, *et al*. Life expectancies of South African adults starting antiretroviral treatment: collaborative analysis of cohort studies. *PLoS Med* 2013;10:e1001418.
4 Boulle A, Van Cutsem G, Hilderbrand K, *et al*. Seven-Year experience of a primary care antiretroviral treatment programme in Khayelitsha, South Africa. *AIDS* 2010;24:563–72.
5 Fatti G, Meintjes G, Shea J, *et al*. Improved survival and antiretroviral treatment outcomes in adults receiving community-based adherence support: 5-year results from a multicentre cohort study in South Africa. *J Acquir Immune Defic Syndr* 2012;61:50–8.
6 Bor J, Herbst AJ, Newell M-L, *et al*. Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment. *Science* 2013;339:961–5.
7 Human Sciences Research Council. *Hiv impact assessment summary: the fifth South African national HIV prevalence, incidence,*

behavior and communication survey, 2017. Pretoria, South Africa, 2018.
8 Phokojoe M. South Africa update presentation to CQUIN network. Available: https://cquin.icap.columbia.edu/wp-content/uploads/2020/12/NDOH-FINAL-4th-CQUIN-Annual-Meeting_MOH-South-Africa-24-NOV-2020.pdf
9 Bärnighausen T, Chaiyachati K, Chimbindi N, *et al*. Interventions to increase antiretroviral adherence in sub-Saharan Africa: a systematic review of evaluation studies. *Lancet Infect Dis* 2011;11:942–51.
10 Andersson N, Cockcroft A, Shea B. Gender-Based violence and HIV: relevance for HIV prevention in hyperendemic countries of southern Africa. *AIDS* 2008;22 Suppl 4:S73–86.
11 Abdool Karim Q, Baxter C. The dual burden of gender-based violence and HIV in adolescent girls and young women in South Africa. *S Afr Med J* 2016;106:1151–2.
12 Schafer KR, Brant J, Gupta S, *et al*. Intimate partner violence: a predictor of worse HIV outcomes and engagement in care. *AIDS Patient Care STDS* 2012;26:356–65.
13 Kidman R, Violari A. Dating violence against HIV-infected youth in South Africa. *J Acquir Immune Defic Syndr* 2017;77:64–71.
14 Machtinger EL, Wilson TC, Haberer JE, *et al*. Psychological trauma and PTSD in HIV-positive women: a meta-analysis. *AIDS Behav* 2012;16:2091–100.
15 Zierler S, Cunningham WE, Andersen R, *et al*. Violence victimization after HIV infection in a US probability sample of adult patients in primary care. *Am J Public Health* 2000;90:208–15.
16 Campbell JC, Baty ML, Ghandour RM, *et al*. The intersection of intimate partner violence against women and HIV/AIDS: a review. *Int J Inj Contr Saf Promot* 2008;15:221–31.
17 Groves AK, Reyes HLM, Moodley D, *et al*. Hiv positive diagnosis during pregnancy increases risk of IPV postpartum among women with no history of IPV in their relationship. *AIDS Behav* 2018;22:1750–7.
18 Kane JC, Vinikoor MJ, Haroz EE, *et al*. Mental health comorbidity in low-income and middle-income countries: a call for improved measurement and treatment. *Lancet Psychiatry* 2018;5:864–6.
19 Amico KR, Harman JJ, Johnson BT. Efficacy of antiretroviral therapy adherence interventions: a research synthesis of trials, 1996 to 2004. *Journal of Acquired Immune Deficiency Syndromes: JAIDS* 2006;41:285–97.
20 Simoni JM, Pearson CR, Pantalone DW, *et al*. Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials. *J Acquir Immune Defic Syndr* 2006;43 Suppl 1:S23–35.
21 Bärnighausen T, Bor J, Wandira-Kazibwe S, *et al*. Interviewer identity as exclusion restriction in epidemiology. *Epidemiology* 2011;22:446.
22 Sikkema KJ, Mulawa MI, Robertson C, *et al*. Improving AIDS care after trauma (impact): pilot outcomes of a coping intervention among HIV-infected women with sexual trauma in South Africa. *AIDS Behav* 2018;22:1039–52.
23 Abas M, Nyamayaro P, Bere T, *et al*. Feasibility and acceptability of a Task-Shifted intervention to enhance adherence to HIV medication and improve depression in people living with HIV in Zimbabwe, a low income country in sub-Saharan Africa. *AIDS Behav* 2018;22:86–101.
24 Chaiyachati KH, Ogbuoji O, Price M, *et al*. Interventions to improve adherence to antiretroviral therapy: a rapid systematic review. *AIDS* 2014;28 Suppl 2:S187–204.
25 Murray LK, Dorsey S, Haroz E, *et al*. A common elements treatment approach for adult mental health problems in low- and middle-income countries. *Cogn Behav Pract* 2014;21:111–23.
26 Kane JC, Skavenski Van Wyk S, Murray SM, *et al*. Testing the effectiveness of a transdiagnostic treatment approach in reducing violence and alcohol abuse among families in Zambia: study protocol of the violence and alcohol treatment (VATU) trial. *Glob Ment Health* 2017;4:1–15.
27 Murray LK, Hall BJ, Dorsey S, *et al*. An evaluation of a common elements treatment approach for youth in Somali refugee camps. *Glob Ment Health* 2018;5:e16.
