

SHORT REPORT

Project Khanya: results from a pilot randomized type 1 hybrid effectiveness-implementation trial of a peer-delivered behavioural intervention for ART adherence and substance use in HIV care in South Africa

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Abstract

Introduction: South Africa (SA) has the highest number of people living with HIV (PLWH) globally, and a significant burden of alcohol and other drug use (AOD). Although integrating AOD treatment into HIV care may improve antiretroviral therapy (ART) adherence, this is not typically routine practice in SA or other low-resource settings. Identifying interventions that are feasible and acceptable for implementation is critical to improve HIV and AOD outcomes.

Methods: A pilot randomized hybrid type 1 effectiveness-implementation trial ($N = 61$) was conducted to evaluate the feasibility and acceptability of *Khanya*, a task-shared, peer-delivered behavioral intervention to improve ART adherence and reduce AOD in HIV care in SA. *Khanya* was compared to enhanced treatment as usual (ETAU), a facilitated referral to on-site AOD treatment. Implementation outcomes, defined by Proctor's model, included feasibility, acceptability, appropriateness and fidelity. Primary pilot effectiveness outcomes were ART adherence at post-treatment (three months) measured via real-time electronic adherence monitoring, and AOD measured using biomarker and self-report assessments over six months. Data collection was conducted from August 2018 to April 2020.

Results and discussion: Ninety-one percent of participants ($n = 56$) were retained at six months. The intervention was highly feasible, acceptable, appropriate and delivered with fidelity (>90% of components delivered as intended by the peer). There was a significant treatment-by-time interaction for ART adherence (estimate = -0.287 [95% CI = $-0.507, -0.066$]), revealing a 6.4 percentage point increase in ART adherence in *Khanya*, and a 22.3 percentage point decline in ETAU. Both groups evidenced significant reductions in alcohol use measured using phosphatidylethanol (PEth) ($F(2,101) = 4.16, p = 0.01$), significantly decreased likelihood of self-reported moderate or severe AOD ($F(2,104) = 7.02, p = 0.001$), and significant declines in alcohol use quantity on the timeline follow-back ($F(2,102) = 21.53, p < 0.001$). Among individuals using drugs and alcohol, there was a greater reduction in alcohol use quantity in *Khanya* compared to ETAU over six months ($F(2,31) = 3.28, p = 0.05$).

Conclusions: Results of this pilot trial provide initial evidence of the feasibility and acceptability of the *Khanya* intervention for improving adherence in an underserved group at high risk for ongoing ART non-adherence and HIV transmission. Implementation results suggest that peers may be a potential strategy to extend task-sharing models for behavioral health in resource-limited, global settings.

Keywords: HIV; substance use; antiretroviral therapy adherence; global mental health; implementation science; South Africa

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

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1 | INTRODUCTION

South Africa (SA) is home to the largest number of people living with HIV (PLWH) globally [1]. Despite a large antiretroviral therapy (ART) programme, limited ART regimens are readily available in the public health sector [2]. ART non-adherence

increases the risk of developing drug resistance and treatment failure, contributing to ongoing viral transmission, morbidity and mortality [3,4].

Alongside the HIV epidemic, alcohol and other drug use (AOD) are highly prevalent among PLWH in SA [5,6]. Individuals with AOD are at greater risk for poor ART adherence, viral

non-suppression, and ongoing HIV transmission [7-14]. Integrating AOD treatment into HIV care can improve ART adherence, yet this is not typically routine practice in SA or other low-resource settings [15-17]. Furthermore, ART adherence interventions are rarely adapted for AOD – a missed opportunity for maximizing HIV treatment outcomes [18-23].

We conducted a hybrid type 1 effectiveness-implementation [24] pilot study to evaluate the feasibility, acceptability, appropriateness and fidelity of a peer-delivered intervention (“*Khanya*”), and preliminarily examine whether *Khanya* was associated with improvements in ART adherence over three months and AOD over six months versus enhanced treatment as usual (ETAU) [25,26].

