Journal of Affective Disorders 370 (2025) 499–510

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Effectiveness of a task-sharing collaborative care model for the detection and management of depression among adults receiving antiretroviral therapy in primary care facilities in South Africa: A pragmatic cluster randomised controlled trial

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ARTICLE INFO

Keywords:
HIV
Depression
Collaborative care
Antiretroviral therapy
Viral load suppression
Psychosocial counselling

ABSTRACT

Background: HIV is characterised by high rates of comorbidity with mental health conditions including depression, as such, the detection and treatment of comorbid depression is critical to achieve viral load suppression. This study evaluated the effectiveness of a collaborative care intervention for depression among adults with comorbid depression symptoms receiving ART in primary health care (PHC) facilities.

Methods: We conducted a pragmatic cluster-randomised trial in 40 clinics in the North West province of South Africa. PHC clinics were stratified by sub-district and randomised in a 1:1 ratio. Participants were ≥ 18 years, receiving ART, and had depression symptoms indicated by Patient Health Questionnaire-9 (PHQ-9) score ≥ 9. Intervention clinics received: i) supplementary mental health training and clinical communication skills for PHC nurses; ii) workshops for PHC doctors on treating depression; and iii) lay counselling services. Using mixed effects regression models, we assessed co-primary outcomes of PHQ-9 response at 6 months (≥50 % reduction in baseline PHQ-9 score) and viral load suppression at 12 months (viral load<1000 copies/mL).

Results: The intervention had no effect in PHQ-9 response (49 % vs 57 %, risk difference (RD) = −0.08, 95 % CI = −0.19; 0.03, $p = 0.184$) or viral load suppression (85 % vs 84 %, RD = 0.02, 95 % CI = −0.01; 0.04, $p = 0.125$). Nurses referred 4298 clinic patients to counsellors, however, only 66/1008 (7 %) of intervention arm participants were referred to counsellors at any point during the study.

Limitations: The highly pragmatic approach of this trial limited exposure to the counselling component of the intervention and referral to doctors for initiation of antidepressant treatment was extremely low.

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https://doi.org/10.1016/j.jad.2024.10.061
Received 7 March 2024; Received in revised form 16 October 2024; Accepted 18 October 2024
Available online 21 October 2024

Conclusion: The trial showed no effect of a district-based intervention to strengthen collaborative care for depression. The trial revealed the extent of the treatment gap in the context of scaling up mental health services.
Trial registration: ClinicalTrials.gov (NCT02407691); Pan African Clinical Trials Registry (201504001078347).

1. Background

HIV is characterised by high rates of comorbidity with mental health conditions (Arseniou et al., 2014; Sikkema et al., 2015). Comorbid depression among adult people living with HIV (PLWH) on antiretroviral therapy (ART) is associated with higher rates of non-adherence to ART, disease progression and mortality (Leserman et al., 2007; Mayston et al., 2012; Schuster et al., 2012). Detection and treatment of comorbid depression is critical to achieve viral load suppression. While interventions are in place to support adherence in primary care is South Africa, there has been limited attention paid to identifying and addressing underlying depression, which may be contributing to low viral load suppression rates (South African Department of Health, 2016).

South Africa is faced with a shortage of mental health specialists (Sorsdahl et al., 2023), resulting in gaps in the diagnosis and treatment of mental health conditions in primary care and in general (Seedat et al., 2008; Sorsdahl et al., 2023; Zani et al., 2020). Primary Health Care (PHC) nurses are not authorised to prescribe antidepressant medication, limiting prescribing to doctors, who are fewer and have limited availability at PHC clinics. In this context, there is a need to consider task sharing of counselling interventions with generalist and lay health care workers available in PHC facilities. There is evidence supporting task sharing of counselling interventions in low- and middle-income countries (LMICs) using trained lay counsellors and community health workers (Connolly et al., 2021; Singla et al., 2017), but evidence is limited for PLWH. Pilot studies of task-shared psychological counselling interventions delivered by lay health workers were associated with reductions in depression symptom scores among PLWH (Nakimuli-Mpungu et al., 2015; Nakimuli-Mpungu et al., 2014; Petersen et al., 2014), however, these pilot studies did not report on HIV treatment outcomes.

The successful delivery of evidence-based interventions for depression including counselling and antidepressant treatment requires that health workers work collaboratively in a structured manner; a method called collaborative care (Gilbody et al., 2006). Collaborative care requires that four key criteria are met: a multi-professional approach to patient care; having a structured case management plan; scheduled patient follow-ups; and enhanced inter-professional communication (Archer et al., 2012; Gunn et al., 2006). Collaborative care for detection and treatment of comorbid depression in South Africa takes lessons from task-shifting for HIV care, where Nurse Initiated Management of Anti-Retroviral Therapy was as effective as doctor-initiated care and eased the burden on overburdened specialist health-care workers (Fairall et al., 2012). Our proposed collaborative care model was developed through the PRogramme for Improving Mental health carE (PRIME) to reduce the treatment gap for mental disorders in five LMICs (Lund et al., 2012). To evaluate this collaborative care model, we conducted the Comorbid Affective Disorders, AIDS/HIV, and Long Term Health (CobALT) trial in primary care facilities in South Africa, enrolling ART patients with depression symptoms. We hypothesized that the intervention would result in greater improvement in depression symptoms at 6 months, and viral load suppression at 12 months.

2. Methods

2.1. Study design

CobALT was a pragmatic, two parallel arm cluster-randomised trial (RCT) conducted in PHC clinics in the North West Province of South Africa phased over two districts, Dr. Kenneth Kaunda (Dr. KK) and Bojanala. The study protocol has been published (Fairall et al., 2018b) and registered with ClinicalTrials.gov (NCT02407691), the Pan African Clinical Trials Registry (201504001078347) and the South African National Clinical Trials Register (SANCTR) (DOH-27-0515-5048, NHREC 4048). Ethical approval was obtained from the University of Cape Town Human Research Ethics Committee (211/2013), King's College London Research Ethics Office (PNM/12/13-159), and the University of KwaZulu-Natal's Biomedical Research Ethics Committee (BFC049/15). Permission to conduct the study was granted by the South African National Department of Health and the North West Provincial Department of Health.

