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Title: Which HIV-infected youth are at risk of developing depression and what treatments help? A systematic review focusing on Southern Africa

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Abstract

Background: Depression is common in people with HIV and is associated with lower quality of life, reduced medication adherence, worse disease progression and higher risk of transmission to others. While the majority of HIV-infected youth live in Southern Africa, research has largely focused on adults from Western countries, with limited generalisability across these populations. This review sought to identify and synthesise research on the risk factors for depression in HIV-infected youth in Southern Africa, and to summarise the available evidence on psychosocial interventions to reduce depression.

Method: A systematic review was conducted of studies using a validated measure of depression in HIV-infected youth (aged ≤19) in Southern Africa. Eligible studies included either analysis of variables associated with depression, or evaluation of the impact of psychosocial interventions on depression in this population.

Results: Twelve studies met inclusion criteria for assessing risk factors, based on nine independent samples, constituting 3,573 HIV-infected youth (aged 9–19 years). Study quality varied, with heterogeneous methodology limiting comparability and conclusions. There is some evidence that female gender, older age, food insecurity, exposure to abuse and internalised stigma are risk factors for depression, while disclosure of HIV status, satisfaction with relationships and social support are protective. Only one study met inclusion criteria for assessing psychosocial interventions (*N*=65; aged 10–13 years). The intervention study did not successfully reduce depression, demonstrating a need for low-cost, large scale interventions to be developed and trialled.

Conclusion: This review has highlighted the dearth of research into depression in HIV-infected youth in Southern Africa. Disclosing HIV status could be an important protective factor.

Keywords: South Africa; mood; HIV; children; adolescents; intervention

Introduction

Globally, rates of depression have been found to be higher among HIV-infected youth than those without HIV (1, 2), including youth with other chronic, life-threatening conditions (3). The presence of depression in HIV-infected youth has been associated with decreased adherence to antiretroviral therapy (ART) (4-6) and higher risk behaviour (7), thus increasing the risk of transmission to others. There are further serious consequences if depression continues into adulthood; depression in HIV-infected adults is associated with poorer quality of life (8-10), faster disease progression (11-13) and, according to some studies, earlier death (12, 14). Early identification and treatment of depression in HIV-infected youth therefore has the potential to improve morbidity and quality of life and reduce transmission to others and mortality.

Southern Africa has the highest HIV prevalence globally (15), with over half of the world's HIV-infected children living within these nine countries (16). Despite this, a 2011 systematic review of interventions for depression in HIV-infected individuals found that just one of the 90 eligible studies originated from Southern Africa, with the vast majority of studies (n=81) based in Europe and North America—often focused on adult male participants (17). There are several developmental, cultural and contextual factors that limit the applicability of these findings to youth in Southern Africa. Factors such as living with caregivers, attending school, higher likelihood of having HIV-infected family, the resource-poor setting and the disproportionate number of females in affected by HIV in Southern Africa (18) all need to be considered when understanding risk factors and developing appropriate interventions.

Previous reviews considering risk factors for depression in HIV-infected populations have neglected critical information about participant characteristics, such as country of origin or age (19, 20). Research in HIV-infected adults in sub-Saharan Africa has identified stage of illness; poor social support; life stressors; and stigma as potential risk factors for depression (21), but, it is unclear to what degree these findings would generalise to HIV-infected youth in Southern Africa.

Developing effective treatments for depression in people living with HIV has far-reaching consequences for improved quality of life, physical health and reduced transmission to others. Psychological interventions are more consistently effective at treating depression in HIV-infected participants than other interventions, including psychotropic drugs (17) and eliminate potential medical interactions with ART (22), providing a strong rationale for developing effective psychological support for HIV-infected youth. Most HIV-infected youth

globally live in Southern Africa, yet current understanding of depression in those living with HIV is based predominantly on adult samples from resource-rich settings. This review aims to synthesise existing research about depression in HIV-infected youth in Southern Africa by addressing the following questions:

1. What factors are associated with depression in HIV-infected youth living in Southern Africa?

2. What does the research tell us about interventions that have been implemented in Southern Africa to reduce depression in HIV-infected youth?

Method

Search Strategy

Searches were conducted according to PRISMA guidelines (23) in July, 2018. Four databases (Embase, PsycNet, PubMed and Scopus) were searched. See Table 1 for Scopus search strategy. In the other databases, filters were used to restrict the age of participants. For the purpose of this review, Southern Africa comprises: Swaziland, Lesotho, Botswana, South Africa, Namibia, Zimbabwe, Zambia, Mozambique and Malawi. To identify grey literature the first 100 references of Google Scholar were searched using adapted search terms and reference lists of included articles were hand-searched.

Selection Criteria

Although the primary focus of this review was youth aged <18 years, we included studies with 19 year olds because demographic data often groups adolescents into 15–19 year-olds, e.g. (16). Further, it is not uncommon for youth to be aged 19 when completing grade 12 in Southern Africa (24).

Eligibility criteria were:

1. Inclusion of participants <19 years old

2. Inclusion of HIV-infected participants, with data separable from any HIV-uninfected participants

3. Recruitment exclusively from Southern Africa

4. Inclusion of depression measure (clinical interview or validated screening tool)

5. Analysis of variables associated with/predictive of depression AND/OR impact of psychosocial intervention on depression

6. English or Afrikaans

A publication cut-off of since 2004 was chosen to account for the roll-out of ART to Southern African countries. ART has impacted prognosis and illness trajectory and may have introduced new factors associated with depression, such as medication regimes.

Selection of Studies

Articles returned from database searches were screened for duplicates (CH). All unique abstracts were then screened by two independent raters (CH and NH-S). Conflicts were discussed and resolved. Full texts of included articles were then screened independently by the same raters using the study eligibility criteria. Where studies comprised a substantial number of eligible participants alongside non-eligible participants, authors were contacted and asked for the data pertaining to the eligible sample (N=11). Requested data was provided from three papers; the remaining eight were excluded.

Quality Assessment and Risk of Bias

Quality assessment tools were developed for each of the review questions to address risk of bias within studies. A 16-point quality assessment tool was developed for cross-sectional and longitudinal studies, informed by previously used tools (25, 26). A second 17-point tool was developed for the assessment of intervention studies, which incorporated additional elements for intervention studies (27).

