

Mental health and HIV: research priorities related to the implementation and scale up of 'treat all' in sub-Saharan Africa

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Abstract

World Health Organization (WHO) guidelines call for antiretroviral therapy (ART) for all people living with HIV (PLWH) regardless of CD4 cell count, a policy often referred to as 'treat all'. This article seeks to: (1) provide an overview of mental health research among PLWH in sub-Saharan Africa (SSA) and interventions or strategies to address comorbid mental illness among those living with HIV; and (2) describe key mental health-related recommendations to inform the successful implementation and scale up of 'treat all' policies in SSA. An initial set of mental health-related research recommendations was developed by a working group comprising investigators affiliated with the International epidemiology Databases to Evaluate AIDS (IeDEA) consortium. Recommendations were shared with those who attended the All-Africa IeDEA Meeting in Kigali, Rwanda in November 2017 and refined following the meeting. Recommendations reflect a need for epidemiological research to examine the prevalence, incidence, and impact of mental health multimorbidities on HIV treatment outcomes, intervention research to examine the extent to which improving the mental health of people living with HIV enhances HIV treatment outcomes, and implementation science research to evaluate promising models of integrated mental health and HIV care. Key research recommendations can advance understanding and treatment of mental illness among those living with HIV in sub-Saharan Africa and beyond.

Keywords: mental health, HIV, Africa, treat all

The World Health Organization (WHO) guidelines call for antiretroviral therapy (ART) for all people living with HIV (PLWH) regardless of their CD4 T cell count, a policy often referred to as 'treat all' [1]. 'Treat all' strategies, increasingly common in low-resource settings, are motivated by evidence that treating HIV as soon as possible after infection can improve patient outcomes and reduce transmission [2,3]. Large-scale success of the implementation and scale-up of 'treat all' requires understanding and addressing known barriers to achieving optimal HIV treatment outcomes. Insufficient attention has been paid to identifying and addressing the mental health needs of PLWH, particularly in sub-Saharan Africa (SSA), a region that accounts for more than 70% of the global burden of HIV [4]. Because mental health disorders are common among PLWH, often underdiagnosed and undertreated in low-resource settings, and associated with suboptimal HIV treatment outcomes, addressing the mental health needs of those living with HIV should be a critical component of successful implementation, scale-up, and achievement of 'treat all' priorities in SSA and beyond [5–11]. This article seeks to: (1) provide an overview of research regarding the mental health of PLWH in SSA and interventions and strategies to address comorbid mental illness among PLWH and (2) describe key mental health-related research priorities to inform the successful implementation and

scale up of 'treat all' policies in SSA and other low-resource settings. Because substance use disorders are the focus of a separate paper in this supplement [12], such disorders are not addressed in this article.

Mental health disorders among PLWH

Mental health disorders (e.g. depression, post-traumatic stress disorder [PTSD]) are among the most prevalent comorbidities in PLWH globally and more common among PLWH than the general population [5,13,14]. It has been estimated that approximately half of PLWH meet criteria for one or more mental health disorder [5]. High rates of mental health disorders have been documented among PLWH residing in low- and middle-income countries (LMICs), including SSA [14]. Research suggests that these are associated with delayed HIV diagnosis [15], and with suboptimal HIV treatment outcomes, including late ART initiation, poor ART adherence, lack of viral suppression, and increased AIDS-related mortality across LMICs [15,16].

It is important to note that most studies focused on the mental health of PLWH in SSA and globally do not distinguish between pre-existing mental health disorders among PLWH and mental health disorders with an onset subsequent to HIV infection or its diagnosis. Two studies from South Africa have revealed that an important proportion of HIV test seekers experience mental health symptoms prior to their diagnosis. In the first, 55% of individuals surveyed displayed depressive symptoms prior to HIV testing and individuals with depressive symptoms prior to HIV

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diagnosis were less likely to receive CD4 cell count testing after diagnosis [17]. In the second, the prevalence of major depressive disorder, generalised anxiety disorder and PTSD among HIV test seekers was 14%, 5% and 5%, respectively [18]. Additional longitudinal research is needed to better understand the course and severity of mental health disorders among PLWH in relation to HIV infection, diagnosis, and treatment.

