AIDS Behav (2018) 22:1–8
https://doi.org/10.1007/s10461-017-1906-3

SUBSTANTIVE REVIEW

Systematic Review of Interventions for Depression for People Living with HIV in Africa

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Published online: 12 September 2017

Abstract Depression interventions for individuals with HIV/AIDS in Africa are being increasingly evaluated. MEDLINE was searched using key terms: depression, Africa, and HIV, to identify depression interventions for HIV-infected adults in Africa. Perinatal women were excluded. Results were extracted and relative change in depression scores for interventions and net effect calculated. The MEDLINE search yielded 18 articles. Six of seven studies evaluating feasibility were positive, and seven of seven studies evaluating acceptability were also positive. Three studies investigated the effect of psychotherapy (% relative decrease of depressive symptoms for intervention: %net decrease compared to controls) (73%:39% decrease). Four studies investigated task-shifting of psychotherapy (47%:34% decrease). Three studies evaluated antidepressants (79%:39% decrease). Three studies investigated task-shifting of antidepressant treatment (82%:65% decrease). An exercise intervention was evaluated (66%:49% decrease). One trial investigated minocycline with non-statistically significant results. Finally, three studies investigated other psychosocial interventions (44%:21% decrease). Overall, the results highlight the need for large, randomized trials to establish efficacy as well as implementation studies.

Resumen Las intervenciones contra depresión para personas con VIH/SIDA en África se están evaluando de forma cada vez más frecuente. Se realizo una busqueda en MEDLINE usando los términos: depresión, África y VIH, para identificar intervenciones contra depresión para adultos infectados por el VIH en África. Se excluyeron las mujeres en estado perinatal. Se extrajeron los resultados y se calculó el cambio relativo en las escalas de depresión para las intervenciones y el efecto neto. La búsqueda en MEDLINE produjo 18 artículos. Seis de los siete estudios que evaluaron la factibilidad fueron positivos y siete de los siete estudios positivos que evaluaron la aceptabilidad. Tres estudios investigaron el efecto de la psicoterapia (% de disminución relativa de la intervención: % de disminución neta en comparación con los controles) (73%:39%). Cuatro estudios investigaron el cambio de tareas de la psicoterapia (47%:34%). Tres estudios evaluaron medicamentos antidepresivos (79%:39%). Tres estudios investigaron el cambio de tareas del tratamiento antidepresivo (82%:65%). Se evaluó una intervención de ejercicio (66%:49%). Un ensayo investigó minociclina con resultados no estadísticamente significativos. Por último, tres estudios investigaron otras intervenciones psicosociales (44%:21%). En general, los resultados enfatizan la necesidad de estudios prospectivos y randomizados para establecer elementos tanto de eficacia, como de implementacion.

Keywords HIV · Depression · Africa · Intervention

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Background

Depression is known to be a major cause of morbidity and mortality with an estimated loss of 63 million disability-adjusted life years (DALY) compared with 82 million for HIV [1]. Depression is also known to cause 2.2 million excess deaths globally in 2010 from suicide and comorbid diseases [2]. Depression is significantly more common in HIV infected persons where the global prevalence is 12.8–78% compared with 4.7% prevalence in the general population [3, 4]. This is especially concerning as people living with HIV and depression are 42% less likely to achieve good antiretroviral therapy (ART) adherence, more likely to develop virologic failure, and are more likely to have HIV progression, independent of ART adherence, than those without depression [3, 5, 6].

In Africa, which has the highest burden of HIV depression, treatment is especially difficult. The paucity of resources, infrastructure, and staff are significant impediments to depression care. In Africa, there are 0.5 psychiatrists per million people compared to 83 per million in Europe 37 per million in South America, 3 per million in India, 124 per million in the USA, and 134 per million in Canada [7]. This also varies across Africa with 7.8 psychiatrists per two million in South Africa versus zero in Eritrea [7]. In spite of difficulties there has been significant research in Africa into the prevalence and incidence of comorbid HIV and depression, confounding factors such as alcohol abuse and trauma. There also has been much work on the validation of depression screening tools. While there have been review articles investigating interventions for mental illness in people living with HIV/AIDS in low and middle income countries these have not been specific to depression interventions in Africa.

The purpose of this systematic review is to evaluate interventions for depression care in Africa, including the use of medications, psychotherapy, or other methods.