Quality of the included papers was assessed by two independent raters (CH and NH-S). Discrepancies were minimal and were resolved by a third rater (ML).

Results

Twelve studies, based on nine independent samples, met inclusion criteria for examining risk factors for depression. Only one study met eligibility for examining effectiveness of interventions for reducing depression. See Figure 1 for flowchart of study selection.

Risk Factors Associated with Depression

Study characteristics and quality. Twelve studies (nine independent samples) were included, comprising HIV-infected youth aged 9–19 years. Of these, three papers (two samples) comprised both eligible and non-eligible participants, with data relevant to this review provided by authors upon request (28-30). Results are therefore based on 3,573 HIV-infected youth from nine samples.

Sample sizes ranged from *n*=31 (eligible participants from Målqvist et al.'s (30) larger dataset) to *N*=1060 (31, 32). Most studies recruited from specialist HIV clinics using convenience sampling (28, 29, 33-37). While this provides a feasible recruitment method for researchers, and is an effective way of verifying the HIV status of participants, the risk of bias is high (38); recruiting from HIV clinics is likely to exclude youth who have not undergone testing, choose not to use HIV services, or are unable to do so. Målqvist et al. (30) used the more robust method of consecutive sampling, but was community-based and relied on self-report of HIV status. The small number of participants eligible for inclusion in this review (*n*=31) reduces the power of the analysis and generalisability of the results. Two samples were recruited through community tracing in addition to directly through HIV clinics, enabling inclusion of participants not attending specialist services (31, 32, 39); thus, providing a less-biased and more representative sample of HIV-infected youth.

Most studies recruited from South Africa (28, 29, 31-33, 37, 39, 40); with some representation from Malawi (34, 35); Zambia (36) and Swaziland (30).

Only one sample was assessed for depression via clinical interview—a method deemed more rigorous than screening tools (34). However, it is worth noting that despite excellent psychometrics internationally, the lack of child mental health research and public sector resource in Southern Africa means the Child Depression Rating Scale-Revised (CDRS-R) has been culturally adapted but not validated in these countries (41). This sample was also assessed using the Beck Depression Inventory-II (BDI-II) screening tool. The remaining studies used screening tools only: one sample used the BDI (28, 29), one used the Edinburgh Postnatal Depression Scale (EPDS) (30), one used the Center for Epidemiological Studies Depression (CESD) (36) and six samples used the Child Depression Inventory Short Form (CDI-S) (31-33, 37, 39, 40). The BDI-II, EDPS and CESD have all been validated for use in Southern Africa, with psychometrics reported (41-43). The CDI-S has been used in Southern Africa, but not adequately validated; whilst Snider and Dawes (44) addressed the wording of items, no psychometrics were provided for Southern African populations. The BDI, which measures different constructs to the BDI-II has not been validated in Southern Africa. Some studies used overall or mean scores on depression measures to create continuous variables (32-35, 37, 40) while others used cut-offs (28-30, 36). In addition to using overall score, Woollett et al. (37) conducted a separate analysis using presence of >50% of symptoms (defined by the authors as scoring one or two, on five or more items), to indicate 'increased risk of depression'. One study did not describe how depression was used as a variable in their analysis (39).

Quality of included studies varied, with quality assessment scores ranging from 3–12 (possible range 0–16). Kim et al. (35) and Sherr et al. (40) were rated highest. Sherr et al. (40) recruited a large sample using robust methods, with clearly described and reported analyses. However, Kim et al. (35) used the methodologically superior clinical interview to determine depression. See Table 2 for quality assessment.

Demographic factors.

Gender. Seven studies assessed the association between gender and depression. Four studies found no association (31, 32, 36, 40). The remaining three found depression to be associated with female gender using scores on screening tools (28, 34, 37). No significant association was found when using clinical interview (34) or 'increased risk of depression' (37), although this approached significance (*p*=.06).

Age. Six studies assessed the association between age and depression; three found depression to be associated with older age (31, 34, 40). Kim et al. (34) found this association when using clinical interview to determine depression. When using the BDI-II, there was no direct effect of age; however, there were significant interactions—older participants who were more dissatisfied with their appearance, or who had a lower height-for-age z-scores, had higher depressive symptoms. The remaining three studies found no association between age and depression (28, 36, 37); studies that found an effect of age recruited younger participants than the studies that found no effect.

Education. Three studies measured schooling variables. Kim et al. (34) found fewer years of schooling was associated with depression using both clinical interview and BDI-II score. Failing a school term/class was also associated with higher BDI-II score. However, the other two studies found no relationship between depression and education (36, 37).

Caregiver demographics. Two studies considered depression in relation to caregiver variables. Lower education of the primary caregiver was associated with higher depressive symptoms (33). Non-significant variables were primary caregiver type (i.e. single parent; both parents; aunt/uncle; grandparent/other); maternal employment status; and changes in caregiver (34); caregiver HIV status; caregiver employment, caregiver depression (measured using screening tools) (33).

Other household variables. Other household variables were assessed by four studies. Increased depression was associated with higher household density, although this did not remain significant when controlling for age, gender and study indicator (33). Surprisingly, Woollett et al. (37) found that youth looking after a sick person in the home was associated

with lower CDI-S score. It is possible that this role provides youths with a sense of purpose, acting as a protective factor. However, the paper found no association between looking after younger children in the family and depression. As a standalone finding in a single paper, this warrants further investigation.

Analysis of Målqvist et al.'s (30) dataset demonstrated significantly lower depression in those renting, rather than being a homeowner/living with parents; whilst this replicated findings from the overall dataset, the eligible sample was very small (n=22), with only one participant owning their home. No other variables from this dataset were significant. Other variables not found to be associated with depression include whether the caregiver is living in their own home (33); location of home; travel time between home and clinic (34); household composition; formal or informal housing; looking after younger siblings at home (37) and rural vs urban location (31).

Socio-economic conditions.

Household income. Five studies measured household income, with no association found with depression (31, 33, 34, 37, 40).