2 | METHODS

2.1 | Recruitment and screening

Individuals were recruited between August 2018 and October 2019 from HIV care in Khayelitsha, a community with the highest HIV prevalence in the Western Cape [27]. Inclusion criteria were as follows: (1) HIV positive and on ART; (2) 18 to 65 years old; (3) at least moderate AOD on the WHO Alcohol, Smoking, and Substance Involvement Screening Test (WHO-ASSIST [28]); (4) ART non-adherence in the past three months, defined by either: (a) missing a pharmacy refill; (b) reinitiating first-line treatment or being on second-line treatment or (c) having unsuppressed viral load (≥ 400 copies/mL). Exclusion criteria were as follows: (1) high-risk opiate or alcohol use warranting medical management; (2) untreated major mental illness; (3) inability to provide informed consent or speak English or isiXhosa; (4) third-trimester pregnancy or (5) currently enrolled in AOD treatment. Eligible and interested participants completed informed consent and baseline assessments. Participants were given a Wisepill device [29] to monitor ART adherence over two weeks. At two-weeks post-baseline, participants were randomly assigned in parallel (1:1) to ETAU or *Khanya* using Research Electronic Data Capture (REDCap). Participants were assessed by a trained, blinded assessor at three- and six-month post-baseline. Participants received a 150ZAR (approximately \$10 USD) grocery voucher for completing study assessments. All procedures were approved by the University of Cape Town Health Sciences Faculty Human Research Ethics Committee (HREC 187/2018). Magidson *et al.*[30] includes full protocol details.

2.2 | Allocation groups

2.2.1 | *Khanya*

Khanya is a six-session peer-delivered behavioral intervention that integrates several evidence-based intervention components [31-34] – behavioral activation, problem solving, motivational interviewing and mindfulness-based relapse prevention – adapted during formative work preceding this trial [35,36]. The intervention aims to support increased ART adherence and individualized goal setting for AOD reduction by teaching evidence-based behavioral skills (i.e. behavioral monitoring, activity scheduling, mindfulness practice, relapse prevention) to support the attainment of these goals. Home practice is assigned between sessions to reinforce skills. Real-time

electronic adherence monitoring is discussed in session in relation to skill practice to address barriers to adherence and relapse prevention. Participants are offered up to six optional booster sessions to further reinforce skills. Participants were not compensated for intervention sessions but travel costs were reimbursed. Sessions lasted approximately 60 minutes. The interventionist was a peer – an individual with lived AOD experience – paid full-time as part of the research team, trained and supervised by clinical psychologists. Intervention, supervision and training details are provided elsewhere [30,37].

2.2.2 | Enhanced treatment as usual

TAU for individuals with AOD in this context is a referral letter to Matrix [38,39], an evidence-based, co-located 16-week AOD programme that includes an initial screening and brief intervention session [25,26]. We enhanced TAU by discussing the referral to Matrix, offering to accompany participants to the intake if they wished, and following up on referral uptake at subsequent visits.

2.3 | Measures

Implementation outcomes were guided by Proctor’s model [40], including feasibility, acceptability, appropriateness and fidelity. *Feasibility* and *acceptability* were assessed based on uptake (percentage who initiated the intervention and session attendance respectively) and a validated quantitative measure was used for assessing implementation outcomes in Low-and-middle-income countries (LMICs) [41], including feasibility, acceptability and appropriateness (ratings on a four-point scale: 0 = “not at all”; 3 = “a lot”). *Fidelity*. A randomly selected 20% of *Khanya* sessions were rated by the interventionist and an independent coder (trained in fidelity monitoring and not involved in this study) following best practices and other studies examining fidelity of task-shared interventions [42]. A 15 to 19 item (depending on session) checklist of core session components was developed a priori. The independent coder also rated common factors (i.e. verbal communication, self-disclosure, normalization, empathy) using the ENhancing Assessment of Common Therapeutic factors (ENACT; 1 to 3 rating scale) [43].

ART adherence was assessed from baseline (past two weeks) through post-treatment (approximately three months) using Wisepill, a real-time adherence monitoring device [29]. Adherence was measured as the percentage of days’ adherent from baseline to the week prior to post-treatment. Observations, where the device battery was dysfunctional, were excluded.