2.2. Participants

Participating clinics were the largest nurse-led public sector primary care clinics providing ART across the two districts. We enrolled the 40 largest eligible clinics, 20 from the Dr. KK district and 20 from the Bojanala district. We excluded the four clinics which participated in the formative research to develop the intervention and pilot the data collection materials as part of the PRIME project in the Dr. KK district. Participants were 18 years or older, receiving ART and had depression symptoms as indicated by a total score of nine or more on the Patient Health Questionnaire-9 (PHQ-9) (Kroenke et al., 2001). As part of the preparatory work for the trial, we validated a Setswana version of the PHQ-9 among 676 chronic care patients in the Dr. Kenneth Kaunda District. We compared the performance of a localised version of the PHQ-9 administered by fieldworkers to that of the Structured Clinical Interview for DSM-IV administered by a clinical psychologist. This showed that the PHQ-9 is a valid tool for measuring depressive symptoms in the trial population (Bhana et al., 2015). However, we showed that a threshold of 9, as opposed to the more widely used threshold of 10, was more appropriate for detecting depression in this population and so applied it to the trial eligibility criteria. A systematic review found the PHQ-9 to have acceptable diagnostic properties for detecting major depressive disorder for cut-off scores between 8 and 11 (Costantini et al., 2021; Manea et al., 2012).

We excluded individuals who planned to relocate and would therefore be unavailable for follow-up, and those who were attending the clinic for acute medical treatment or judged to be unable to provide informed consent, for example due to psychosis or dementia. We did not exclude participants with active suicidal ideation, but urgently referred them for clinical review in both intervention and control arms. In Dr. KK, we co-enrolled alongside the PRIME South Africa (PRIME-SA) trial, recruiting patients on hypertension medication and with depression symptoms (Petersen et al., 2018).

2.3. Randomization and masking

Within each district, the trial statistician (CLo) randomised prior to recruitment clinics with a 1:1 allocation ratio, within five sub-district strata to the intervention and control groups (Fig. 1). Stratification and clustering considered the geographical distribution of clinics within sub-districts for two reasons, i) to limit intervention contamination through geographically determined management of clinics, and ii) to limit the exposure of participants allocated to the control arm of the trial to some of the components of the intervention based at the facilities that they usually receive care in. Details of the randomization process have been reported (Fairall et al., 2018b). We randomised PHC facilities and collected outcome measures on individual participants. Staff in the intervention clinics were not blinded to intervention status because they

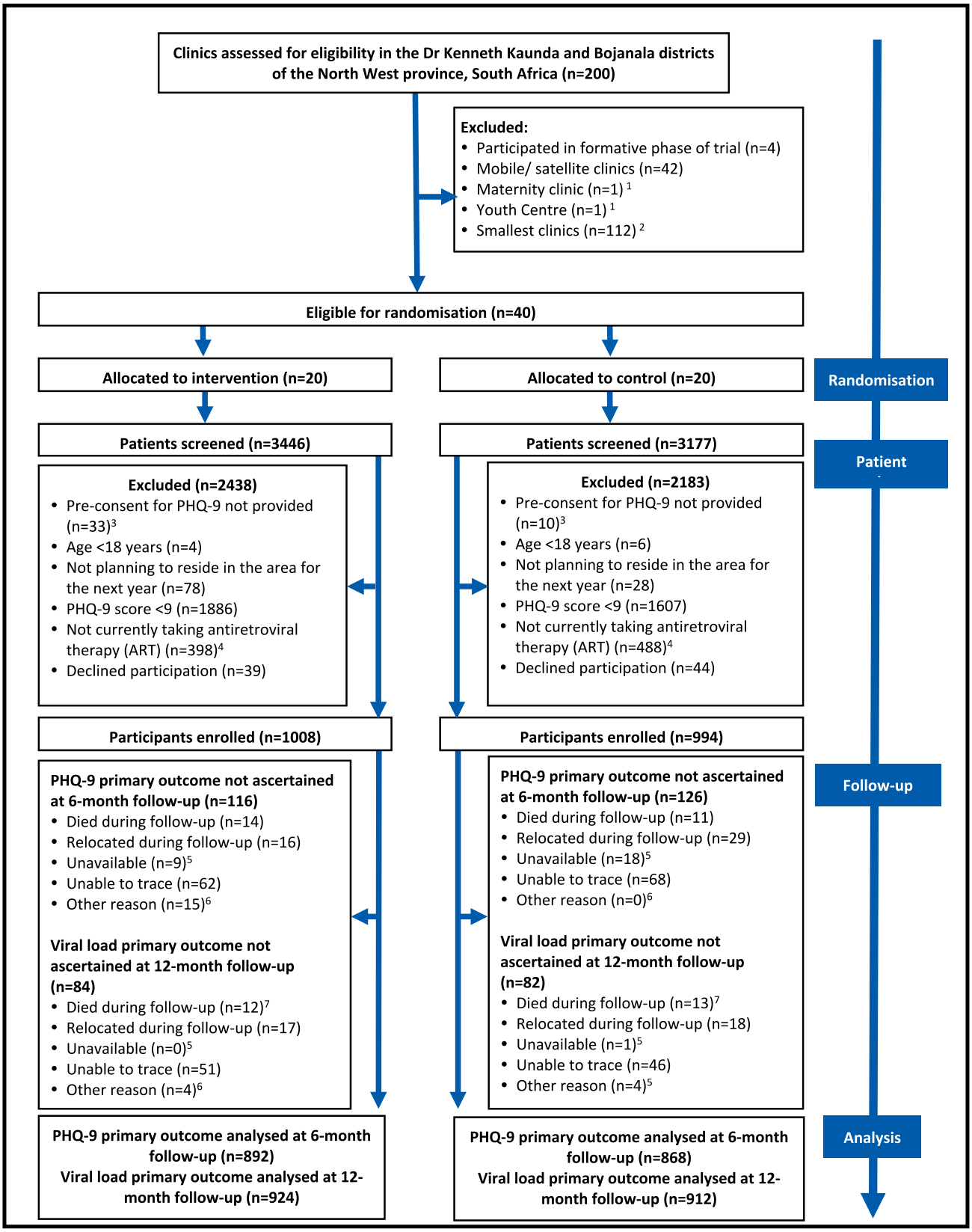

Fig. 1. Inclusion and follow-up of participants
[1]Clinics that focus on a specific target population excluding the study population; [2]Clinics with a headcount <24,900. [3]Declined screening for enrolment. [4]Attending the clinic for chronic care but not taking ART. [5]Patients successfully contacted but unavailable to participate in the follow-up interview or draw blood samples. [6]In prison, hospitalized, psychotic or recently suffered domestic violence. [7]21 of the 46 participants who died had a follow-up viral load result that could be analysed.

were recipients of the training component of the intervention. Trial patient participants were not informed whether their clinic received the intervention or not. Blinding of fieldworkers could not be guaranteed given implementation activities of the intervention. All fieldwork activities were standardised across both groups with training manuals, standard operating procedures and daily supervision (Fairall et al., 2018b). Outcome assessment for viral loads was conducted blindly by independent laboratories.