Food security. Three studies looked at measures of food security. Two found an association between less food security and higher depression scores (33, 37), although this did not remain significant in Bhana et al.'s (33) adjusted analysis. This may be due to differing levels of food insecurity between the two included samples (pilot and main RCT). Analysis of eligible participants from Målqvist et al.'s (30) dataset (n=28) found that, in contrast to the overall dataset, there was no association between depression and their three measures of food security.

HIV-specific factors.

Disclosure. Three studies looked at disclosure in relation to depression. Kim et al. (34) found that participants who were aware of their HIV status and had disclosed it to others had lower depression than those who had not disclosed to others, or who were not aware of their status. While Woollett et al. (37) found that participants who knew their HIV status had significantly lower depression scores than those who did not know, they found no difference between those who had disclosed their status to others (27% of the sample) and those who had not. Boyes et al. (31) found no difference in depression between those who were disclosed to about their HIV status before or after 12 years old.

ART. Two studies assessed ART adherence, with limited evidence of a relationship with depression. Although Kim et al.'s (35) univariate analyses found poorer ART adherence was associated with depression using BDI-II and clinical interview, this did not remain significant in multivariate analyses. Okawa et al. (36) found no relationship between depression and ART non-adherence.

Two studies examined the role of other ART-related variables. Presence of ART side-effects was associated with higher depression (31), while ART use (93.6% of the sample); an efavirenz-based regimen; and second-line ART (34) were not.

Health. Three studies assessed associations with other health variables. Boyes et al. (31) found worse overall health and negative clinic interactions predicted higher depression. More severe immunosuppression classification (based on CD4) predicted depression using BDI-II, but not clinical interview (34). No other bio-clinical parameters assessed by Kim et al. (34) were associated with depression, including: history of tuberculosis; most recent CD4 count; nutritional status; alcohol use and hospital admission in the past year. Woollett et al. (37) found no association between depression and history of tuberculosis or being hospitalised.

Mode of transmission. Two studies assessed the relationship between depression and mode of HIV infection. Sherr et al. (40) found higher depression scores in those who had acquired HIV behaviourally compared with perinatally, while Boyes et al. (31) found no differences. However, it is worth noting that Boyes et al. (31) used an age cut-off and algorithm in the absence of clinic notes regarding the mode of infection.

Other HIV factors. Pantelic et al. (32) found HIV-related disability to be associated with depression via higher abuse victimisation and more enacted HIV stigma.

Social and community support.

Relationships. Four studies assessed relationships between youth and their family/caregivers. Okawa et al. (36) found unsatisfactory relationships with family was related to depression. Bhana et al. (33) found lower youth ratings of caregiver supervision was associated with higher depression, as was lower likelihood of youths seeking social support. In contrast, Boyes et al. (31) found no association between depression and youth-rated parental monitoring, nor parent communication. They did, however, find that youth-rated positive parenting was associated with lower depression, as was better self-rated social support. Surprisingly, Woollett et al. (37) found higher depression scores in youth who

reported receiving praise at home; getting the same things as other children in the home; and feeling like they belonged in the family they were being raised in.

Two studies examined other relationships. Unsatisfactory relationships with friends and healthcare workers were both associated with depression (36). Those with a current or past boyfriend/girlfriend had higher BDI-II scores than those who had never had a boyfriend/girlfriend (34).

Community. Two studies looked at youth engagement with the wider community. Having a safe place in the community and accessing a clinic support group were associated with lower depression (31, 37).

Past trauma/stressors.

Violence and abuse. Six studies assessed various forms of violence and abuse in relation to depression. Although there was heterogeneity in how sexual abuse history was measured, four studies found an association with depression (28, 31, 32, 37). Four studies found an association between depression and experiences of violence (28, 29, 32, 37). Measures of violence also varied, including 'being hit', interpersonal violence among females, collective violence and peer violence. Having witnessed somebody being stabbed or shot was not associated with depression (37).

Feeling unsafe at home, emotional abuse and cumulative adverse/abuse experiences were also associated with depression in this review (28, 31, 32, 37). In contrast to the other studies, Kim et al. (34) found no association between depression and experience of forced sex, physical abuse or witnessing physical abuse in the home.

Bereavement. Four studies assessed parental survival status; all found no association with depression (31, 36, 37, 40).

Two studies assessed other bereavement variables, with mixed findings. Kim et al. (34) found a death in the family/household was associated with higher BDI-II score, whilst Woollett et al. (37) found no association between bereavement and depression.

Bullying. Two studies looked examined bullying. Boyes et al. (31) found bullying victimisation was associated with higher depressive symptoms. Kim et al. (34) found being bullied for taking medication was associated with depression when measured by both the BDI-II and CDRS-R, but being bullied for appearance was not.

Psychosocial factors.

Stigma. Five studies explored the relationship between depression and stigma; all five found an association (31-33, 36, 39). Three of these measured enacted, anticipated and internalised stigma separately using the Adolescents Living with HIV Stigma Scale (31, 32, 39). Only Pantelic et al. (39) found an association between depression and anticipated stigma; two found an association with enacted stigma (32, 39); and all three found an association with internalised stigma.

Other psychosocial factors. Three studies explored various other psychosocial factors. As to be expected from the overlap between psychosocial factors and characteristic symptoms of depression, many of the psychosocial factors examined were found to be associated with depression. Woollett et al. (37) found that suicidality; feeling unable to control one's future and not having dreams for one's future were all predictive of CDI-S score and 'increased risk of depression'. Higher depression score was also associated with higher score on the Revised Child Manifestation of Anxiety Scale. Depression was not associated with score on the Child PTSD Checklist. Boyes et al. (31) found that lower self-efficacy was related to higher depression. Bhana et al. (33) found lower self-concept (measured using a scale validated for use in Southern Africa) was associated with higher depression. Two of the ten coping styles measured by the Kidcope were associated with higher depression score: social withdrawal and resignation, although this was only assessed in the pilot-study participants (*n*=66).

Potential Treatments for Depression

Study characteristics and quality. Only one identified study examined psychosocial interventions for depression in HIV-infected youth (45). Participants (10–13 years) were clinically-verified as being HIV-infected and were randomly allocated to a family-based intervention (*n*=33) or wait list control group (*n*=32). The intervention used a cartoon-based storyline about a boy with HIV to deliver information and promote discussion within and between families over six sessions. The curriculum covered a range of topics relevant to HIV in youth (listed in Table 5). The intervention was delivered by lay counsellors, supervised by a psychologist. Depression was measured pre and post intervention using the CDI-S. Study quality is described in Table 4.