Depression

Depression is the most prevalent mental health disorder among PLWH globally and in SSA [5,19,20]. Estimates of depressive symptoms among PLWH on ART in SSA have varied between 14% and 32%, with substantial variability within and between measurement scales [21]. A meta-analysis of studies conducted in Western countries found the prevalence of major depressive disorder to be nearly two-fold higher among PLWH compared to those who did not have HIV [22].

Little is known about the relationship between depression and delayed HIV diagnosis in SSA. However, depression has been associated with suboptimal HIV treatment outcomes in SSA, including late ART initiation and poor adherence, lack of viral suppression, more rapid decline in CD4 cell count, faster progression to AIDS and increased AIDS-related mortality [8,9,23]. Similar to other mental health disorders, depression remains underdiagnosed and undertreated throughout SSA, compromising timely ART initiation and treatment adherence at individual and population levels, and attainment of ‘treat all’ objectives [10,11,23].

Anxiety disorders

Estimates of the prevalence of anxiety-related symptoms or anxiety disorders among PLWH in SSA have varied between 9% and 34% [5,24] compared to 3–7% among general populations throughout SSA [25].

Among PLWH in South Africa, anxiety was significantly associated with delayed engagement in HIV care following diagnosis, but not significantly associated with ART adherence [11,24]. Little is known about the relationship between anxiety symptoms or diagnoses and viral suppression or HIV disease progression in SSA. In high-income settings, anxiety symptoms have been associated with poor adherence to ART, higher viral load and lower CD4 cell count [26,27].

Post-traumatic stress disorder

Exposure to traumatic events in childhood and adulthood, including child physical and sexual abuse, intimate partner violence, sexual assault, and war is also prevalent among PLWH and associated with mental health disorders and suboptimal HIV treatment outcomes [28]. Estimates of PTSD among PLWH in SSA are limited and vary widely. Studies conducted with PLWH in South Africa estimated PTSD prevalence at 5–20% [29,30] compared to approximately 2% among the general population [31,32].

Little is known about the relationship between PTSD and ART initiation, care engagement, or HIV disease progression globally and throughout SSA [5]. Findings regarding the relationship between PTSD and ART adherence remain equivocal [33,34].

Bipolar disorder and psychotic disorders

Estimates of the prevalence of bipolar disorder and psychotic disorders such as schizophrenia among PLWH in SSA are largely lacking. However, one study of PLWH in South Africa estimated a prevalence of bipolar disorder of 6% while a study with PLWH in Nigeria found a prevalence of psychotic disorders of 6% [35,36]. Estimates of bipolar disorder among the general population in

SSA are largely unavailable. However, estimates of bipolar disorder among the general population across 11 countries in the Americas, Europe and Asia range from 0.4% to 2% [37]. Little is known about the relationship between bipolar disorder or psychotic disorders and HIV treatment outcomes in SSA. One study with PLWH in Uganda found that serious mental illness at ART initiation was associated with worse retention in HIV care [38]. While limited, research in high-income settings has found bipolar disorder to be associated with poor ART adherence [39,40].

Psychiatric multimorbidity

Among individuals with mental health disorders, psychiatric multimorbidity (i.e. having more than one concurrent mental health or substance use disorder) is common and associated with greater symptom severity and worse health outcomes. Among PLWH in the US with a past-year mental health disorder, half met criteria for multiple mental health diagnoses [41]. Co-occurring mood and anxiety disorders and co-occurring mood and substance use disorders were particularly common. In the US, psychiatric multimorbidity has been associated with greater HIV symptomatology and worse quality of life [42]. Among veterans living with HIV in the US, multimorbidity (co-occurring substance use disorder, psychiatric disorder, and medical disease) was associated with having a detectable viral load [43]. Research into the prevalence and impact of psychiatric multimorbidity among PLWH in SSA and other low-resource settings is particularly limited.