2.4. Procedures

Usual care in all participating clinics included the introduction of a clinical decision support tool called Primary Care 101 (PC101), later known as Adult Primary Care (APC) and internationally, the Practical Approach to Care Kit (PACK) (Fairall et al., 2018a). This tool integrates the management of communicable and non-communicable diseases, mental illness, and women's health. APC was rolled out through 12 facility-based two-hour interactive training sessions, including two sessions on mental health. Patients identified with depression symptoms were referred for treatment to PHC doctors for antidepressant medication initiation, district-based psychologists providing outreach counselling services to PHC clinics, or psychology outpatient clinics based at the district hospitals.

The details of the intervention activities have been described elsewhere (Fairall et al., 2018b; Petersen et al., 2022). Briefly, the collaborative care model comprised a strengthened APC training – where the standard APC training was strengthened by a supplementary APC Mental Health Module comprising four additional onsite sessions on mental healthcare. These sessions contain nine mental health case scenarios covering common mental disorders, including depression, anxiety and alcohol use disorder. The model included strengthened referral pathways for depression, to; i) lay depression counsellors who provided manualized counselling for mild depression and were placed at each intervention facility, ii) PHC doctors for initiation of antidepressant medication, and iii) mental health specialists for more severe and treatment resistant depression. PHC nurses also provided a detection and case management function, reviewing patient progress and referring complex and treatment resistant cases to specialist mental health services. Two workshops were held with PHC doctors who were appointed to PHC clinics focusing on mental health care for adults attending primary care facilities. The APC Supplementary Mental Health Module was augmented by four sessions on Clinical Communications Skills for nurse-led chronic care and a strengthened employee assistance programme for PHC providers experiencing personal problems and burn-out. The clinical communication skills sessions orientated clinic staff to the collaborative care model within other health systems strengthening initiatives.

Lay depression counsellors gave waiting room educational talks designed to help adult patients to identify and report their symptoms to the consulting health worker. Within the collaborative care model, PHC nurses were responsible for the screening and diagnosis of people with depression, referring where appropriate to lay-counsellors for psychological counselling, and to doctors for initiation of antidepressants. Referrals were made for patients with chronic conditions who were depressed, not only those who were on ART. The lay counsellors were trained and supervised to provide manualized evidence-based counselling for patients with depression symptoms under the supervision of a project-employed clinical psychologist. The initial session was psychoeducation on depression symptoms; with the middle sessions ($n = 6$), introducing common triggers of depression in the target community (poverty; interpersonal conflict; social isolation; grief and bereavement; externalised stigma; internalised stigma using narrative vignettes); and the last being closure (Petersen et al., 2013). Depending on the trigger, evidence-based problem solving and cognitive behavioural techniques, including behavioural activation were used to work through issues raised in the vignettes (Dua et al., 2011). An additional individual adherence session was added bringing the total number of counselling sessions to nine. Lay counsellors, with a minimum of 12 years of schooling, were selected, trained and employed to provide this service for the duration of the trial.

In Dr. KK, we started with training in the intervention facilities in March 2015 and placed lay depression counsellors in intervention clinics in July 2015, two weeks before the start of recruitment in intervention clinics. This proved to be insufficient time for embedding the intervention as it took longer for referrals to depression counsellors to be adopted into routine care by the PHC nurses. Consequently, in Bojanala, we extended the embedding period, starting with training in March 2016, and placing lay depression counsellors in clinics in April 2016, three months before the start of trial recruitment. Fieldworkers introduced the study and recruited patients through waiting room talks. Patients who qualified through verbal pre-screening conducted privately were given information about the nature of the screening tool and were required to consent for screening using the PHQ-9. Participants gave a valid written informed consent. Fieldwork interviewers conducted interviews in one of the three local languages (Setswana, English, Afrikaans), chosen by each participant. Follow-up interviews were conducted 6 and 12 months after the baseline interview. Viral load results captured from the patient clinic files were enriched through linkage with research-funded and routinely collected viral loads from the National Health Laboratory Services (NHLS).

The trial was pragmatic in nature (Loudon et al., 2015; Zwarenstein et al., 2008), in that i) we employed broad eligibility criteria, enrolling any participant who would be a candidate for the intervention in real settings; ii) we recruited participants at the facilities where they usually seek care; iii) the intervention was implemented in usual settings, iv) study recruitment and data collection occurred independent of clinical care or receipt of the counselling component of the intervention, in that recruitment to the study did not guarantee referral for counselling, as much as referral for counselling did not guarantee recruitment into the study; and v) all the enrolled participants were analysed in their allocated group – whether they received counselling or not, and whether they sought care at another facility or not.

2.5. Outcomes

The co-primary patient mental and physical outcomes were (1) PHQ-9 response at 6 months, defined as at least a 50 % improvement in PHQ-9 score compared with baseline and (2) viral load suppression 12 months after patient enrolment, defined as a viral load value of <1000copies/mL. Our co-primary outcome, PHQ-9 response was based on three cluster trials (Huijbregts et al., 2013; Menchetti et al., 2013; Richards et al., 2016) which had baseline PHQ-9 scores similar to those previously reported in our PHQ-9 tool validation study (Bhana et al., 2015). Secondary outcome measures and safety outcome measures included remission of depression symptoms, defined as a PHQ-9 score of 5 or less at 12 months, PHQ-9 response at 12 months, mean scores at 6 and 12 months and ART adherence, measured as taking 90 % of the doses in the prior month using a visual analogue scale (Amico et al., 2006).

2.6. Statistical methods

We based our estimates of viral load suppression on data from our previous RCT on task-shifting HIV care in which 70 % of ART patients had suppressed viral loads at follow-up with an intra-cluster correlation coefficient (ICC) of 0.046 (Fairall et al., 2012). We assumed that rates of viral load suppression would be slightly lower in a group of patients suffering from depression (65 %) (Moussavi et al., 2007; Nakimuli-Mpungu et al., 2012). Designing CobALT as a superiority trial, a sample size of 2000 participants provided 80 % power to detect a 10 % difference in viral load suppression at 12-months, and between 10 % and 12 % in PHQ-9 response at 6 months at the 5 % significance level assuming an ICC of 0.04, accounting for 20 % loss to follow-up (Fairall et al., 2005). We estimated the effects of the intervention by comparing the primary

outcomes of intervention and control group patients using generalised regression models, with identity link functions, adjusting for the intra-cluster correlation of outcomes within clinics. We included the stratum as a covariate in the regression models using Stata/IC 16.0 statistical software. All clinics and patients were analysed in the treatment group to which they were randomly assigned to facilitate an intention to treat analysis. We performed a modified intention to treat analysis assuming the missing data to be completely missing at random. We used binomial regression to estimate differences in proportions of patients with suppressed viral loads and who had responded in terms of their depression symptoms and reported these estimates with 95 % confidence intervals.