Effect on depression. Bhana et al. (45) used generalised linear models to compare intervention and control groups over time, accounting for the effect of repeated measures. The intervention did not have a significant effect on depression.

Discussion

This review sought to identify risk factors for depression in HIV-infected youth in Southern Africa and evaluate potential psychosocial interventions.

Only one intervention study was identified, consisting of a family programme; this was not effective at significantly reducing youth depression. Literature on interventions for HIV-infected youth outside of Southern Africa is also sparse. A global review of interventions for depression in HIV-infected individuals (17) identified just one study of adolescents, which was USA-based and used massage as the intervention (46). Although the review found psychological interventions to be particularly effective in reducing depression, the populations studied make the findings unlikely to be generalisable to Southern African youth. In addition, interventions to be implemented in Southern Africa need to take account of the resource-poor context. One review of low and middle-income countries identified 18 community and school-based intervention studies that assessed depression as an outcome in youth (47). Of these, seven demonstrated a significant reduction in depression. These interventions, though not tailored to HIV-infected youth, are evidence for the feasibility of community-based interventions in resource-poor settings and indicate they have potential to reduce depression. In South Africa, attendance at community-based organisations (CBOs) is associated with reduced depression (48) and it may be that CBOs provide a potential target for future interventions.

Twelve studies (nine samples) were identified that pertained to risk factors for depression. Some key findings from these studies are discussed in relation to wider literature below.

Demographic factors

This review found some evidence that female gender is a risk factor for depression. Female gender has been identified as a risk factor for depression in the general population, including in Southern Africa (49-52), as well as HIV-infected adults (53). Salk et al.'s (51) meta-analysis found gender differences in depression are not present in young childhood, but start emerging around age 12 in the general population. This could explain the mixed findings in the current review, as studies including younger participants found no effect of gender, with no studies exploring gender and age interactions.

Only one study examined caregiver depression and found no association with youth depression. This contrasts with other studies that have found caregiver depression is associated with increased emotional difficulties in Southern African HIV-infected youth (54,

55), although Louw et al. (55) found this association was weaker in HIV-infected, compared with HIV-uninfected, participants.

Some evidence was found for an association between food insecurity and depression, but not between household income and depression. In line with this, American studies that have distinguished between food insecurity and poverty, have found only the former to be associated with depression in youth (56, 57). Food insecurity is also a predictor of depression in the broader Southern African youth population (58, 59).

HIV-specific factors

The results of this review suggest that youth being aware of their HIV status is protective, but findings were mixed regarding the effect of disclosure to others. Wider research on disclosure to others is also mixed. In Namibian HIV-infected youth, disclosure to others was associated with more mental health difficulties, although there was no direct association with emotional symptoms (60). Qualitative studies have found that South African youth who disclosed to teachers generally experienced increased academic support, but disclosure revealed via gossip sometimes result in discrimination and stigma (61). Lam et al.'s (62) study of American 16–25 year olds found disclosure to acquaintances was associated with increased distress, while disclosure to close family friends was not, indicating that perhaps measures of disclosure need to be more nuanced than those employed in this review.

This review did not find evidence of an association between ART adherence and depression. This contrasts with findings outside of Southern Africa, where there is a well-established association between poor ART adherence and depression in HIV-infected youth (63-65).

Social and community support

The findings indicate that satisfaction with relationships and seeking social support are protective against depression, which is consistent with wider literature about the positive impacts of social support for HIV-infected youth (21, 60, 62, 66).

Past trauma/stressors

In line with these findings, a study of Southern African youth found interpersonal violence in the home was associated with higher depression, but community violence was not; this remained the case when controlling for HIV status (67). Community violence was,

however, related to trauma symptoms, suggesting while it does have a psychological impact on youth in Southern Africa, it may not manifest as depression.

Orphanhood status was not found to be associated with depression. In line with this, a study of HIV-infected and uninfected South African youth found no significant association between orphanhood status and depression (68) and a Nambian study found no relationship between orphanhood status and broader mental health problems in HIV-infected youth (60).

Psychosocial support

Findings regarding the relationship between depression and internal stigma are convincing and replicate wider research on the role of stigma in HIV-infected populations (21, 60, 69, 70).

Clinical Implications

Based on the intervention study identified in this review, it is not possible to make recommendations for reducing depression in HIV-infected youth. However, findings regarding risk factors for depression offer potential targets for intervention. For example, interventions aimed at reducing stigma, violence and abuse, and food insecurity should be considered. In support of this, a stigma-reducing intervention for South African HIV-infected adults significantly reduced depressive symptoms (71). Cluver et al. (72) ran a parent programming intervention with youths and their caregivers in South Africa, aimed at reducing child abuse. They found parenting improved, and abuse and youth depression reduced. HIV-infected youth could therefore potentially benefit from a similar intervention, perhaps with further support for caregivers to inform youths of their HIV status.

Schools offer a viable method of delivering large-scale, low-cost interventions and could be a good target for reducing stigma and bullying, as well as supporting safe disclosure of HIV status to others. Having a safe community space was identified as a protective factor, yet not all youths had access to one. CBOs may be able to provide this and offers another potential target for delivering large-scale, low-cost interventions.

Based on the results of this review, increasing self-concept, reducing social withdrawal and resignation could be potential aims for psychosocial interventions.

Limitations

There are several limitations of this review. Measures of depression used in this review mainly relied on the adaptation of Western-developed measures, using Western conceptualisations of depression, with alternative terminology either agreed by researchers or developed from a small sample of participants (41, 44). The construct validity of these measures can therefore be questioned. In addition, data on risk factors were derived exclusively from cross-sectional studies, making it difficult to determine causality between depression and associated variables. The lack of control groups in the risk factor studies, and the lack of mental health research in Southern Africa more generally, means it is unclear which risk factors are specific to HIV-infected youth and which are relevant to youth generally.