Mediators and moderators of the relationship between mental health disorders and HIV treatment outcomes

Several factors have been found to mediate or moderate the relationship between mental health and HIV treatment outcomes among PLWH in SSA including ART adherence, HIV care self-efficacy and motivation, among others. Research with PLWH in Uganda found that cognitive and affective (e.g. depressed mood and loss of interest in activities that are normally pleasurable), but not somatic symptoms of depression (e.g. fatigue, difficulty sleeping) were associated with ART adherence [44]. Furthermore, depression alleviation was associated with improved ART adherence and HIV clinic attendance among this population [44]. HIV care self-efficacy and adherence motivation have been found to mediate the relationship between depression and ART adherence among PLWH in SSA [44]. In high-income settings, integrated interventions that address depression and ART adherence have been effective at improving both depression and ART adherence [45].

Priority populations

UNAIDS has identified ambitious treatment goals of having 90% of PLWH know their HIV status, 90% of those diagnosed with HIV receiving ART, and 90% of those on ART virally suppressed by 2020 [46]. The identification and treatment of mental health disorders may be of particular importance in the successful attainment of 90-90-90 goals among specific priority or underserved populations, including children and adolescents living with HIV, pregnant and postpartum women living with HIV, and additional key populations living with HIV, including men who have sex with men, sex workers and transgender individuals.

Children and adolescents living with HIV

Adolescence represents a period of particular vulnerability among PLWH. Among the general population, most mental health disorders first emerge during adolescence and are associated with

poor physical and mental health in adolescence and into adulthood [47]. In addition, adolescents living with HIV are often in transition to adult care and may be particularly vulnerable to disruptions and disengagement from HIV care. While limited, research indicates that many adolescents living with HIV experience mental health disorders and may have higher prevalence of mental health disorders than adolescents without HIV [48,49]. Studies of children and adolescents living with HIV in SSA have estimated the prevalence of depression to be 18–25% [50–52]. A study of children and adolescents living with HIV in Kenya found that the prevalence of anxiety disorders to be 32% [50]. Comparative research examining the mental health of children and adolescents with and without HIV in SSA is rare. However, a study of children and adolescents in Rwanda found that HIV-affected children (i.e. children who are living with HIV, living with a caregiver who has HIV, or had a caregiver who died from HIV) had a significantly higher likelihood of depression, anxiety, and conduct disorder compared to HIV-unaffected children and adolescents [53]. However, there was no significant difference in the likelihood of mental health problems between children who were living with HIV and those who did not have HIV [53].

Similar to adults living with HIV, symptoms of depression and anxiety among adolescents living with HIV have been associated with worse HIV treatment outcomes, including poor ART adherence and lack of viral suppression, and greater HIV sexual risk behaviour [49]. However, most research on the relationship between adolescent mental health and HIV treatment outcomes has been conducted in high-income countries [54]. More research is needed to understand the prevalence and impact of mental health disorders among adolescents living with HIV in SSA and how to effectively identify and address these disorders in this population.

Pregnant and postpartum women living with HIV

Pregnancy and the postpartum period represent periods of vulnerability among women living with HIV during which mental health disorders are common. Mental health disorders are more common among pregnant women living with HIV compared to pregnant women in the general population [55]. In non-African settings, perinatal depression (i.e. depression occurring during pregnancy or the postpartum period) has been associated with non-adherence to ART [56]. Few studies have examined the effects of perinatal depression on HIV treatment outcomes among women in SSA. Among women newly diagnosed with HIV in the Democratic Republic of Congo, antenatal depression (i.e. depression occurring during pregnancy) was not associated with engagement in HIV care [57]. Factors associated with perinatal depression among women living with HIV in SSA remain poorly understood. Identifying and addressing mental health disorders among women during pregnancy and the postpartum period has the potential to improve HIV outcomes among women living with HIV, reduce vertical transmission of HIV, and foster attainment of 'treat all' objectives among mothers and children. Data on other mental health disorders among women living with HIV in SSA during pregnancy and the postpartum period are largely unavailable. One study found that pregnant women living with HIV in South Africa had significantly higher levels of anxiety compared to pregnant women without HIV [58]. Additional research on mental disorders beyond depression among women living with HIV during pregnancy and the postpartum period is warranted.