We analysed secondary outcomes as follows: binomial regression for binary outcomes, linear regression for numerical outcomes comparing values at follow-up adjusted for baseline values and ordinal logistic regression of depression symptom severity. For the safety outcome death, these time to event outcomes were analysed using a cox regression model adjusted for clustering of events within clusters. The effect measure estimated was the hazard ratio and reported with 95 % confidence intervals.

2.7. Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit the manuscript for publication.

3. Results

Between April 21, 2015 and December 14, 2016, we screened 6623 patients, of whom 2002 were enrolled; 1008 in intervention clinics and 994 in control clinics. Fig. 1 illustrates the trial profile, showing the enrolment, follow-up of participants and reasons for exclusion. Baseline characteristics of the enrolled participants are presented in Table 1, and clinics in Table 2. Patient participant characteristics were similar across arms; 82 % were women, the median age was 42 (±11) years, 73 % were unemployed, 35 % had a history of TB and 33 % had a history of NCD. The mean PHQ-9 score was 14 (±4) and the median duration on ART was 38 (inter-quartile range: 15; 66) months. Overall, 94 % of the participants had viral load results available at baseline; of these, 85 % were virally suppressed using a threshold of 1000 copies/mL in the intervention arm and 84 % in control. Control group clinics tended to be slightly larger and had fewer pharmaceutical services before randomization (Table 2).

All clinics completed the trial although one control clinic was closed because of arson following community protests. Affected participants were followed up at a neighbouring control clinic. Eighty-eight percent of the participants were interviewed at 6 months in the intervention arm and 87 % in control. At 12 months, 84 % of the participants were interviewed and 92 % had viral load results. The reasons for loss to follow-up were similar between the groups and are shown in Fig. 1. Participants who were lost to follow-up did not differ from those interviewed in PHQ-9 scores but were more likely to be younger and not virally suppressed.

The uptake of the intervention in both districts has been described in more detail elsewhere (Petersen et al., 2022). In Dr. KK, 59 % of eligible staff received at least one mental health training session and 39 % completed all sessions. In Bojanala, the corresponding rates were 85 % and 78 %. Intervention clinic nurses referred 4298 clinic patients to counsellors, and 2200 of these attended at least one session (Petersen et al., 2022). In total, 6418 counselling sessions were provided. Patients who took up counselling in Dr. KK received an average of 3.61 counselling sessions and those in Bojanala received an average of 1.55 sessions. However, the overlap between referred patients and those enrolled in the data collection component of the trial was low: only 66

Table 1
Patient participant characteristics at enrolment.

Characteristic	Intervention n (%), *N* = 1008	Control n (%), *N* = 994
Sociodemographic characteristics		
Women (%)	850 (84 %)	787 (79 %)
Age in years: mean (SD); median (IQR)	42 (11); 42 (33, 50)	42 (11); 41 (34, 50)
Socioeconomic status		
Highest level of education achieved		
Never attended school	89 (9 %)	75 (8 %)
Some primary school education	356 (36 %)	371 (37 %)
Some secondary school or tertiary education	556 (55 %)	544 (55 %)
Employed or self employed	270 (27 %)	261 (26 %)
Receiving a government social grant	447 (44 %)	438 (44 %)
Depression symptoms and depression care		
Patient Health Questionnaire (PHQ)-9 score: mean (SD); median (IQR)	14 (4); 13 (11, 16)	14 (4); 13 (11, 16)
PHQ-9 score category		
9–14: mild to moderate symptoms	667 (66 %)	635 (64 %)
15–27: moderately severe to severe symptoms	341 (34 %)	359 (36 %)
History of depression	173 (17 %)	189 (19 %)
On antidepressants at a therapeutic dose	1 (0.1 %)	2 (0.2 %)
Antiretroviral treatment		
Duration on ART in months: mean (SD); median (IQR)	44 (34); 37 (16, 64)	46 (37); 38 (14, 67)
Viral load available[a]	949 (94 %)	927 (93 %)
Viral suppression defined as viral load<1000 copies/ml[b]	802/949 (85)	772/927 (84 %)
Viral suppression defined as viral load<400 copies/ml[b]	777/949 (82 %)	742/927 (80 %)
Medical history	*N* = 1004	*N* = 993
Previous myocardial infarction	99 (10 %)	83 (8 %)
Previous stroke	47 (5 %)	57 (6 %)
Previous myocardial infarction or stroke	138 (14 %)	118 (12 %)
Hypertension	331 (33 %)	302 (30 %)
Diabetes	34 (3 %)	42 (4 %)
At least one non-communicable disease	342 (34 %)	323 (32 %)
Previous tuberculosis	355 (35 %)	347 (35 %)
Reported a hospitalisation in the last 3 months (%)	32 (3 %)	45 (5 %)
Cardiovascular disease risk profile		
Blood pressure	*N* = 1003	*N* = 992
Systolic blood pressure: mean (SD); median (IQR)	116 (20); 113 (102, 129)	116 (20); 114 (103; 126)
BP ≥180/110 mmHg	38 (4 %)	41 (4 %)
BP ≥140/90–179/109 mmHg	246 (24 %)	210 (21 %)
BP <140/90	719 (72 %)	741 (75 %)
Smoking history	*N* = 1001	N = 992
Current smokers	135 (13 %)	175 (18 %)
Pack Year History: mean (SD); median (IQR)	6 (6); 4 (2, 7)	7 (9); 5 (2, 9)
Body Mass Index (BMI)	*N* = 991	*N* = 979
Mean BMI (kg/m^2): mean (SD); median (IQR)	25 (7); 23 (20; 29)	25 (7); 23 (20; 28)
BMI >30: obese	208 (21 %)	190 (19 %)
Cardiovascular risk percent>20 %[c]	53/870 (6 %)	52/876 (6 %)
World Health Organization Disability Assessment Schedule 2 score[d]: mean (SD); median (IQR)	10 (7); 9 (4; 14)	10 (8); 9 (4; 15)

IQR = interquartile range; SD = standard deviation.