AOD was assessed using biomarker and self-report at baseline, three months and six months. *Phosphatidylethanol* (PEth) testing was conducted from dried blood spots (≥ 50 ng/mL reflects unhealthy drinking up to 21 days [44]). *Urinalysis* assessed cocaine, marijuana, amphetamines, opiates, phencyclidine and alcohol (<80 hours; 300 ng/mL; [45,46]), and methaqualone (Mandrax), a local sedative. The WHO-ASSIST assessed past three-month self-reported AOD [28] using defined risk categories (*alcohol*: ≥ 27 high risk; 11 to 26 moderate; 0 to 10 low; *drugs*: ≥ 27 high risk; 4 to 26 moderate; 0 to 3 low). The *Timeline Follow-Back* (TLFB) [47], a calendar-aided assessment of AOD, assessed the quantity of alcohol

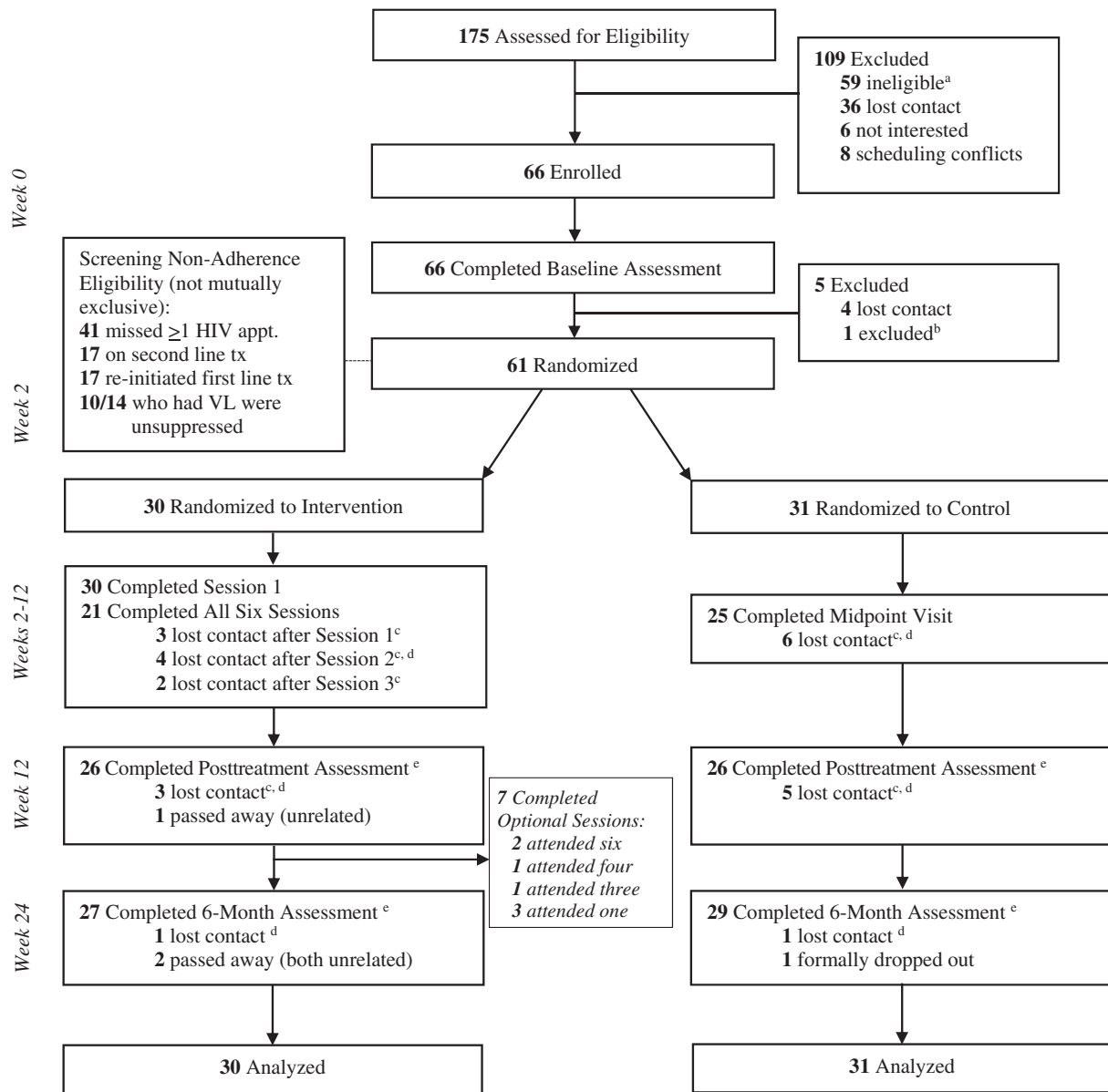


Figure 1. Consort diagram.^aWHO-ASSIST too low only (n = 54); not struggling with adherence only (n = 1); WHO-ASSIST too low and not struggling with adherence (n = 1); undertreated major mental illness (n = 2); incomplete screening (n = 1). ^b1 participant excluded pre-randomization for severe alcohol dependence (medical management of withdrawal symptoms needed). ^cParticipants uncontactable for specific event, but attended later events. ^d1 participant was uncontactable for remainder of study. ^eDue to staffing resource restraints, only 36/52 assessments were blinded at post-treatment (69%), and only 19/56 assessments were blinded at six-month follow-up (34%).