Methods

Systematic Search

MEDLINE was searched using the terms HIV and Africa and Depression. This resulted in the following MeSH terms being used "HIV," "depressive disorder," "depression," and "Africa." All Fields were searched for "HIV," "depressive," "disorder," "depressive disorder," "depression," and "Africa." This returned 545 articles.

Selected articles had to meet the following criteria: (1) have depression as an objective, measure depression using a validated tool and show outcome results, (2) target adults living with HIV, (3) be conducted in Africa, (4) be an intervention other than antiretroviral medication, and (5) focus on depression treatment, not just screening. Article exclusion criteria included (1) peri-partum depression and (2) pediatric studies. These were excluded as there was a recent excellent review on peri-partum depression [14], and as the interventions for children, especially young children, are distinct from adults. A wide range of rigor was allowed in this systematic review in order to summarize the available data. Thus, we included those with or without a control arm, feasibility studies, and pilot studies.

Data Analysis

From each selected article, data were extracted regarding study population, country, year, and study design. Additionally, we assessed if depression was a primary or secondary objective, the depression scale(s) utilized, sample size, inclusion criteria, and outcome data. Descriptive comparisons were performed using Microsoft Excel. Feasibility and acceptability were defined by the individual studies.

The studies were grouped by intervention type and compared by relative change in depression score. Since the studies used different depression scores to measure the depression, we compared the result by relative change in the depression score. The effect score was divided by the baseline score. Since this fraction gave the remaining depression and not the reduction in depression, the fraction was subtracted from one and the result multiplied by 100%. Control reduction was calculated in the same way. If there was a control arm a net reduction of depression score was calculated by subtracting the control reduction from the intervention reduction. This methodology was also chosen as several studies gave the mean depression scores at baseline and after the intervention but not the number or percentage of those who went from depressed to not depressed defined as the response rate.

Results

We completed our search on February 3, 2017 and did not limit articles by date. Our search yielded 545 articles. The article titles were screened for inclusion/exclusion, leaving 50 articles. The abstracts were reviewed and 24 were removed. The full texts of the remaining 26 were reviewed and eight more were removed. Full search details can be seen in Fig. 1.

The 18 included articles were read and data abstracted. Their main points are summarized in Table 1. Although the search was not limited to Sub-Saharan Africa, all of the studies were from there. Most of the articles described pilot