Future Research

Much of the psychosocial research on Southern African youth focuses on those *affected* by HIV (i.e. caring for HIV-infected family members or orphaned by HIV/AIDS). Despite being at increased risk of HIV-infection, most of these studies failed to record the HIV status of youth themselves. HIV-infection is associated with biological changes and specific psychological and social consequences. This review identified several HIV-specific variables that appear to be associated with depression, including immunosuppression, disclosure of status and being bullied for taking medication. Future research should therefore record HIV status of youth to improve our understanding of risk factors relevant to this population so that interventions can be tailored appropriately.

As research on interventions is severely lacking, further research in this area is needed. To optimise viability, interventions would likely need to be community or school-based, and may involve training of teachers or other community workers to deliver interventions.

Conclusions

Despite the high prevalence of HIV in youth in Southern Africa, this review has identified limited research considering depression in this population. Some preliminary evidence for potential risk factors is presented, which offer possibilities for the focus of interventions, but more research is needed. Future research should consider measuring HIV status as standard and conducting separate or comparative analysis for this participant group.

Wider literature can offer some suggestions for community-based interventions that take account of the impoverished setting.

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Table 1. Scopus search strategy

Field code	Search terms used
Title-Abstract-Keywords	depress* OR "affective disorder*" OR "adjustment disorder*" OR dysthymi* OR mood OR distress
	AND
Title-Abstract-Keywords	hiv OR aids OR "human immunodeficiency virus" OR "acquired immune deficiency"
	AND
Title-Abstract-Keywords	botswana* OR batswana OR swazi* OR zimbabwe* OR namibia* OR mozambi* OR lesotho OR basotho OR "south africa*" OR malawi* OR tonga* OR zambia* OR "southern africa*"
	AND
Title-Abstract-Keywords	child* OR teen* OR young OR pediatric OR paediatric OR adolescen* OR youth* OR juvenile* OR infant*
	AND
Database filters applied	Publication year > 2003 Language: English or Afrikaans Document type: article, article in press, conference paper

Table 2. Quality assessment of papers examining risk factors for depression

Study	Recruitment	Eligibility criteria	Sample size justified?	Sample size	Participation rate	Criteria for depression	Criteria for HIV	Confounding	Statistical analysis	Reporting of results	Total score
Bhana et al. (2016)	Convenience	Specified (+)	Not justified	177 (+)	Not reported	Screening tool not validated in Southern Africa	Clinically verified (+)	Adjusted for age and gender (+)	Statistical methods adequate, but some details missing (+)	Reporting incomplete	+++++ 5
Boyes et al. (2019)	Consecutive (++)	Specified (+)	Not justified	1060 (++)	Reported. Over 75% (++)	Screening tool not validated in Southern Africa	Clinically verified (+)	Adjusted for age and gender (+)	Clearly described, robust and appropriate (++)	Reporting incomplete	++++ ++++ +++ 11
Kidman et al. (2018)	Convenience	Specified (+)	Not justified	196 (+)	Not reported	Screening tool not validated in Southern Africa	Clinically verified (+)	Adjusted for age and gender (+)	Statistical methods adequate, but some details missing (+)	M and SD for continuous variables, and CI reported (+)	++++ ++ 6
Kidman and Violari (2018)	Convenience	Specified (+)	Not justified	105	Not reported	Screening tool not validated in Southern Africa	Clinically verified (+)	Adjusted for age and gender (+)	Statistical methods adequate, but some details missing (+)	M and SD for continuous variables, and CI reported (+)	++++ + 5
Kim et al. (2015)	Convenience	Not specified	Not justified	562 (++)	Reported. Over 75% (++)	Clinical interview (++)	Clinically verified (+)	Adjusted for age and gender (+)	Statistical methods adequate, but some details missing (+)	Reporting incomplete	++++ ++++ + 9
Kim et al. (2017)	Convenience	Specified (+)	Not justified	519 (++)	Reported. Over 75% (++)	Clinical interview (++)	Clinically verified (+)	Adjusted for age and gender (+)	Clearly described, robust and appropriate (++)	M and SD for continuous variables, and CI reported (+)	++++ ++++ ++++ 12

Målqvist et al. (2016)	Consecutive (++)	Not specified	Not justified	31 with HIV	Not reported	Screening tool validated in Southern Africa (+)	Self-report	N/A	N/A [a]	M and SD for continuous variables, and CI reported (+)	++++ 4
Okawa et al. (2018)	Convenience	Specified (+)	Not justified	190 (+)	Not reported	Screening tool validated in Southern Africa (+)	Clinically verified (+)	Not adjusted for sex and age	Statistical methods adequate, but some details missing (+)	M and SD for continuous variables, and CI reported (+)	++++ ++ 6
Pantelic et al. (2017)	Consecutive (++)	Specified (+)	Not justified	1060 (++)	Reported. Over 75% (++)	Screening tool not validated in Southern Africa	Clinically verified (+)	Adjusted for sex and age (+)	Clearly described, robust and appropriate (++)	M and SD for continuous variables, and CI reported (+)	++++ ++++ +++ 11
Pantelic et al. (2018)	Consecutive (++)	Specified (+)	Not justified	721 (++)	Reported. Over 75% (++)	Screening tool not validated in Southern Africa	Clinically verified (+)	Not adjusted for sex and age	Statistical methods adequate, but some details missing (+)	M and SD for continuous variables, and CI reported (+)	++++ ++++ ++ 10
Sherr et al. (2018)	Consecutive (++)	Specified (+)	Not justified	1024 (++)	Reported, 90.1% (++)	Screening tool not validated in Southern Africa [b]	Clinically verified (+)	Moderation analysis for sex and age (+)	Clearly described, robust and appropriate (++)	OR and CI reported (+)	++++ ++++ ++++ 12
Woollett et al. (2017)	Convenience	Not specified	Not justified	343 (+)	Not reported	Screening tool not validated in Southern Africa	Clinically verified (+)	Not adjusted for sex and age	Statistical methods adequate, but some details missing (+)	No mean, range or SD for depression score. Reporting unclear.	+++ 3

CI, confidence intervals; OR, odds ratio; AOR, adjusted odds ratio; SE, standard error

[a] Study itself did not analyse HIV-infected sample separately, but authors provided data to allow analysis for this review. Analysis available in Appendix B.