use in the past two weeks and the percentage of days used (any substance). Recall was aided by the use of empty, locally recognizable alcohol containers.

Viral load (exploratory) was extracted from medical records (within three months before baseline, 30 days of follow-ups) or drawn and tested by the National Health Laboratory Service when unavailable. Viral suppression was defined as <400 copies/mL per local clinic standards.

2.4 | Data analytic plan

This pilot study aimed to establish the feasibility and acceptability of *Khanya*, examined using descriptive statistics (means

and standard deviations) of implementation outcomes. The study sample size followed recommendations for pilot studies [48,49]. Effectiveness outcomes were examined using multi-level modelling to account for repeated measurements [50]. Time was treated categorically to capture differing rates of change between time points, and all models included a random intercept. Analyses used an intent-to-treat framework [51], including all available data. Missing data were treated as missing at random. All analyses were run using SAS version 9.4 [52]. Presented models were adjusted for baseline age and gender, determined a priori [30], and observed baseline differences in theoretically relevant factors (relationship status, viral suppression and substance use severity). As

Table 1. Baseline demographic and clinical characteristics of sample by treatment group

Characteristic	Total sample (N = 61)	Khanya (n = 30)	ETAU (n = 31)
Age, M (SD)	37.00 (9.63)	39.80 (10.47)	34.29 (7.99)
% Female (n)	54.1 (33)	43.3 (13)	64.5 (20)
% Graduated high school or above (n)	23.0 (14)	26.7 (8)	19.4 (6)
% Casual or full-time employment (n)	21.3 (13)	13.3 (4)	29.0 (9)
% Married or common-law (n)	26.2 (16)	10.0 (3)	41.9 (13)
HIV characteristics			
Years since HIV diagnosis, M (SD)	6.27 (4.87)	7.14 (5.97)	5.43 (3.39)
% Suppressed viral load (<400 copies/mL) (n)	63.9 (39)	50.0 (15)	77.4 (24)
CD4 count	376 (253)	330 (210)	420 (285)
% Days adherent via Wisepill over two weeks, M (SD) ^a	51.4 (30.7)	53.6 (32.1)	49.3 (29.7)
% On second-line (n) ^b	26.7 (16)	24.1 (7)	29.0 (9)
Substance use characteristics			
% Positive alcohol urine test (n)	88.5 (54)	86.7 (26)	90.3 (28)
% PEth unhealthy drinking (n)	83.6 (51)	90.0 (27)	77.4 (24)
WHO-ASSIST alcohol score, M (SD) ^c	25.66 (6.88)	25.93 (6.70)	25.39 (7.16)
% Days consumed any substance on TLFB, M (SD)	34.1 (23.5)	38.8 (24.6)	29.5 (21.7)
% Days consumed alcohol on TLFB, M (SD)	30.3 (21.0)	37.1 (22.9)	23.7 (16.9)
Average number of drinks on days drinking on TLFB, M (SD)	7.60 (4.75)	7.17 (3.79)	8.03 (5.59) ^d
% Positive (any) drug urine test (n)	31.2 (19)	40.0 (12)	22.6 (7)
WHO-ASSIST (any) drug score, M (SD) ^e	13.10 (9.47)	9.25 (6.34)	15.67 (10.84)
% Days consumed other drugs on TLFB, M (SD) ^f	39.8 (26.0)	47.6 (35.9)	33.9 (19.7)

^aData from randomization visit; ^bn = 29 for Khanya arm; ^cdata from screening visit; ^dn = 30; ^escore for those who reported using substance in past 3 months (N = 11 WHO ASSIST scores from 10 participants, n = 4 Khanya arm, n = 7 ETAU arm); ^fCannabis was the only substance reported at this assessment; n = 3 for Khanya arm, n = 4 or ETAU arm. TLFB, Timeline Follow-Back; SD, Standard deviation

sensitivity analyses, models were re-run without covariates and with age and gender only. Models were also run with time treated continuously and a random slope. The pattern of results for sensitivity analyses did not differ. We also examined all results separately for a subsample who also used drugs in the past three months (n = 21). See supplemental materials for the more detailed data analytic plan.