[a] Viral load values from the past 12 months were considered and compiled from blood tests done specifically for the trial and medical and laboratory records.

[b] Proportion of patients with a viral load result.

[c] Ten-year risk of cardiovascular disease death (sudden cardiac or stroke death).

[d] WHO-DAS 12-item schedule used. Maximum score is out of 37, with a score of 0–1 considered no disability, and 2–37 considerable disability (37 is the lowest level of functioning (Hanass-Hancock et al., 2015).

Table 2
Clinic characteristics prior to enrolment.

Clinics	Intervention	Control
Number of clinics	20	20
Headcount[a]: median (IQR)	38,832 (33,554, 54,359)	42,463 (35,665, 50,200)
Number of nurses per clinic: median (IQR)	11 (7, 20)	11 (8, 13)
Patient to nurse ratio (headcount/ number of nurses): median (IQR)	3806 (2994, 4534)	4110 (2986, 5088)
Doctor support:		
Daily: n (%)	8 (40 %)	7 (35 %)
Sessional: n (%)	11 (55 %)	13 (65 %)
None: n (%)	1 (5 %)	0 (0 %)
Pharmacist/assistant on-site: n (%)[b]	7 (35 %)	4 (20 %)
Off-site medication collection[c]	15 (75 %)	9 (45 %)
Cluster size[d]: harmonic mean (95 % CI)	50 (50, 51)	50 (48, 51)

IQR: Interquartile range.
[a] Headcount: Dr. Kenneth Kaunda district: number of attendances of patients ≥5 years in 2013; Bojanala district: number of attendances of patients ≥5 years in 2015.
[b] All clinics dispense onsite, but not all have dedicated pharmacy staff.
[c] Collection of chronic medication available at pharmacies at no cost for clinically stable patients.
[d] Number of participants enrolled in each clinic for the trial (target of 50 participants per clinic).

(7 %) of the 1008 intervention group patient participants were linked to the counselling database containing referrals by PHC nurses to a project counsellor. Control group participants in the Dr. KK district reported increased referral to mental health specialists including other counsellors, social workers, psychologists and psychiatrists (Table 3). Only 11 participants (0.55 %) were on antidepressants at a therapeutic dose at any point during the study – four in the intervention group arm and seven in the control. At follow-up, more participants from the control group reported receiving treatment from specialist mental health workers compared to collaborative care clinics – these included psychologists, psychiatrists and social workers (Table 3).

Regarding primary outcomes, 439/892 (49 %) of intervention group participants and 498/868 (57 %) of the control group participants had a 50 % reduction in PHQ-9 scores at 6-months (risk difference (RD) = 0.08, 95 % CI -0.19-0.03, $p = 0.184$) (Table 4). Twelve-month viral load suppression outcomes were high and did not differ by arm: 785/924 (85 %) of intervention group participants had viral load of <1000 copies/mL compared to 770/913 (84 %) of control group participants (RD = 0.02, 95 % CI -0.01-0.04, $p = 0.125$).

There were no significant differences in secondary outcomes between the intervention and control groups; in mean PHQ-9 scores at 6 and 12 months, PHQ-9 response at 12 months and ART adherence at 12 months (Tables 4 and 5). In total, 46 deaths occurred during the trial, 25 in the intervention arm and 21 in control. The intervention was not significantly associated with death (hazard ratio = 1.18, 96 % CI = 0.65; 2.15, $p = 0.589$). One participant died by suicide during follow-up: a 42-year-old man enrolled at an intervention facility. At enrolment, the participant's PHQ-9 score was 10, corresponding to 'moderate depression', and he responded '1–7 days' to the PHQ-9 item-9 (Over the last 2 weeks, how often have you been bothered by: Thoughts that you would be better off dead or of hurting yourself in some way). There was no evidence that the participant was referred to the counsellor, and there is no record of him attending any study counselling sessions. The adverse events were reported to the data and safety monitoring board, and the deliberations concluded that the death by suicide was not related to the intervention or the data collection component of the study.

4. Discussion

This trial showed no effect of a collaborative care model for depression among people receiving ART on either depression symptoms or viral load suppression. Depression symptoms in general were mild, and only 35 % had moderate to severe symptoms at enrolment. Viral load suppression rates at enrolment were higher than anticipated and remained high at follow-up.

Table 3
Receipt of the components of collaborative care model for depression.

Component of care	Treatment prior to the trial		Treatment during the trial	
	Intervention n (%), N = 1008	Control n (%), N = 994	Intervention n (%), N = 1008	Control n (%), N = 994
Project employed lay depression counsellors				
Referred to project employed counsellors over 12 months period[a]			66 (7 %)	0 (0 %)
Received counselling from intervention counsellors[b]	26 (3 %)	13 (1 %)[c]	90 (9 %)	2 (0 %)[c]
State employed mental health provider				
Referred to or received counselling from a state employed mental health provider	194 (19 %)	272 (27 %)	121 (12 %)	187 (19 %)
Received counselling from a state employed mental health provider	180 (18 %)	245 (25 %)	106 (11 %)	172 (17 %)
Clinic counsellor (excluding intervention counsellors)	140 (14 %)	204 (21 %)	52 (5 %)	113 (11 %)
Social Worker	47 (5 %)	79 (8 %)	249 (25 %)	255 (27 %)
Psychologist	21 (2 %)	28 (3 %)	11 (1 %)	40 (4 %)
Psychiatrist	18 (2 %)	16 (2 %)	3 (0 %)	16 (2 %)
Antidepressant treatment				
On antidepressants at a therapeutic dose at any point[d]			4 (0 %)	7 (1 %)
Initiated or intensified antidepressants[e]			4 (0 %)	6 (1 %)

[a] Referrals by primary health care nurses obtained from the counselling database, managed separately from data collection for the trial.
[b] Receipt of counselling self-reported by trial participants during data collection.
[c] Some participants enrolled and attending control facilities reported having received counselling from project-employed lay depression counsellors based at the intervention clinics.
[d] Excludes those who were on antidepressant medication on low doses deemed not therapeutic according to South African and primary care clinical guidelines
[e] Includes only therapeutic doses, 1 % patient stayed at a therapeutic dose.