28 Bolton P, Lee C, Haroz EE, *et al*. Transdiagnostic community-based mental health treatment for comorbid disorders: development and outcomes of a randomized controlled trial among Burmese refugees in Thailand. *PLoS Med*.
29 Weiss WM, Murray LK, Zangana GAS, *et al*. Community-Based mental health treatments for survivors of torture and Militant attacks in southern Iraq: a randomized control trial. *BMC Psychiatry* 2015;15:249.
30 Bolton P, Lee C, Haroz EE, *et al*. A transdiagnostic community-based mental health treatment for comorbid disorders: development and outcomes of a randomized controlled trial among Burmese refugees in Thailand. *PLoS Med* 2014;11:e1001757.
31 Bonilla-Escobar FJ, Fandiño-Losada A, Martínez-Buitrago DM, *et al*. A randomized controlled trial of a transdiagnostic cognitive-behavioral intervention for Afro-descendants' survivors of systemic violence in Colombia. *PLoS One* 2018;13:e0208483.
32 Murray LK, Dorsey S, Bolton P, *et al*. Building capacity in mental health interventions in low resource countries: an apprenticeship model for training local providers. *Int J Ment Health Syst* 2011;5:30.
33 Mbuagbaw L, Thabane L, Ongolo-Zogo P. The Cameroon mobile phone SMS (camps) trial: a randomized trial of text messaging versus usual care for adherence to antiretroviral therapy. *PLoS One* 2012;7:6–12.
34 Pop-Eleches C, Thirumurthy H, Habyarimana JP, *et al*. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. *AIDS* 2011;25:825–34.
35 Burton J, Brook G, McSorley J, *et al*. The utility of short message service (SMS) texts to remind patients at higher risk of STIs and HIV to reattend for testing: a controlled before and after study. *Sex Transm Infect* 2014;90:11–13.
36 Rana Y, Haberer J, Huang H, *et al*. Short message service (SMS)-based intervention to improve treatment adherence among HIV-positive youth in Uganda: focus group findings. *PLoS One* 2015;10:1–14.
37 Marko-Holguin M, Cordel SL, Van Voorhees BW, *et al*. A two-way interactive text messaging application for low-income patients with chronic medical conditions: Design-thinking development approach. *JMIR Mhealth Uhealth* 2019;7:e11833.
38 Chiang N, Guo M, Amico KR, *et al*. Interactive two-way mHealth interventions for improving medication adherence: an evaluation using the behaviour change wheel framework. *JMIR Mhealth Uhealth* 2018;6:e87.
39 Fox MP, Maskew M, MacPhail AP, *et al*. Cohort profile: the Themba Lethu clinical cohort, Johannesburg, South Africa. *Int J Epidemiol* 2013;42:430–9.
40 Fox MP, Maskew M, Brennan AT. Cohort profile: the right to care clinical HIV cohort, South Africa. *BMJ Open* 2017;7.
41 Rosen S, Maskew M, Fox MP. Initiating Antiretroviral Therapy for HIV at a Patient's First Clinic Visit: The RapIT Randomized Controlled Trial. *PLoS Med*2016;13.
42 Maskew M, Brennan AT, Fox MP, *et al*. A clinical algorithm for same-day HIV treatment initiation in settings with high TB symptom prevalence in South Africa: the Slate II individually randomized clinical trial. *PLoS Med* 2020;17:e1003226.
43 Fox MP, Pascoe SJS, Huber AN, *et al*. Effectiveness of interventions for unstable patients on antiretroviral therapy in South Africa: results of a cluster-randomised evaluation. *Trop Med Int Health* 2018;23:1314–25.
44 Marshall LL. Development of the severity of violence against women scales. *J Fam Violence* 1992;7:103–21.
45 Langhaug LF, Sherr L, Cowan FM. How to improve the validity of sexual behaviour reporting: systematic review of questionnaire delivery modes in developing countries. *Trop Med Int Health* 2010;15:362–81.
46 Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1:385–401.
47 Mollica RF, Caspi-Yavin Y, Bollini P, *et al*. The Harvard trauma questionnaire. validating a cross-cultural instrument for measuring torture, trauma, and posttraumatic stress disorder in Indochinese refugees. *J Nerv Ment Dis* 1992;180:111–6.
48 Humeniuk R, Ali R, Babor TF, *et al*. Validation of the alcohol, smoking and substance involvement screening test (assist). *Addiction* 2008;103:1039–47.
49 Tsai AC, Tomlinson M, Comulada WS, *et al*. Intimate partner violence and depression symptom severity among South African women during pregnancy and postpartum: population-based prospective cohort study. *PLoS Med* 2016;13:e1001943.
50 Hatcher AM, Gibbs A, McBride R-S, *et al*. Gendered syndemic of intimate partner violence, alcohol misuse, and HIV risk among peri-urban, heterosexual men in South Africa. *Soc Sci Med* 2022;295:112637.
51 Cohen J. *Statistical power analysis for the behavioral sciences*. New York, NY: Routledge Academic, 1988.
52 Drummond M, Schulpher M, Claxton K, *et al*. *Methods for the economic evaluation of health care programs*. Fourth Edi.. Oxford University Press,, 2015.
53 Vassall A, Sweeney S, Kahn J. *Reference case for estimating the costs of global health services and interventions*, 2017.