3 | RESULTS AND DISCUSSION

3.1 | Participants

A total of N = 61 participants were enrolled and randomized; see Figure 1 for consort diagram. The sample was largely Black African and 54% female. Individuals were ART adherent 51.4% of days over two weeks at baseline, over 80% had unhealthy drinking, and approximately one-third had current drug use. Table 1 includes baseline characteristics, and Table 2 includes all outcomes by treatment group by time point.

3.2 | Outcomes

3.2.1 | Implementation outcomes

Although AOD treatment utilization is typically low in SA [53], treatment uptake was high in this sample. Of the participants randomized to *Khanya*, 100% initiated the intervention, and 70% attended all six sessions (M = 4.77; SD = 1.96); 88% of *Khanya* participants reported satisfaction with the number of

treatment sessions. Feasibility, acceptability and appropriateness of *Khanya* were rated very highly (feasibility: M = 2.98; SD = 0.18; acceptability: M = 2.98; SD = 0.04; appropriateness: M = 2.94, SD = 0.09). For ETAU, 80.6% (n = 25) attended the Matrix referral, of whom 68% (n = 17) attended only one session (range 0 to 11). Interventionist self-reported fidelity was 96.5% (SD = 7.2) for *Khanya*; average independent rater fidelity was 91.7% (SD = 13.3). Peer therapeutic common factors, such as warmth and non-judgement, were rated highly using ENACT (M = 2.69; SD = 0.28).

3.2.2 | Effectiveness outcomes

Overall model results for all effectiveness outcomes are presented in Table 3. Drug subsample results for all outcomes are in Tables S1-S6.

ART adherence

There was a significant treatment-by-time interaction (estimate = -0.287 [95% CI = -0.507, -0.066]), such that ETAU's pre-post treatment change in days' adherent was 28 percentage points lower than *Khanya*. Average adherence increased 6.4 percentage points in *Khanya*, whereas adherence declined by 22.3 percentage points in ETAU (see Figure S1).

Although the study was focused on implementation, the fact that we saw large effects on behavioral adherence in this small sample is noteworthy. Improving ART adherence among individuals with AOD is a known challenge [15]. Interventions to enhance adherence are critical for improving individual HIV outcomes and supporting treatment as prevention.

Table 2. Sample means and percentages for primary outcomes at assessment time points by treatment group

Outcome measure	Khanya			ETAU		
	Baseline (N = 30)	Three-month (N = 26)	Six-month (N = 27)	Baseline (N = 31)	Three-month (N = 26)	Six-month (N = 29)
% Days adherent via Wisepill, M (SD)	53.6 (32.1) ^a	60.0 (37.1) ^b	–	49.3 (29.8)	28.2 (32.1) ^c	–
% (n) suppressed viral load, <400 copies/mL	50.0 (15)	65.4 (17)	59.3 (16)	77.4 (24)	73.1 (19)	75.9 (22)
PEth score, M (SD)	686.0 (639.9)	484.2 (398.7)	538.4 (554.4) ^d	456.1 (530.8)	414.7 (389.6) ^d	386.1 (392.6)
% Positive alcohol or drug urine test (n)	90.0 (27)	96.2 (25)	83.3 (20)	93.6 (29)	88.5 (23)	82.8 (24)
% Moderate or high risk on WHO-ASSIST	100 (30)	88.5 (23)	88.9 (24)	100 (31)	96.2 (25)	75.9 (22)
% Days consumed any substance on TLFB, M (SD)	38.8 (24.6)	29.1 (24.6)	30.7 (25.9)	29.5 (21.7)	24.5 (20.2)	25.1 (23.2)
Average number of drinks on days drinking on TLFB, M (SD)	7.17 (3.79)	5.36 (3.84)	4.61 (3.29)	8.03 (5.59) ^e	5.47 (3.77) ^d	4.96 (4.25)