Additional key populations living with HIV

Little is known about the mental health of additional key populations living with HIV in SSA, including sex workers, men who

have sex with men and transgender individuals. Research from outside SSA indicates that mental health symptoms and disorders are common among these key populations and more common among young key populations than older key population peers [59–62]. Research with key populations in high-income countries suggests that mental health symptoms are associated with increased risk of HIV acquisition and suboptimal HIV treatment outcomes [59,60]. Little is known about the extent to which poor mental health influences HIV treatment outcomes among key populations living with HIV in SSA.

Systems interventions and strategies to address co-morbid mental illness among PLWH

Despite the prevalence of mental health disorders among PLWH in SSA and associations with suboptimal HIV outcomes, many HIV providers neither screen nor treat patients for mental health disorders, contributing to underdiagnosis of mental health disorders and a substantial mental health treatment gap among PLWH [63,64]. Numerous factors contribute to challenges identifying and treating PLWH with mental health disorders in SSA including: a substantial mental health workforce shortage, especially in rural areas; limited time available in HIV and primary care settings; limited mental health training of HIV and primary care clinicians; few validated and culturally appropriate screening and diagnostic tools for mental health disorders; limited availability of psychiatric medications; competing priorities; and poor integration of mental health services into HIV care [5,23,65].

Integrating mental health care into HIV care has been identified as a promising strategy for improving the mental health and HIV treatment outcomes of PLWH in SSA and may facilitate attainment of 'treat all' objectives [63]. More research is needed into the feasibility, acceptability and effectiveness of models of integrated mental health and HIV care throughout SSA. The scale up and implementation of 'treat all' objectives adds challenges to already overburdened health systems (e.g. increased workload) in SSA that must be better understood [66]. The Mental Health Gap Action Programme (mhGAP), published in 2008 and updated in 2015, provides evidence-based guidelines for diagnosis and management of priority mental health conditions in non-specialised health settings and presents a promising model for integration of mental health care into HIV care in SSA [67]. Integration of the mhGAP into primary care in Nigeria was associated with increased identification, treatment, and referral for mental health disorders [68]. To the authors' knowledge, the feasibility, acceptability or effectiveness of integrating mhGAP specifically into HIV care settings in SSA has not yet been evaluated. The Programme for Improving Mental Health Care (PRIME) is a multi-country initiative evaluating the implementation and scale up of mental health services in primary and maternal health care settings in Ethiopia, India, Nepal, South Africa and Uganda [69]. Results from this work are forthcoming and will contribute to the knowledge base regarding the implementation and scale up of evidence-based mental health care in non-specialty settings in LMICs.

Task-shifting and task-sharing have emerged as promising strategies to increase access to evidence-based mental health care in SSA. Evidence suggests that mental health screening, evaluation and pharmacological interventions can be effectively implemented by non-specialists in SSA when appropriate training, supervision and mentorship are available [70,71]. Evidence also indicates that psychological interventions can be effectively delivered in non-specialty settings and by lay health workers in SSA. Randomised trials of the Friendship Bench intervention in Zimbabwe in which trained, supervised lay health workers delivered individual problem-solving therapy in primary care, found that the intervention was

associated with significant improvement in symptoms of depression and other common mental health disorders [72,73]. While integration of this intervention into HIV care has not yet been evaluated, previous trials were conducted among a population with high HIV prevalence [74,75]. Although this intervention has been shown to improve depressive symptoms, the extent to which this intervention impacts HIV treatment outcomes remains unknown.

Individual- and group-level interventions to improve outcomes among PLWH with mental health disorders

Evidence-based, individual- and group-level mental health interventions offer promising strategies to manage mental health disorders among PLWH and improve health and HIV treatment outcomes. Their implementation and scale up in SSA may begin to address the mental health treatment gap among PLWH.