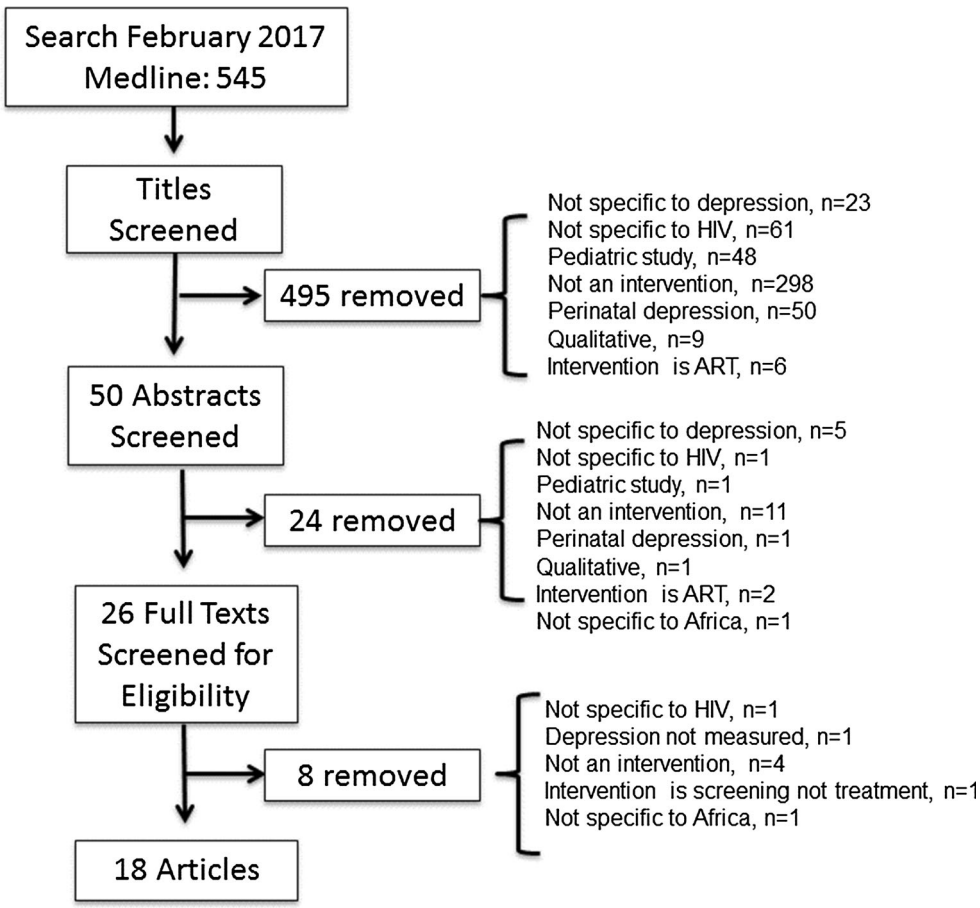

Fig. 1 Search strategy for depression interventions in those with HIV in Africa

studies. The type of interventions and depression scales are varied.

Several trials investigated the feasibility and/or acceptability of the intervention. The feasibility was generally defined as by the ability to recruit staff and participants, retention of participants, the ability to collect desired data, and the fidelity of completing the intervention as defined. Seven studies accessed feasibility of their methods, six assessing psychotherapy as well as the three looking at task shifting of antidepressant assessment and delivery. Of the seven, only one, Andersen et al. expressed concerns about feasibility given the difficulty lack of fidelity of the intervention [8], all of the other six studies found that providing the intervention was feasible [9–14]. Seven studies evaluated acceptability and all found the respective interventions acceptable. The acceptability was defined as either as patient retention and adherence to the intervention or through qualitative interviews or surveys. The seven studies included psychotherapy (n = 5) [8–11, 14] and task shifting of antidepressant delivery (n = 2) [12, 13]. Thus, feasibility and acceptability was high for their respective interventions.

To evaluate the validity of our comparison of results between studies, we examined two studies which used two different depression scores. Andersen, et al. used both Center for Epidemiological Studies Depression Scale (CES-D) and the Hamilton Depression Scale (HAM-D) which yielded percent reduction of intervention scores of 16 and 22% respectively [11]. Hoare et al. used both the HAM-D and the Montgomery-Asberg depression rating scale [12] (MADRS) which yielded percent reduction of intervention scores of 60 and 56% [15]. Thus, the percent reduction appeared to generally result in approximately similar relative responses across different metrics.

Psychotherapy

Overall in the psychotherapy trials, there was significant reduction in depression as summarized in Table 2a [16–18]. Overall weighted reduction in the score of the intervention group was 73% and the weighted net reduction was 39% when removing the effect observed in the control group. The authors did not report the percent response; however, the means for each group are below the cutoff for even borderline depression. Of note the participants in Nakimuli-Mpungu et al. were allowed to utilize antidepressants as needed [16].

Table 1 Included prospective studies on interventions for depression of those with HIV in Africa

Intervention	Author	Country	Year	N	Study type	Depression primary outcome?
Psychotherapy	Nakimuli-Mpungu [15]	Uganda	2014	77	Comparison trial[a]	Yes
	Nakimuli-Mpungu [16]	Uganda	2015	109	RCT	Yes
	Olley [17]	Nigeria	2006	77	RCT	Yes
Psychotherapy task shifting	Abas [8]	Zimbabwe	2017	32	RCT	Yes
	Andersen [7]	South Africa	2016	14	Intervention trial	Yes
	Chibanda [9]	Zimbabwe	2011	320	Intervention trial	Yes
	Petersen [10]	South Africa	2014	34	RCT	Yes
Antidepressant	Hoare [14]	South Africa	2014	102	RCT	Yes
	Ngo [18]	Uganda	2015	184	2 cohorts	Yes
	Wagner [19]	Uganda	2014	105	Cohort	Yes
Antidepressant task shifting	Adams [11]	Tanzania	2012	20	Intervention trial	Yes
	Gaynes [20]	Cameroon	2015	41	Intervention trial	Yes
	Pence [21]	Cameroon	2014	55	Intervention trial	Yes
Exercise	Aweto [22]	Nigeria	2016	33	RCT	No
Novel drug	Nakasujja [23]	Uganda	2013	73	RCT	No
Other psychosocial intervention	Chidrawi [24]	South Africa	2015	18	Intervention trial	No
	Prinsloo [25]	South Africa	2016	62	Intervention	No
	Thomson [26]	Rwanda	2014	610	Comparison trial	No