^an = 29; ^bn = 28; ^cn = 27; ^dn = 25; ^en = 30. SD, standard deviation; TLFB, Timeline Follow-Back

Table 3. Overview of all model results by time and time by treatment interaction

Effect	Time only (effect of Khanya on outcome)				Time by Treatment (effect of ETAU on outcome)			
	Estimate (SE) or DF	95% CI	F or t	p	Estimate (SE) or DF	95% CI	F or t	p
Wisepill adherence	–	–	–	–	–	–	–	–
PT	0.064 (0.078)	[–0.092, 0.220]	0.82	0.41	–0.287 (0.110)	[–0.507, –0.066]	–2.61	0.01
FU	–	–	–	–	–	–	–	–
PEth	2, 101	–	4.16	0.01	2, 101	–	0.97	0.38
PT	–227 (80)	[–385, –69]	–2.85	0.005	157 (113)	[–67, 382]	1.39	0.16
FU	–169 (81)	[–329, –9]	–2.09	0.03	84 (111)	[–136, 304]	0.76	0.44
Alcohol/drug urine test	2, 101	–	1.67	0.19	2, 101	–	0.59	0.55
PT	–1.14 (1.36)	[–3.85, 1.56]	–0.84	0.40	1.95 (1.79)	[–1.61, 5.50]	1.09	0.27
FU	0.80 (1.04)	[–1.26, 2.87]	0.77	0.44	0.71 (1.49)	[–2.24, 3.67]	0.48	0.63
Categorical ASSIST	2, 104	–	7.02	0.001	2, 104	–	0.10	0.90
PT	–1.35 (0.67)	[–2.67, –0.03]	–2.03	0.04	0.25 (0.89)	[–1.51, 2.00]	0.28	0.77
FU	–1.68 (0.66)	[–2.98, –0.37]	–2.55	0.01	–0.14 (0.87)	[–1.85, 1.58]	–0.16	0.87
TLFB average drinks	2, 102	–	21.53	<0.001	2, 102	–	0.05	0.94
PT	–0.32 (0.11)	[–0.54, –0.10]	–2.91	0.004	–0.05 (0.16)	[–0.36, 0.26]	–0.32	0.74
FU	–0.46 (0.11)	[–0.69, –0.24]	–4.07	<0.001	–0.03 (0.16)	[–0.34, 0.28]	–0.18	0.85
Viral suppression (<400)	2, 104	–	0.27	0.76	2, 104	–	0.72	0.49
PT	1.01 (0.77)	[–0.52, 2.53]	1.31	0.19	–1.31 (1.13)	[–3.56, 0.93]	–1.16	0.24
FU	0.81 (0.75)	[–0.69, 2.30]	1.07	0.28	–0.89 (1.10)	[–3.08, 1.29]	–0.81	0.41

Alcohol and other drug use

Biomarker There was a significant main effect of time in the model predicting PEth ($F(2,101) = 4.16, p = 0.01$) and a non-significant treatment-by-time interaction ($F(2,101) = 0.97, p = 0.38$), indicating both groups demonstrated reductions in PEth. In the model predicting negative urinalysis results for drug use or past three-day alcohol use, the time ($F(2,101) = 1.67, p = 0.19$) and treatment-by-time interaction were not significant ($F(2,101) = 0.59, p = 0.55$).

WHO alcohol, smoking, and substance involvement screening test There was a significant main effect of time in the model

predicting the likelihood of moderate or high-risk WHO-ASSIST category ($F(2,104) = 7.02, p = 0.001$), but not the treatment-by-time interaction ($F(2,104) = 0.10, p = 0.90$). The probability of being in the high-risk category reduced 30 percentage points at three months and 40 percentage points at six months.

Timeline follow-back There was a significant effect of time in the model predicting the average number of drinks consumed for Khanya ($F(2,102) = 21.53, p < 0.001$). Participants in Khanya consumed on average 5.3 and 4.6 drinks at the subsequent time points, compared to 7.3 at baseline.

However, the treatment-by-time interaction was not significant, indicating similar changes across groups over time. For the subsample who also used drugs, there was a marginally significant treatment-by-time interaction ($F(2,31) = 3.28, p = 0.05$); *Khanya* had a greater reduction in the number of drinks at six months compared to ETAU (see Figure S2). Given the *Khanya* intervention did not require abstinence, it can be understood that individuals reduced amounts of alcohol consumed rather than abstinence.