Depression

Pharmacological interventions have been implemented by non-specialists in SSA. A pilot trial of a measurement-based care (MBC) approach to antidepressant medication management trained non-specialists to screen and monitor depression symptoms in an HIV treatment setting in Cameroon. This study found that the intervention was associated with improvements in depression symptoms and HIV treatment outcomes [71,76]. A cluster randomised trial in Uganda compared two task-shifting models of pharmacological depression care: a structured protocol model and a model focused on clinical acumen [70]. The two models performed similarly in the prescription of antidepressants to clinically depressed participants. However, those who screened positive for depressive symptoms were significantly more likely to receive a diagnostic evaluation in the structured protocol arm as compared to the clinical acumen arm [70].

Group interpersonal psychotherapy (IPT-G), recommended by the WHO, has been successfully adapted for delivery in LMICs and has demonstrated effectiveness at reducing depression [77,78]. The effectiveness of IPT-G should be evaluated with PLWH in SSA. A group support psychotherapy intervention for depression among PLWH in Uganda has also been associated with lower mean depression scores; changes in HIV treatment outcomes were not reported [79]. Cognitive behavioural interventions have also demonstrated effectiveness in LMICs [80]. Research in the US found that integrating evidence-based treatment for depression and evidence-based adherence counselling improved adherence and depression among PLWH [45]. Similar research is needed with PLWH in SSA.

Anxiety disorders

Although selective serotonin reuptake inhibitors (SSRIs) are a common and effective treatment for anxiety disorders in middle- and high-income countries, access to SSRIs and health professionals trained to prescribe SSRIs are limited in SSA. One US-based study reported 66% of medications prescribed for anxiety among PLWH were benzodiazepines [81]. Benzodiazepines should be used cautiously due to their potential for abuse. To our knowledge, there are no published studies of pharmacological, psychotherapeutic or behavioural interventions for anxiety disorders among PLWH in SSA.

Post-traumatic stress disorder

Little is known regarding the effectiveness of interventions for PTSD among PLWH in LMICs. A review of psychological interventions for PTSD among PLWH in resource-poor settings identified

seven such studies, six of which used cognitive behavioural therapy and none of which was conducted in SSA [82].

Children and adolescents living with HIV

Few evidence-based mental health interventions have been studied with children or adolescents living with HIV in SSA. One intervention that shows promise is the VUKA family-based programme, which has been implemented with pre-adolescents living with HIV and their caregivers in South Africa [83]. A pilot found that the intervention was associated with improved mental health and ART adherence [83].

Pregnant and postpartum women living with HIV

Similarly, few evidence-based mental health interventions have been studied with pregnant or postpartum women living with HIV in SSA. A randomised controlled trial (RCT) of a group counselling intervention which used a problem-solving therapy approach was associated with a marginally significant reduction in depression compared to standard of care (i.e. pre- and post-test voluntary counselling and testing for HIV and information on how to access prevention of vertical transmission of HIV services) among pregnant women living with HIV in Tanzania [84].

Additional key populations living with HIV

The effectiveness of mental health interventions with additional key populations living with HIV in SSA remains largely unknown. However, an RCT of a cognitive behaviour therapy intervention for ART adherence and depression was conducted with PLWH who had depression and were in treatment for injection drug use in the US [85]. The intervention was significantly associated with improvements in depression, ART adherence, and CD4 cell count post treatment. Similar research is needed with key populations living with HIV in SSA.

Key research priorities to improve the mental health and HIV treatment outcomes of PLWH with mental health disorders in SSA

Numerous research gaps exist in our understanding of how to effectively identify and manage mental health needs and optimise HIV treatment outcomes of PLWH in SSA. The authors recommend the following mental health-related research priorities to inform effective and efficient scale up and implementation of 'treat all' in SSA and beyond.