Intervention trial a trial with just an intervention arm and no control, *RCT* randomized controlled trial

[a]Trial was not randomized, instead those with worse depression were prioritized to intervention

Cognitive Behavioral Therapy Task-Shifted Intervention

Also, in the task shifted psychotherapy groups, there was significant reduction in depression as summarized in Table 2b [8–11]. Overall weighted reduction of the score in the intervention group was 47%. Only two of the task-shifted psychotherapy studies included controls. The weighted average net reduction was 34% in those studies. The studies did not report response rates, however again the average score in each study was below the cutoff for depression. In Abas et al., the participants were allowed to take antidepressants as needed. Those participants were also on ART but poorly adherent and adherence counseling was part of the intervention. Anderson et al. allowed participants to take antidepressants but the doses could not have been adjusted in the 3 months prior to enrolling in the study. Those participants were also on ART and two-thirds were maintaining >80% adherence.

Antidepressants Trials

There were three antidepressants trials, two reported positive response [19, 20], while one reported no significant results as summarized in Table 2c [15]. The average weighted reduction of intervention score was 79%. Only the negative study had a control with the net reduction of 0% [15]. These studies did give response rates. The negative study showed only 3% of their participants going from depressed to not depressed; however, the other two reported a 79 and 86% result. The overall weighted rate was 61% response rate. All participants were drawn from HIV clinics. Rates of ART use was only described in one of study, the Wagner et al. cohorts, in which all participants were about to start ART at enrollment [20].

Antidepressant Task-Shifted Studies

There were three studies examining task shifting in the screening for and administration of antidepressants as summarized in Table 2d [12, 21, 22]. Since these studies were pilot studies looking at feasibility none of them have controls. Each reported positive responses and all showed feasibility. The weighted average reduction of intervention score was 82%. Two studies reported response rates for weighted average of 65%. The third study's mean follow up score was below the threshold for depression. Participants from Adams et al. were drawn from the HIV clinic, although ART history was not provided. Participants from Gaynes et al. were on ART although poorly adherent with 53% reporting 95% or more adherence at baseline and 63% at 4 months. They also had 0% virologically suppressed at baseline and 18% at 4 months. In Pence et al. the participants were drawn from ART clinic but none were

Table 2 Depression interventions of those with HIV in Africa by group

First author	Scale	Intervention N	Reduction in intervention score (%)	Control N	Reduction in control score (%)	Net N	Net reduction in score (%)	Response rate
(a) Psychotherapy intervention group								
Nakimuli-Mpungu	SRQ-20	48	67	29	10	77	57	–
Nakimuli-Mpungu	SRQ-20	57	79	52	62	109	17	–
Olley	BDI	34	70	33	18	77	52	–
Total		139[a]	73[b]	114[a]	36	263	39[b]	–
(b) Psychotherapy task-shifted intervention								
Abas	PHQ-9	14	78	18	38	32	40	–
Andersen	CES-D	14	84	–	–	–	–	–
Chibanda	SSQ-20	320	43	–	–	–	–	–
Peterson	PHQ-9	17	56	17	28	34	28	–
Total		365	47	35	33	66	34	–
(c) Antidepressant studies group								
Hoare	MADRS	51	44	51	44	102	0	3%
Ngo	PHQ-9	184	83	–	–	–	–	79%
Wagner	PHQ-9	105	89	–	–	–	–	86%
Total		340	79	51	44	102	0	61%
(d) Antidepressant task-shifted group								
Adams	PHQ-9	20	59	–	–	–	–	–
Gaynes	PHQ-9	41	89	–	–	41	–	90%
Pence	PHQ-9	55	85	–	–	55	–	46%
Total		116	82	–	–	96	–	65%
(f) Novel drug group								
Nakasujja	CES-D	36	–	37	–	73	Not Significant	–
(e) Exercise intervention group								
Aweto	BDI[a]	18	66	15	17	33	49	–
(g) Other psychosocial intervention group								
Chidrawi	PHQ-9	18	28	–	–	–	–	–
Prinsloo	PHQ-9	62	16	–	–	–	–	–
Thomson	HSCL-15	304	44	306	23	610	21	44% greater decrease
Total		80	39%	306	23%	610	21%	

SRQ-20 self reporting questionnaire 20-Item, *BDI* beck depression inventory, *PHQ-9* patient health questionnaire- 9, *CES-D* Center for Epidemiological Studies Depression Scale, *SSQ* Shona symptom questionnaire, *MADRS* Montgomery–Åsberg depression rating scale, *PHQ-9* patient health questionnaire-9, *HSCL-15* Hopkins symptom checklist- 15

[a]Ns are analyzed numbers

[b]Weighted average

virologically suppressed at baseline. Only one participant had ever been treated for depression before although 96% reported at least one prior depressive episode.