Viral load (exploratory)

There was no treatment effect on viral load ($F(2,104) = 0.72, p = 0.49$). However, we were not adequately powered in this pilot study to detect changes in viral load over a relatively short follow-up period [54,55], especially since 63.9% of the sample was suppressed at baseline. However, there was a significant relationship between viral suppression and adherence; individuals with higher adherence at post-treatment were more likely to be virally suppressed ($t = 2.31; p = 0.02$). Results are consistent with other behavioral intervention trials with a primary focus on ART adherence that did not demonstrate treatment effects on viral load [56-58].

4 | CONCLUSIONS

This pilot trial provides initial evidence of the feasibility and acceptability of the peer-delivered *Khanya* intervention for improving adherence alongside AOD in South African HIV care. Peers offer a potential solution to known implementation barriers of task-sharing behavioral interventions with CHWs, including high caseloads and other clinical demands [35,59]. Peers bring with them lived experience, which can foster connection with patients and potentially reduce HIV and AOD stigma [60,61]. Initial results regarding the implementation success of *Khanya* and ART adherence improvements are promising. Results suggest that engagement in AOD treatment alone without integrated adherence support may not be sufficient to improve ART adherence; however, a larger trial is needed to evaluate longer term effectiveness outcomes, including viral suppression, and to consider a stepped care approach to efficiently allocate resources to support individuals most in need of intensive intervention.

Strengths of this trial included a rigorous comparison condition, prioritization of individuals most in need of intervention – with both AOD and ART non-adherence – use of a hybrid effectiveness-implementation design, and high retention rates. Primary limitations relate to this being a pilot trial, including small sample size and relatively short follow-up. As a pilot study, we were not powered to detect differences in viral load – an exploratory outcome. Furthermore, our urinalysis assessment of substance use included detection of alcohol use in the past three days; based on the alcohol use severity in this population and *Khanya's* focus on reduction of use and harms rather than abstinence, we also had limited power to detect changes in urine-verified abstinence. Finally, although real-time electronic adherence monitoring is a strength, it has its limitations; Wisepill can act as an intervention in itself, and non-use of Wisepill may be conflated with ART non-adherence – although we limited our assessment to three months to minimize potential non-use over time [29]. Despite these

limitations, this pilot study contributes new knowledge about incorporating peers as AOD interventionists within HIV care in SA. As SA Department of Health refines its strategy for integration of behavioral health services into primary care, findings may have important implications for the feasibility and acceptability of incorporating peers into task-shared services for improving ART adherence among PLWH with AOD.

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COMPETING INTERESTS

Dr. Safren receives royalties from Oxford University Press, Guilford Publications, and Springer/Humana Press for books related to cognitive behavioral therapy. All other authors declare no conflicts of interest.

AUTHORS' CONTRIBUTIONS

JFM conceptualized the idea and secured funding for the project with JAJ, BM and SAS. JM led all aspects of the study and wrote the first draft of the manuscript. JAJ, BM, COC and SAS provided guidance throughout the study and provided a critical review and edits of the manuscript. JMB conducted the analyses, oversaw data management and provided edits to the manuscript. LSA provided oversight of study operations, contributed to idea conceptualization and provided a critical review of the manuscript. KSR developed the protocol with JFM and SM and led all aspects of study start up, operations, data oversight and regulatory compliance, along with SM, and contributed to manuscript writing. ALR oversaw study operations, procedures for biomarker specimen testing and analysis along with SM, and contributed to manuscript writing. All authors approve of the final manuscript to be submitted for publication.

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SUPPORTING INFORMATION

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

Figure S1. Model-implied Wisepill adherence at baseline and post-treatment (three-months) for ETAU and Khanya intervention groups

Figure S2. Model-implied alcohol use quantity at baseline, post-treatment, and follow-up time points for ETAU and intervention groups among the subsample who used both drugs and alcohol ($n = 21$)

Table S1. Linear model predicting wisepill adherence

Table S2. Linear model predicting continuous PEth and categorical model predicting dichotomous urine

Table S3. Cumulative logit model predicting moderate and high risk categories of WHO-ASSIST

Table S4. Count model predicting average number of drinks consumed on days drinking on the timeline followback

Table S5. Linear model predicting percentage days used any substance on the timeline followback

Table S6. Categorical model predicting binary viral load suppression