The failure to demonstrate effectiveness could be explained by several factors. Arguably the most important is that we used a highly pragmatic approach to participant enrolment which was completely independent of intervention delivery and processes. The result was that only 7 % of intervention group participants were referred to project counsellors and almost no-one was referred to a doctor for initiation of antidepressant treatment. Similar studies of psychosocial counselling, one conducted in South Africa and another in Uganda, used a less pragmatic approach to participant recruitment and intervention delivery, with 74–78 % of their trial participants receiving all counselling sessions, and 94–99 % receiving at least one counselling session (Myers et al., 2022; Nakimuli-Mpungu et al., 2020).

The uptake of the counselling component of the intervention, which was low, has been described elsewhere (Petersen et al., 2022). Common reasons for not attending follow-up counselling sessions included changes in the circumstances the patients experienced, including employment. Some expressed "feeling better" after being equipped to face their current challenges in the initial sessions. While some patients may have discontinued counselling due to the improvement of their symptoms or the resolution of the stressors, intervention fidelity may

Table 4
Effect of the intervention on depressive symptoms and viral load suppression.

Outcome	Intervention n (%)	Control n (%)	Effect type	Estimate[a] (95 % CI)	p-value	ICC[b]
Primary outcomes						
PHQ-9 response: 50 % improvement in PHQ-9 score at 6 months from enrolment	439/892 (49 %)	498/868 (57 %)	Risk difference	−0.08 (−0.19; 0.04)	0.184	0.144
Viral suppression defined as viral load<1000 copies/ml at 12 months	785/924 (85 %)	770/913 (84 %)	Risk difference	0.02 (−0.01; 0.04)	0.125	0.025
Secondary outcomes at 6 months	*N* = 892	*N* = 868				
PHQ-9 score: mean (SD)	8 (7)	7 (5)	Mean difference	0.89 (−0.53; 2.31	0.164	0.182
Severity of depressive symptoms at 6 months						
PHQ-9 score 0–4: no depressive symptoms	277 (31 %)	358 (41 %)	Ordinal based	1.39 (0.83 to 2.31)	0.210	0.099
PHQ-9 score 5–9: mild depressive symptoms	351 (39 %)	262 (30 %)	Odds ratio			
PHQ-9 score 10–14: moderate depressive symptoms	153 (17 %)	167 (19 %)				
PHQ-9 score 15–27: moderately severe depressive symptoms	111 (12 %)	81 (9 %)				
Secondary outcomes at 12 months	*N* = 843	*N* = 832				
PHQ-9 score: mean (SD)	7 (6)	7 (5)	Mean difference	0.25 (−1.31; 1.81)	0.745	0.190
PHQ-9 response: 50 % improvement in PHQ-9 score from baseline	448 (53 %)	462 (56 %)	Risk difference	0.02 (−0.14; 0.10)	0.743	0.151
Remission of depression symptoms: PHQ-9 score of ≤5 at 12 months	340 (40 %)	375 (45 %)	Risk difference	−0.06 (−0.18; 0.06)	0.338	0.189
PHQ9 recovery: PHQ-9 score of ≤5 at both 6 and 12 months	192/877 (22 %)	269/861 (31 %)	Risk difference	−0.08 (−0.19 to 0.02)	0.117	0.210
Severity of depressive symptoms at 12 months						
PHQ-9 score 0–4: no depressive symptoms	279 (33 %)	321 (39 %)	Ordinal based	1.18 (0.70; 1.99)	0.570	0.166
PHQ-9 score 5–9: mild depressive symptoms	320 (38 %)	278/832 (33 %)	Odds ratio			
PHQ-9 score 10–14: moderate depressive symptoms	141 (17 %)	129/832 (16 %)				
PHQ-9 score 15–27: moderately severe depressive symptoms	103 (12 %)	104 (12 %)				
Viral suppression defined as viral load<400 copies/ml at 12 months[c]	761/924 (82 %)	746/913(82 %)	Risk difference	0.01 (−0.03; 0.04)	0.688	0.025
Follow-up viral suppression for those who were not suppressed at enrolment	55/133 (41 %)	59/141 (42 %)	Risk difference	0.01 (−0.11; 0.10)	0.915	0.019
Virological failure defined as two consecutive viral loads ≥1000 copies/ml at least two months but no >24 months apart.[3]	83/1004 (8 %)	99/992 (10 %)	Risk difference	−0.01 (−0.03; 0.02)	0.644	0.028
Virological failure restricted to those with follow-up viral load results[3]	83/924 (9 %)	99/913 (11 %)	Risk difference	−0.01 (−0.04; 0.02)	0.610	0.029

[a] Adjusted for trial design and baseline characteristics.
[b] ICC = intraclass correlation coefficient.
[c] Adjusted for trial design only.

have contributed to the discontinuation of treatment. Intervention fidelity for counselling averaged 66 % (Petersen et al., 2022). Fidelity has been found to impact the uptake and the effectiveness of lay counselling services (Selohilwe et al., 2019). While other evidence-based therapies like cognitive behavioural therapy have better fidelity, they have higher effectiveness only in the long-term and when higher attendance to sessions has been recorded (Pybis et al., 2017). Counselling has potential to benefit patients in the short term and even when its uptake is low.

The low exposure to the counselling among our trial participants was despite >4000 patients attending intervention clinics being referred to counsellors and >2000 taking up the service. Intervention delivery was very sensitive to project-specific augmentation. In Dr. KK, where we had a full-time project psychologist overseeing the counsellors, patients attended more sessions and counselling fidelity was higher. In Bojanala, where we had a dedicated nurse trainer, more nurses were exposed to training sessions and completed the course (Petersen et al., 2022). Nurse referrals to counsellors were also sensitive to a counsellor being available on the same day, which was not always consistent because of turnover of counselling staff. In Dr. KK, the district was more engaged in intervention delivery and had participated in the original development and pilot in four clinics (Petersen et al., 2016). Considering our trial design, a less pragmatic approach would have been to task PHC nurses with referring patients to both the intervention and data collection components of the trial, instead of recruitment running independent of referral to counsellors. This more controlled approach, however, would not have highlighted the implementation challenges our trial exposed.

Interviews with district managers found that they had deliberately redirected their limited mental health resources to control clinics which may explain why participants attending these facilities reported receiving more referrals to existing mental health services (Selohilwe et al., 2023). This may have contributed to the lack of difference in outcomes between arms. Observational analysis of data collected within this trial showed that nurses tended to refer patients with more severe depression symptoms or greater disability (Zani et al., 2020). This is consistent with other local studies (Kemp et al., 2020).