Exercise Study

A novel study used exercise to improve pulmonary function as well as mental health as summarized in Table 2e [23]. They had 66% reduction in the depression symptoms and a net reduction of 49%. There was no response rate reported, however, the mean final score is below the cutoff for depression. The participants were all on ART but adherence information was not given. It was not noted if they could be on antidepressants or not.

Novel Drug

In 2013 a trial in Uganda examined minocycline utilization for cognitive function. The authors measured depression as well; their results are summarized in Table 2f [24]. The participants were allowed to be on antidepressants as needed. Unfortunately, the effect of minocycline was not significant for cognitive function or depression and the trial was stopped early.

Other Psychosocial Intervention

Finally, there were three studies analyzing other psychosocial interventions that evaluated depression as summarized in Table 2g [25–27]. These included two stigma reduction interventions of people living with HIV and those around them and a community accompaniment intervention using community health workers. Their response rates were more modest; however not all participants started with depression and depression was a secondary endpoint. The weighted reduction in the intervention score was 39% and net reduction in the intervention result was 21%. The intervention arm from the community accompaniment trial had 44.3% greater response than the other arm. Information regarding ART use was not noted in Chidrawi et al. or Prinsloo et al. although both studies were drawn from people in care. Those in Thomson et al. were initiating ART. None of the studies mentioned antidepressants.

The results of this analysis are shown in Fig. 2. Note that while all three of the psychotherapy studies included control arms, only two of those with task shifted psychotherapy did. Most notably, in the antidepressant studies only one had a control arm and overall there was no net change in that study. Those in the task shifted antidepressant trials did not have control arms and only one in the other psychosocial interventions had a control arm.

Discussion

This review demonstrates that a variety of depression treatment modalities have been tried in Africa. These trials are diverse and were completed across the continent which suggests wide applicability. While there were challenges, such as pharmacy outages in drug delivery, a high percentage of patients experienced favorable results. While it is difficult to compare between studies and across modalities, both psychotherapy and antidepressants seem to have efficacy in low-resource areas, the same as in high-resource areas.

As mentioned above, since we were comparing depression scores from different scales, we did relative reductions in score. To evaluate the validity of this approach we looked at two studies that used more than one depression score. Andersen et al. used both Center for Epidemiological Studies Depression Scale (CES-D) and the Hamilton Depression Scale (HAM-D) which yielded percent reduction of intervention scores of 16.1 and 22% respectively. Hoare et al. used both the Montgomery-Asberg depression rating scale (MADRS) and the HAM-D which yielded percent reduction of intervention scores of 56.2 and 60.2%. We felt that these differences were