- Research is needed to advance understanding of the prevalence and incidence of mental health multimorbidities among PLWH and their impact on HIV treatment outcomes. Greater understanding of the prevalence of mental health symptoms and disorders among PLWH in SSA compared to people without HIV is also needed. Longitudinal studies that examine the onset and trajectory of mental health symptoms and disorders in relation to HIV infection, diagnosis and treatment are needed in SSA.
- Factors, such as ART adherence, that mediate or moderate the relationship between mental health and HIV treatment outcomes should be evaluated as potential intervention targets to improve mental health and HIV treatment outcomes among PLWH with mental health disorders. Additional mediators and moderators of the relationship between mental health and HIV treatment outcomes should be identified and evaluated as potential intervention targets.
- Research is needed to understand the prevalence, incidence, impact and treatment of mental health disorders among children and adolescents living with HIV in SSA. Such research should include the examination of whether, and in what ways,

the burden and impact of mental health disorders among children and adolescents living with HIV varies between children and adolescents who acquired HIV perinatally or behaviourally. In addition, research is needed to understand the burden and impact of mental health disorders among children and adolescents living with HIV compared to both HIV-affected (but not infected) children and adolescents in SSA as well as HIV-unaffected and uninfected children and adolescents in SSA.

- Research to examine the prevalence of and factors associated with mental health disorders during pregnancy and the post-partum period among women living with HIV is needed. Interventions to optimise mental health and HIV treatment outcomes among this population should be developed, implemented and evaluated. Such research should examine mental health disorders beyond perinatal depression, including perinatal anxiety disorders.
- Research to examine the prevalence of and factors associated with mental health disorders among key populations living with HIV is needed. Research that examines the extent to which mental health disorders influence HIV treatment outcomes among key populations living with HIV in SSA is needed. Interventions to optimise mental health and HIV treatment outcomes among sex workers, men who have sex with men, transgender individuals and other key populations should be developed, implemented and evaluated. The effectiveness of mental health interventions with such key populations living with HIV in SSA warrants investigation.
- The effectiveness of promising strategies to address psychiatric multimorbidity, such as a common elements treatment approach, a transdiagnostic intervention developed to treat mood and/or anxiety disorders in low-resource settings, needs to be evaluated among PLWH at critical points throughout HIV treatment.
- Intervention research is needed to understand the extent to which improving the mental health of PLWH improves HIV treatment outcomes. Research has consistently found that mental health disorders are associated with suboptimal HIV treatment outcomes. However, less is known about whether improvement in one's mental health is associated with subsequent improvement in HIV treatment outcomes. Research is needed that examines the relationship between improvements in symptoms and severity of mental health disorders among PLWH and improvements in HIV treatment outcomes including uptake in HIV care, adherence to ART, immunological response and sustained viral suppression. Research that examines mechanisms through which changes in mental health are associated with changes in HIV treatment outcomes is also warranted. Such research should incorporate longer-term follow-up when possible to examine intervention sustainability and long-term effectiveness.
- Promising models of integrated mental health and HIV care should be implemented and evaluated. Although screening and treatment for mental health conditions are limited in many healthcare settings in SSA and globally [86], the integration of mental health care into HIV testing and care settings must be a priority. The International AIDS Society supports integrated healthcare systems as an important element of not only strengthening the HIV response, but also advancing global health [87]. There is a critical need for research to identify effective and efficient strategies to integrate mental health interventions into HIV service delivery programmes in the context of 'treat all' implementation. Implementation research is needed to more fully understand multilevel (e.g., patient-, provider-, and systems-level) barriers and facilitators to integrating mental health care into HIV care in the context of

'treat all' and to develop and evaluate strategies to address identified barriers. To address barriers to ART adherence and reach the 90-90-90 objectives, screening and treatment of mental health disorders is necessary at HIV diagnosis and throughout the patients' life. Screening and treatment protocols for mental health disorders that can be integrated into HIV treatment and implemented by non-specialists need to be developed, implemented and evaluated. Strategies to effectively supervise non-specialists delivering mental health interventions with PLWH and to strengthen health systems to effectively integrate mental health care into HIV are also needed.

Conclusion

Key mental health-related recommendations have been identified to advance understanding and treatment of mental health disorders among PLWH and attainment of 'treat all' objectives in SSA and beyond. Key recommendations include a call for epidemiological research to examine the prevalence and impact of mental health multimorbidities on HIV treatment outcomes, intervention research to examine the extent to which improving the mental health of people living with HIV improves HIV treatment outcomes, and implementation research to evaluate promising models of integrated mental health and HIV care.

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