Doctors proved difficult to enlist in the intervention across both districts. Despite doctor workshops, very few participants saw doctors and antidepressant prescribing was almost non-existent, an observation documented elsewhere in South Africa (Bouwer et al., 2021; Kathree et al., 2023). Doctor support in public sector primary care clinics tends to focus more on physical conditions and comorbidities, and for mental illness, is often limited to psychiatric emergencies requiring admission. South Africa's National Mental Health Policy Framework and Strategic Plan 2023–2030 calls for a review of the regulatory environment to support nurse-initiated antidepressant treatment with fluoxetine (South African National Department of Health, 2023). This requires amendment of the Nursing Act that governs what nurses may prescribe and possible down-scheduling of fluoxetine from a controlled prescription-only substance to a prescription-only substance. South Africa is one of only two countries, alongside Brazil, to classify antidepressants as controlled substances, subject to high levels of regulation regarding their distribution and use (National Health Surveillance Agency -

Table 5
Effect of the intervention on blood pressure and risk for cardiovascular disease.

Outcome	Intervention n (%)	Control n (%)	Effect type	Estimate (95 % CI)	p-value	ICC
Outcomes at 6 months	$N = 886$	$N = 864$				
Systolic blood pressure: mean (SD); median (IQR)[a]	114 (±19); 112 (101; 125)	114 (±19); 111 (102, 124)	Mean difference	0.23 (−2.12; 2.58)	0.845	0.052
Blood pressure < 140/90	684 (77 %)	688 (80 %)	Risk difference	−0.002 (−0.05; 0.04)	0.921	0.042
Blood pressure ≥ 140/90	202 (23 %)	176 (20 %)				
Outcomes at 12 m	$N = 835$	$N = 816$				
Systolic blood pressure: mean (SD); median (IQR)[a]	116 (±19); 113 (103; 128)	117 (±19); 115 (104, 127)	Mean difference	−0.47 (−3.07; 2.13)	0.717	0.083
Blood pressure < 140/90	619 (74 %)	633 (78 %)	Risk difference	−0.01 (−0.03; 0.02)	0.690	0.054
Blood pressure ≥ 140/90	216 (26 %)	183 (22 %)				
CVD risk percent >20 %[a,b]	36/711 (5 %)	38/708 (5 %)	Risk difference	−0.003 (−0.02; 0.02)	0.777	0.013

[a] Adjusted for the cluster design of the trial only and not baseline characteristics.
[b] Ten-year risk of cardiovascular disease death (sudden cardiac or stroke death).

Anvisa, 2016; South African Health Products Regulatory Authority, 2022). This is further supported by a thorough review of the mental health section of the WHO's Essential Medicines List in 2023 which includes prescribing of fluoxetine for depression and anxiety by non-specialist health providers.

Our findings raise serious concerns about the use of the PHQ-9 at one time point to identify people at risk of depression, which was common practice among community mental health trials at the time this study was designed. The threshold of 9, identified in our validation study of the Setswana version of the PHQ-9, was perhaps too low. Some trials have attempted to get around these limitations by using higher thresholds for enrolment, repeating the PHQ-9 scores at least two weeks apart (Aragonès et al., 2014; Coventry et al., 2015; Gensichen et al., 2009), or completing a follow-on clinical assessment (Indu et al., 2018; LaRocco-Cockburn et al., 2013; Pence et al., 2007), which we could not resource across such a wide geography and time period. A systematic review evaluating the PHQ-9 as a screening tool recommended the use of the tool in a two-stage screening process, with most studies including a structured interview carried out by primary care and mental health professionals (Costantini et al., 2021). Studies which have repeated the PHQ-9 scores or completed a clinical assessment after two weeks report a high number of patients who do not qualify at second assessment (Ell et al., 2008; Gensichen et al., 2009). Our experience suggests caution in using a single PHQ-9 score with which to enrol people in a trial of depression management. Observing high rates of remission in both groups in our trial further supports this possibility. Remission is further supported by the effect of stressors on depression symptoms. Psychological stressors may be linked to depression symptoms (Yang et al., 2015) and some of these stressors or the inability to manage them may be short lived. These stressors are also likely to result in less severe depression symptoms. Evidence suggests that people with less severe symptoms are more likely to have remission of symptoms (Whiteford et al., 2013).

In contrast with our expectations about people with comorbid depression (Pence et al., 2007; Yehia et al., 2015), viral load suppression at enrolment was already high in our trial. There was thus a ceiling effect, with little room for improvement during the follow-up period. This was also the case in the two trials of psychotherapy delivered by lay depression counsellors in South Africa and Uganda (Myers et al., 2022; Nakimuli-Mpungu et al., 2020). Like viral load suppression, adherence at baseline was higher than expected, and did not significantly differ between groups at enrolment and at follow-up. Our trial may thus have experienced a ceiling effect. The study predated the introduction of dolutegravir-based regimens (South African Department of Health, 2023) which are associated with higher viral load suppression rates (Dorward et al., 2023). This transition benefits patients in care. This emphasizes the need to identify candidates for interventions such as these among those who are lost to care through CHW tracing and possibly screening efforts. In addition, depression screening should be adopted in primary care for patients who return to care. The APC guide recommends screening using PHQ-2, if positive, further clinical assessment (Knowledge Translation Unit, 2023).

While the proportion of participants at follow-up with suppressed viral loads was high and the proportion with severe depression symptoms low, we noted poor control of blood pressure with 184/299 (46 %) of participants at 6 months and 179/371 (47 %) at 12 months on treatment for hypertension with a blood pressure of >140/90 mmHg. This is in keeping with discordant levels of control and unmet needs for communicable and NCDs documented in South Africa (Singh et al., 2023) and underlines the importance of integrating care and addressing all health needs of people on ART. The level of disability among our trial participants was also concerning with 184/399 (54 %) having moderate to severe functional disability. The level of functional disability was higher than previously reported in PLWH in South Africa (Hanass-Hancock et al., 2015).

4.1. Limitations and strengths

The most important limitation of this trial is the highly pragmatic approach of this trial that limited exposure to the counselling component of the intervention and that almost no-one was referred to a doctor for initiation of antidepressant treatment. The trial enrolled participants with predominantly mild depression symptoms and higher rates of viral load suppression.

Strengths of the trial include the meeting of patient recruitment targets in all facilities, the high rates of follow-up and ascertainment of primary outcomes, and collection of data on comorbidities and a wide range of outcomes despite a very challenging context. These difficulties included a multi-year moratorium on new staff appointments, nurses foregoing annual leave to provide a continuous service, high rates of sexual violence along the platinum mining belt (Médecins Sans Frontières, 2016), an earthquake and community protests.