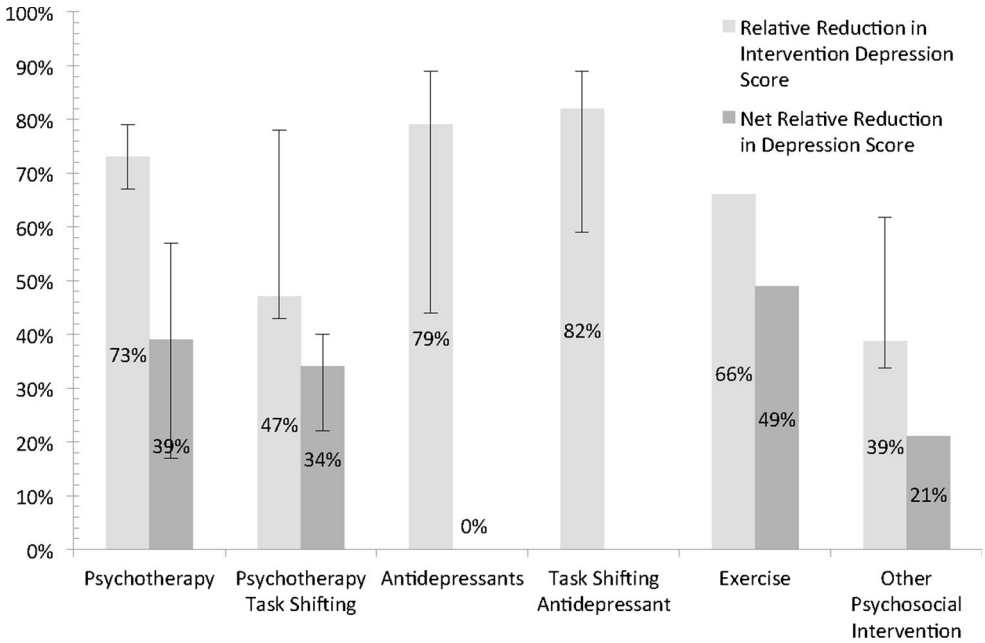

Fig. 2 Relative change in depression by intervention type

acceptable and added support to our procedure for comparison of relative depression scores.

All of the psychotherapy studies reported at least a 40% decrease in initial depression score and one study reported a reduction of over eighty percent. All of those with control arms showed a reduction over the control reduction as well. The studies were small and underpowered to show efficacy. Thus, while we think it is reasonable to summarize the data, this review is not purporting that the efficacy is proved. In spite of that, the results are promising given the high acceptability and feasibility.

Five of the antidepressant trials showed reduction in depression score of at least 59%. There was one negative trial; however, they only allowed a fixed dose of escitalopram 10 mg and no titration up in spite of 20 mg being a safe dose. Seeing a trial that allowed titration of the escitalopram dose would provide more information. However, even including the results of that trial, the response in Africa is quite positive.

Aweto et al. showed that patients with HIV had significant benefit from exercise. These findings are encouraging given the low cost and wide applicability of such an intervention. Given the rising rates of obesity in the developing world, exercise interventions for depression would likely have other beneficial side effects.

While the trials looking at other psychosocial interventions did not have as much reduction in depression score as some of the other interventions, they also did not choose only depressed patients. Thus, it is impressive they saw a treatment benefit at all. The community accompaniment study had significant reductions in rates of depression. Subanalysis using only people testing as depressed initially, or developing a new trial analyzing stigma would be valuable to determine benefit from intervention within these groups of people.

Finally, nearly all of these studies were pilot studies, many with small sample sizes. However, it seems possible to conclude that depression treatment is feasible, acceptable, and worthwhile in resource-limited settings in Africa. Given low personnel costs in Africa as well as the ability to task-shift, psychotherapy would likely not be resource intensive. Antidepressants seem to have promise in Africa, likely limited by pharmacy supply. Novel approaches such as exercise, sigma reduction, or community accompaniment when starting ART appear to have merit. There is clearly a need for larger trials to be more certain of efficacy and response rates. However, given the known poorer HIV outcomes of those with depression [3, 5], treating depression seems a necessary target to try to achieve the UNAIDs 90–90–90 goals in people living with HIV in Africa.

Limitations

Many of these trials were feasibility or pilot studies so were not powered for response. Negative response would not necessarily mean no response. The fact that there were significant responses in many of these articles is all the more impressive given their power. There were many depression scales used, and in an effort to compare across scales, we used relative change. This is useful but not perfect and would certainly not imply high precision of measurement. Greater agreement in depression scales in Africa would help compare depression rates and efficacy. Finally MEDLINE was the only database searched. However, all the references found were searched to look for articles cited by the authors to looked for missed articles. No missed articles were found.

Conclusion

Depression is an important modulating factor in HIV outcomes in Africa. In spite of that, research into depression interventions have largely only come recently. These interventions show that there are many impactful ways to improve the lives of those with HIV in Africa, and in turn improve HIV outcomes. While larger studies are needed to show efficacy, there is clear evidence that psychotherapy and antidepressant delivery are feasible and acceptable in Africa. Also, there are some promising alternatives such as exercise or community accompaniment strategies which would not just impact depression but overall physical or psychosocial health. Work into implementation of these strategies are needed to put interventions into practice as part of holistic HIV care in Africa.

Acknowledgements This research was supported by the National Institute of Neurologic Diseases and Stroke (NINDS) and Fogarty International Center (R01NS086312, R25TW009345), National Institute of Allergy and Infectious Diseases (U01AI089244, T32AI055433). The authors would like to thank Jose Debes, MD, MS for his assistance in translating our abstract into Spanish.

Compliance with Ethical Standards

Conflict of interest None.

Ethical Approval This article does not contain any studies with human participants performed by any of the authors.

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