[b] The authors of this review did not consider validation to be adequate

Table 3. Data extraction from studies examining risk factors for depression

Study	Sample	Design	Key measures	Associated with depression	Not associated with depression
Bhana et al. (2016)	Perinatally-infected HIV+ children and carer dyads recruited for VUKA family program (N=177) Age: 9–14 (M=11.68; SD=1.42) 49% female Country: South Africa	Cross-sectional, using baseline data from RCT and pilot-RCT	*HIV status*: Clinically verified *Depression*: CDI-S; total score used as variable α=.30	Higher depressive score associated with: 1) Lower caregiver education (β=–0.412, p=.010)[a] 2) Higher household density (β=0.092, p=.041) 3) Less food security (ie. Caregiver less reported hunger in the past month) (β=0.254, p=.029) 4) Lower self-concept (β=–0.076, p<.001)[a] 5) Higher internal stigma (β=0.655, p=.027)[a] 6) Lower levels caregiver supervision (β=–1.667, p<.001)[a] 7) Lower likelihood of seeking social support (β=0.429, p=.003)[a] 8) Use of social withdrawal as coping method (β=1.297, p=.022) 9) Use of resignation as coping method (β=1.156, p=.036)[a]	1) Caregiver living in own place 2) Caregiver receiving any grants for child 3) Household income 4) Caregiver employment 5) Caregiver HIV status 6) Caregiver depression (measured by BDI-II or CES-D)
Boyes et al. (2019)	HIV+ youth (N=1060) Age: 10–19 (M=13.31; SD=2.51) 55% female Country: South Africa	Cross-sectional	*HIV status*: Clinically verified *Depression:* CDI-S; mean score used as variable α=.59	Higher depression score associated with: 1) ART side-effects (β=0.12, p<.001) 2) Negative clinic interactions (β=0.07, p<.01) 3) Internalised stigma (β=0.17, p<.001) 4) Past year emotional abuse (β=0.12, p<.001) 5) Lifetime sexual abuse (β=0.10, p<.01) 6) Bullying victimisation (β=0.07, p<.05) 7) Age (β=0.11, p<.001) Lower depression scores associated with: 8) Better health (β=−0.06, p<.05) 9) Accessing a clinic support group (®=−0.09, p<.001) 10) Social support (β=−0.13, p<.001) 11) Positive parenting (β=−0.11, p<.001) 12) Self-efficacy (β=−0.07, p<.05)	1) Gender 2) Mode of infection 3) Disclosed to before age 12 4) Enacted stigma 5) Anticipated stigma 6) Poor parental monitoring 7) Parent communication 8) Orphaned 9) Poverty 10) Rural/Urban location
Kidman et al. (2018)	HIV+ youth aged 13–24 years (N=250) Country: South Africa	Cross-sectional	*HIV status*: Clinically verified *Depression*: BDI; depression defined as score ≥20	Presence of depression (cut-off on BDI) associated with: 1) Gender (OR 1.72, p=.008) 2) Total adverse childhood experiences (OR 4.28, p<.001)[b] 3) Experience of sexual abuse (OR 3.23, p<.001)[b] 4) Experience of collective violence (OR 3.48, p<.001)[b]	1) Age

	Data obtained from authors for those aged 13–19 years (n=196) 53.6% female		α = .91		
Kidman and Violari (2018)	HIV+ females aged 13–24 years (*N*=129) Age: 13–24 (M= ; SD=) 100% female Country: South Africa Data obtained from authors for those aged 13–19 (n=105)	Cross-sectional	*HIV status*: Clinically verified *Depression*: BDI; depression defined as score ≥20 α = not reported	Presence of depression (cut-off on BDI) associated with: 1) Past-year interpersonal violence (OR=4.98, *p*<.001) [b] 2) Lifetime interpersonal violence (OR=5.15, *p*=.003) [b]	
Kim et al. (2017)	Perinatally-infected HIV+ youth (*N*=519) Age: 12–18 (*M*=14.5; *SD*=2) 56.1% female Country: Malawi	Cross-sectional	*HIV status*: Clinically verified *Depression*: Chichewa version of BDI-II; total score used as variable α =.80 CDRS-R; depression defined as score ≥ 55	In univariate analysis, higher depression score (BDI-II) associated with: 1) ART adherence (OR 1.02, *p*=.05) In univariate analysis, presence of depression (CDRS-R) associated with: 1) ART adherence (OR 1.71 p=0.02) [b]	1) ART adherence in multivariate analysis

Kim et al. (2015)	HIV+ adolescents (*N*=562)	Cross-sectional	*HIV status*: Clinically verified	In multivariate analysis, higher depression score (BDI-II) associated with:	1) School grade
				1) Female gender (β= 2.13, *p*=.002)	2) Family income
	Age: 12–18			2) Fewer years of schooling (β= 3.84, *p*=.0005)	3) Location of home
	(*M*=14.5; *SD*=2)		*Depression*:	3) Death in the family/household (β= –1.77, *p*=.01)	4) Time it takes from clinic to home
	56.1% female		Chichewa	4) Failing a school term/class (β= –1.46, *p*=.003)	5) Primary caregiver type
	Country: Malawi		version of BDI-II; total score	5) Being bullied for taking medications (β= 5.31, *p*<.0001)	6) Maternal death or employment status
			used as variable	6) Experience of a romantic relationship (β= –2.38, *p*=.002)	7) Change in caregiver
				7) Not disclosing and sharing HIV status (β= –1.83, *p*=.02)	8) Experience of forced sex,
				8) Worse level of immunosuppression (β= –2.58, *p*=.0009)	physical abuse, or witnessed
			CDRS-R;	9) Older age*low satisfaction with appearance (β= –0.93, *p*=.03)	physical violence in home
			depression	10) Older age*lower height-for-age z score (β= –20.39, *p*=.007)	9) Being bullied for appearance
			defined as score ≥ 55		10) Hospital admission in last year
					11) Satisfaction with physical appearance
				In multivariate analysis, presence of depression (CDRS-R) associated with:	12) Use of alcohol in past 30 days
				1) Age (β= 1.23, *p*=.004)	13) Age of HIV disclosure
				2) Fewer years of schooling (β= 3.30, *p*=.005)	14) Whether on ART or not
				3) Being bullied for taking medications (β= 4.20, *p*<.0001)	15) History of tb treatment
					16) Initial who stage
					17) Most recent CD4 count
					18) Nutritional status
Målqvist et al. (2016)	HIV+ and HIV-pregnant women (*N*=1038)	Cross-sectional	*HIV status*: Self-report	Presence of depression (cut-off on EPDS) associated with:	1) Mother's education
				1) Being a home-owner or living in the parental homestead (compared with being a tenant; *p*=.047)	2) Marital status
			Depression:		3) Employment
	Data obtained from lead author for adolescent HIV+ participants: (*n*=31)		EPDS; depression defined as score ≥13	Trend towards:	4) Sharing toilet
				2) Household water sourced from surface (compared with communal tap or tap on site; *p*=.058, SR =2.2)	5) Cut size of meals
			α = not reported		6) Not eaten for whole day
					7) Cut meals for children
	Age: 14–19, (*M*=17.88; *SD*=1.15) 100% female Country: Swaziland				