4.2. Study impact and future steps

The findings have assisted to highlight structural barriers to the integration of mental health with HIV care in South Africa. These include antidepressant prescribing restrictions and the lack of a suitable cadre of health care workers who can provide task sharing counselling within PHC settings. The need to be more focussed in terms of targeting PLWH with severe illness or who have disengaged from care and may not be attending services, has also been foregrounded by the trial outcomes.

Since completion of the trial, the intervention has been refined and expanded for implementation and scale-up across different contexts using implementation science to understand the modifications required for the different contexts through the Mental health INTegration (MhINT) and Southern African Mental health INTegration (SMhINT) projects in KwaZulu-Natal (KZN) province of South Africa (Grant et al., 2021; Petersen et al., 2021). Important elements that have been added are demand creation through community-based screening and detection by community health-workers, targeting of people who have disengaged from their chronic care and are more likely to have significant depression, and embedding the intervention through continuous monitoring of screening and uptake indicators. Further effort is required to expand antidepressant prescribing through task-sharing.

Looking at possible future steps, there are considerations for discussion with the South African National Department of Health. Given the scale of untreated depression and the limited availability of evidence-based resources in primary care, the current discourse on mass screening for mental illness needs to be reviewed, and a targeted approach to identify people with more severe depression may be more prudent. These targeted approaches include the screening of patients with chronic conditions attending primary care facilities, screening participants returning to care after periods of missed clinic visits, and screening of patients identified through community health worker tracing efforts as well as those receiving routine CHW visits. Screening instruments and thresholds may need to be reviewed to limit the numbers of people who screen positive so that the health system can cope with the burden. Guidelines from South Africa are not clear about screening in primary care. Internationally, the PHQ-9 is recommended on a two-stage diagnostic process –PHQ-9 screening followed by structured or unstructured diagnostic interviews (Costantini et al., 2021). The APC guide recommends screening using PHQ-2, if positive, further clinical assessment based on mhGAP and included in the comprehensive APC guide (Knowledge Translation Unit, 2023).

There is evidence to support manualised psychosocial counselling delivered by lay health workers, a task-sharing approach (Chibanda et al., 2011; Myers et al., 2022; Nakimuli-Mpungu et al., 2020; Petersen et al., 2014; Singla et al., 2017). This strategy is supported by the WHO's mental health Gap Action Programme (World Health Organization, 2010), which aims to scale up services for mental health in low resource settings through task-sharing. Facility-based counselling has a role to play in the treatment of depression but the discussion about who should provide this counselling, and how they should be trained, mentored, supervised and regulated needs to continue. Some of these potential workers are already embedded in the health system. The scope of the existing HIV counsellors, who currently focus on HIV counselling and testing, ART initiation counselling and adherence counselling, could be expanded to include manualised depression counselling. This project employed workers who previously held such positions in Dr. KK district and provided training and supervision. CHWs could be trained and supervised to provide counselling, whether some could have their responsibilities shifted to be dedicated to depression counselling or expanded to include depression counselling. HIV counsellors and CHWs are often secondary school graduates. Myers and colleagues (Myers et al., 2022) evaluated these two approaches and found them to be equally effective. In Bojanala District, this project employed mainly university graduates with a 4-year psychology degree. These graduates are widely available in the country as only 5 % of undergraduate students with a major in psychology gain entry to master's degree programmes (Shisana et al., 2024). Many are employed in the private sector or by NGOs, are registered counsellors while many remain unemployed with no clear career paths (Durrheim et al., 1998; Kotze, 2005). Questions remain whether government would be able to absorb these and adequately compensate for their level of education. This project employed a clinical psychologist to provide supervision for project-employed counsellors. While the intensity of this supervision may not be replicated in clinic settings, district-based psychologists could provide supervision to clinic-based counsellors.

Nurses need to be able to prescribe first-line antidepressant treatment, perhaps in the first instance restricted to fluoxetine, which is effective, well-tolerated, safe and inexpensive. Guides such as the APC guide could be used to provide support for screening and diagnosis by primary care nurses.

5. Conclusion

The trial showed no effect of a district-based intervention to strengthen collaborative care for depression among patients receiving ART on either mental or physical health outcomes. Viral load suppression at enrolment was higher than expected and may have experienced a ceiling effect, and PHQ-9 scores reflected predominantly milder symptoms which we expect would be more likely to resolve at follow-up without intervention. Viral load suppression did not worsen during the study and depression symptoms tended to resolve with both groups. This trial showed the implementation gap between introducing interventions for PLWH with depression and the large clinic population in need, highlighting the need to be more focussed in terms of targeting those with severe illness or who have disengaged from care and may not be attending services, and the requirement for a broader health system strengthening paradigm.

CRediT authorship contribution statement

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Funding

The research reported in this publication was supported by the National Institute of Mental Health of the National Institutes of Health under Award Number R01MH100470. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This study is also an output of the PRogramme for Improving Mental health carE-SA (PRIME) and was supported by the UK Department for International Development [201446]. The views expressed do not necessarily reflect the UK Government's official policies.

LF is supported by the UK's National Institute of Health Research (NIHR) using Official Development Assistance (ODA) funding (NIHR Global Health Research Unit on Health Systems Strengthening in Sub-Saharan Africa at King's College London (16/136/54)). The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care, England.

GT is supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care South London at King's College London NHS Foundation Trust. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. GT also receives support from the National Institute of Mental Health of the National Institutes of Health under award number R01MH100470 (CobALT study). GT is also supported by the UK Medical Research Council in relation the Emilia (MR/S001255/1) and Indigo Partnership (MR/R023697/1) awards.

BZ received funding by the South African Medical Research Council through the Division of Research Capacity Development under the Researcher Development Grant. The contents thereof are the sole responsibility of the authors and does not necessarily represent the official views of the SAMRC.

Declaration of competing interest

All authors declare no competing interests.

Acknowledgements

The authors thank the clinic managers, PC101/APC trainers, nurses, data capturers, counsellors and community health workers at the participating facilities, project employed counsellors and district-based psychologists. We thank Mrs. Deanna Carter for supporting preparation, training and fieldwork activities; the fieldworkers who collected the data and the residents who assisted with tracing patients for follow-up. We are greatly indebted to the patients who participated in this research and ultimately contributed to science.

Data availability

The de-identified data set and a data dictionary will be made available after publication of the trial after obtaining relevant Institutional Research Ethics Board approval of a proposal and signed data access agreement.

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