Okawa et al. (2018)	HIV+ youth, aware of status (*N*=190) Age: 15–19; (*M*=17.02; *SD*=1.32) 57.9% female Country: Zambia	Cross-sectional	*HIV status*: Clinic-verified *Depression*: CES-D short form; depressive symptoms defined as score ≥10; α =.74	Depressive symptoms (cut-off on CES-D) associated with: 1) Unsatisfactory relationships with family (AOR 3.01, *p*<.01) 2) Unsatisfactory relationships with health workers (AOR 2.68, *p*<.01) 3) Experiencing stigma (AOR 2.99, *p*=.01) 4) Unsatisfactory relationships with friends (AOR 1.75, *p*=.03)	1) Gender 2) Age 3) Education 4) Parental survival status 5) Level of basic HIV knowledge 6) Non-adherence to ART
Pantelic et al. (2017)	HIV+ youth (*N*=1060) Age: 10–19 (*M*=13.8; *SD*=2.83) 55.2% female Country: South Africa	Cross-sectional	*HIV status:* Clinic-verified *Depression*: CDI-S; mean score used; α =.62	Depressive symptoms were associated with: 1) Internalised HIV stigma (β= .445, *p*<.001) 2) Enacted HIV stigma (β= .294, *p*<.001) 3) Abuse victimisation (β= .396, *p*<.001). 4) Indirectly associated with HIV-related disability via more abuse victimization (β= .147, *p*<.001) 5) Indirectly associated with HIV-related disability via more enacted HIV stigma (β= .145, *p*<.001)	1) Gender
Pantelic et al. (2018)	HIV+ youth aware of their status (*N*=721) Age: 10–19 (*M*=14.65; *SD*=2.75) 56.5% female Country: South Africa	Cross-sectional	*HIV status:* Clinic-verified *Depression*: CDI-S; α =.62	Depressive symptoms associated with: 1) Enacted stigma (*r*= .092, *p*<.01) 2) Internalised stigma (*r*= .340, *p*<.01) 3) Anticipated stigma (*r*= .203, *p*<.01)	
Sherr et al. (2018)	Perinataly and horizontally infected HIV+ youths a (*N*=1024) Age: 10–19 (*M*=13.76; *SD*=2.82) 54% female	Cross-sectional	*HIV status*: Clinic-verified *Depression*: CDI-S; mean score used as variable; α=.64	Higher depressive scores associated with: 1) Having acquired HIV behaviourally rather than perinatally (β= 0.81 *p*≤0.001) [c] 2) Older age (β = 0.09, *p*<.001) 3) Moderation analyses suggest that behaviourally-infected youth who are also maternal orphans are more likely to report higher rates of depression (β = 1.075, *p*<.001)	1) Gender 2) Poverty 3) Maternal orphan 4) Paternal orphan

	Country: South Africa				
Woollett et al. (2017)	HIV+ youth (*N*=343) Age: 13–19 (*M*=16; *SD*=not reported) 52% female Country: South Africa	Cross-sectional	*HIV status*: Clinic-verified *Depression*: CDI-S; total score used as variable AND symptomatic defined as experiencing >50% of symptoms <u>α</u> =.70;	Higher depressive score (CDI-S) associated with: 1) More days hungry (*p*<.001) 2) Higher anxiety score (*p*<0.001) 3) Higher peer violence score (*p*<0.001) 4) Higher PTSD score (*p*<0.001) 5) Female gender (*p*<0.001) 6) Not looking after sick person in the home (*p*=.04) 7) Feeling they belong (*p*<0.001) 8) Gets praise (*p*<0.001) 9) Get same things as other children in home (*p*<0.001) 10) Suicidality (*p*<0.001) 11) Peer violence inside and outside of school (*p*=.01) 12) Experienced violence: inappropriate touch (*p*=.01) 13) Experienced violence: been hit (*p*<0.001) 14) Experienced violence: don't feel safe at home (*p*<0.001) 15) Not know their status (*p*<0.001) 16) Do not feel control future (*p*<0.001) 17) Do not have dream (*p*<0.001) Associated with presence of >50% of symptoms: 1) Been hit (*p*=.02) 2) Been inappropriately touched (*p*=.01) 3) Do not feel control future (*p*=.04) 4) Do not feel safe at home (*p*<.001) 5) Do not have dream (*p*<.001) 6) Do not have safe place in the community (*p*<.001) 7) Have experienced forced sex (*p*=.02) 8) Experienced peer violence outside of school (*p*=.01) or in and outside school (*p*=.04) 9) Any form of suicidality (*p*<.001)	1) Age 2) Ethnicity 3) Household composition 4) Formal/informal housing 5) Grade 6) Highest school grade achieved 7) Orphanhood status 8) Looks after young children in home 9) Has had sex 10) Seen someone shot 11) Seen someone stabbed 12) Receiving grants 13) Has had TB 14) Significant bereavement (parent, sibling, primary carer) 15) Knowing how contracted HIV 16) Disclosed status to others 17) Age by sex 18) Times things stolen 19) Number of losses 20) Years since loss 21) Often drink

Note. Målqvist et al.'s results derived from analysis of dataset provided by authors. See Appendix B for full analysis.

CDI-S, child depression inventory short form; BDI-II, Beck depression inventory-II; CDRS-R, children's depression scale revised; EPDS, Edinburgh postnatal depression scale; SR, adjusted standardised residual

[a] remained significant after adjusting for age, gender and study indication (pilot or RCT)

[b] remained significant after adjusting for age

[c] remained significant after adjusting for age and gender

Table 4. Quality assessment of studies examining interventions for depression

Study	Recruitment	Eligibility criteria	Sample size justified?	Participation rate	Criteria for depression	Criteria for HIV	Allocation to condition	Description of intervention	Assessment of outcome	Confounding	Follow up	Statistical analysis	Reporting of results	Total score
Bhana et al. (2014)	Convenience	Specified (+)	Not justified	Reported. Over 75% (+)	Screening tool not validated for use in Southern Africa	Clinically verified (+)	Random (+)	Clearly described (+)	Unclear	None	Reported (+)	Appropriate and robust (++)	No CI	++++ ++++ 8

CI, confidence intervals

Table 5. Data extraction from studies examining interventions for depression

| Study	Sample	Design	Key measures	Intervention	Effect of Intervention
Bhana et al. (2014)	HIV+ youth and caregiver dyads (*N*=65) Intervention: (*n*=33) Control: (*n*=32); Completed follow-up: (*N*=59) Age: 10-13 (*M*=11.57) Country: South Africa	Pilot-RCT	*HIV status:* Clinic-verified *Depression:* CDI-S (α= .54)	VUKA family program: culturally-adapted CHAMP model intervention 6 sessions over 3-month period Session topics included: (a) AIDS-related loss and bereavement; (b) HIV transmission and treatment knowledge; (c) Disclosure of HIV status to others; (d) Youth identity, acceptance and coping with HIV; (e) Adherence to medical treatment; (f) Stigma and discrimination; (g) Caregiver-child communication, particularly on sensitive topics such as puberty and HIV; (h) Puberty; (i) Identifying and developing strategies to keep children safe in high-risk situations where sexual behaviour and drug use are possible; and (j) Social support	No significant effect of VUKA on youth depression (β= −.736, *p*=.417)

CDI, Child depression inventory
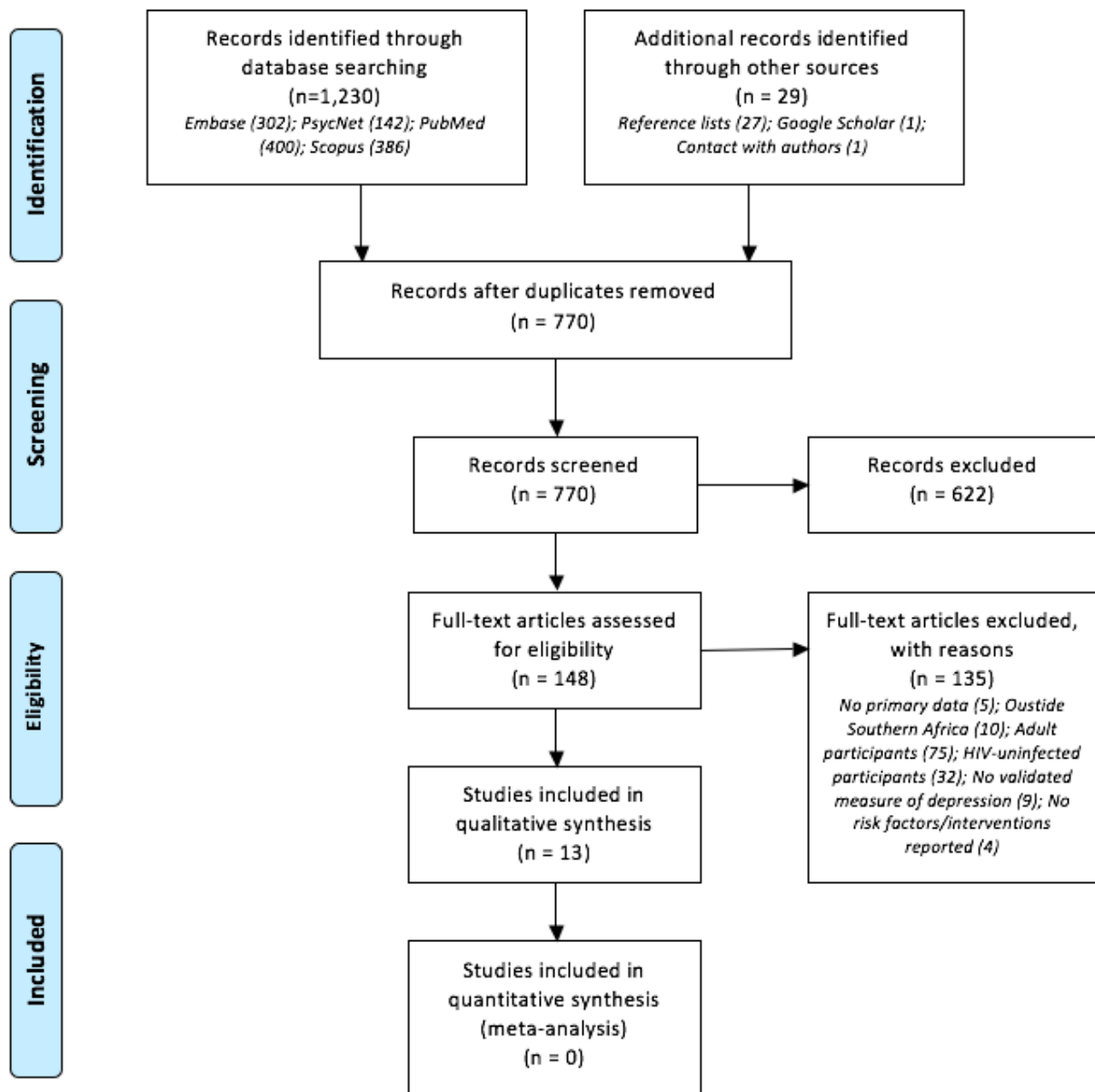
Figure 1. PRISMA flowchart of study selection (23).