

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

Angela M Parcesepe<sup>1,2\*</sup>, Charlotte Bernard<sup>3,4</sup>, Robert Agler<sup>5</sup>, Jeremy Ross<sup>6</sup>, Marcel Yotebieng<sup>7</sup>, Judith Bass<sup>8</sup>, Edith Kwobah<sup>9</sup>, Adebola Adedimeji<sup>10</sup>, Joseph Goulet<sup>11,12</sup> and Keri N Althoff<sup>13</sup>

<sup>1</sup>Department of Maternal and Child Health, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

<sup>2</sup>Institute for Implementation Science in Population Health, City University of New York, NY, USA

<sup>3</sup>Bordeaux Population Health Research Center, University of Bordeaux, INSERM, Bordeaux, France

<sup>4</sup>INSERM, ISPED, Bordeaux Population Health Research Center, Bordeaux, France

<sup>5</sup>Department of Psychology, Ohio State University, Columbus, OH, USA

<sup>6</sup>TREAT Asia, amfAR - The Foundation for AIDS Research, Bangkok, Thailand

<sup>7</sup>College of Public Health, Division of Epidemiology, Ohio State University, Columbus, OH, USA

<sup>8</sup>Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

<sup>9</sup>Department of Mental Health, Moi Teaching and Referral Hospital and Moi University, Eldoret, Kenya

<sup>10</sup>Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, USA

<sup>11</sup>Yale School of Medicine, Department of Emergency Medicine, New Haven, CT, USA

<sup>12</sup>VA Connecticut Healthcare System, West Haven, CT, USA

<sup>13</sup>Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

## 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

\*Corresponding author: Angela M. Parcesepe; University of North Carolina at Chapel Hill, Gillings School of Global Public Health, Department of Maternal and Child Health, CB#7445 Chapel Hill, NC, 27599-7445, USA  
Email: angela\_parcesepe@unc.edu

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.

## References

1. World Health Organization. *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV*. Geneva, Switzerland, WHO, 2015.
2. Lundgren JD, Babiker AG, Gordin F *et al*. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *N Engl J Med* 2015; **373**: 795–807.
3. Cohen MS, Chen YQ, McCauley M *et al*. Antiretroviral therapy for the prevention of HIV-1 transmission. *N Engl J Med* 2016; **375**: 830–839.
4. Kharsany AB, Karim QA. HIV Infection and AIDS in Sub-Saharan Africa: Current Status, Challenges and Opportunities. *Open AIDS J* 2016; **10**: 34–48.
5. Brandt R. The mental health of people living with HIV/AIDS in Africa: a systematic review. *Afr J AIDS Res* 2009; **8**: 123–133.
6. Daar AS, Jacobs M, Wall S *et al*. Declaration on mental health in Africa: moving to implementation. *Glob Health Action* 2014; **7**: 24589.
7. Collins PY, Musisi S, Frehywot S, Patel V. The core competencies for mental, neurological, and substance use disorder care in sub-Saharan Africa. *Glob Health Action* 2015; **8**: 26682.
8. Nakimuli-Mpungu E, Bass JK, Alexandre P *et al*. Depression, alcohol use and adherence to antiretroviral therapy in sub-Saharan Africa: a systematic review. *AIDS Behav* 2012; **16**: 2101–2118.
9. Ickovics JR, Hamburger ME, Vlahov D *et al*. Mortality, CD4 cell count decline, and depressive symptoms among HIV-seropositive women: longitudinal analysis from the HIV Epidemiology Research Study. *J Am Med Assoc* 2001; **285**: 1466–1474.
10. Memiah P, Shumba C, Etienne-Mesubi M *et al*. The effect of depressive symptoms and CD4 count on adherence to highly active antiretroviral therapy in sub-Saharan Africa. *J Int Assoc Provid AIDS Care* 2014; **13**: 346–352.
11. Nel A, Kagee A. The relationship between depression, anxiety and medication adherence among patients receiving antiretroviral treatment in South Africa. *AIDS Care* 2013; **25**: 948–955.
12. Lancaster KE, Hetrick A, Jaquet A *et al*. Substance use and universal access to HIV testing and treatment in sub-Saharan Africa: Implications and research priorities. *J Virus Erad* 2018; **4** (Suppl 2): 26–32.
13. Narayan KM, Miotti PG, Anand NP *et al*. HIV and noncommunicable disease comorbidities in the era of antiretroviral therapy: a vital agenda for research in low- and middle-income country settings. *J Acquir Immune Defic Syndr* 2014; **67** Suppl 1: S2–7.
14. Chibanda D, Benjamin L, Weiss HA, Abas M. Mental, neurological, and substance use disorders in people living with HIV/AIDS in low- and middle-income countries. *J Acquir Immune Defic Syndr* 2014; **67** Suppl 1: S54–67.
15. Mayston R, Lazarus A, Patel V *et al*. Pathways to HIV testing and care in Goa, India: exploring psychosocial barriers and facilitators using mixed methods. *BMC Public Health* 2016; **16**: 765.
16. Mayston R, Kinyanda E, Chishinga N *et al*. Mental disorder and the outcome of HIV/AIDS in low-income and middle-income countries: a systematic review. *Aids* 2012; **26** Suppl 2: S117–135.
17. Ramirez-Avila L, Regan S, Giddy J *et al*. Depressive symptoms and their impact on health-seeking behaviors in newly-diagnosed HIV-infected patients in Durban, South Africa. *AIDS Behav* 2012; **16**: 2226–2235.
18. Kagee A, Saal W, De Villiers L *et al*. The Prevalence of Common Mental Disorders Among South Africans Seeking HIV Testing. *AIDS Behav* 2017; **21**: 1511–1517.
19. Nanni MG, Caruso R, Mitchell AJ *et al*. Depression in HIV infected patients: a review. *Curr Psychiatry Rep* 2015; **17**: 530.
20. Ayano G, Solomon M, Abraha M. A systematic review and meta-analysis of epidemiology of depression in people living with HIV in east Africa. *BMC Psychiatry* 2018; **18**: 254.
21. Bernard C, Dabis F, de Rekeneire N. Prevalence and factors associated with depression in people living with HIV in sub-Saharan Africa: a systematic review and meta-analysis. *PLoS One* 2017; **12**: e0181960.

22. Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *Am J Psychiatry* 2001; **158**: 725–730.
23. Abas M, Ali GC, Nakimuli-Mpungu E, Chibanda D. Depression in people living with HIV in sub-Saharan Africa: time to act. *Trop Med Int Health* 2014; **19**: 1392–1396.
24. Rane MS, Hong T, Govere S *et al.* Depression and anxiety as risk factors for delayed care-seeking behavior in HIV positive individuals in South Africa. *Clin Infect Dis* 2018.
25. Baxter AJ, Vos T, Scott KM *et al.* The regional distribution of anxiety disorders: implications for the Global Burden of Disease Study, 2010. *Int J Methods Psychiatr Res* 2014; **23**: 422–438.
26. Shacham E, Morgan JC, Onen NF *et al.* Screening anxiety in the HIV clinic. *AIDS Behav* 2012; **16**: 2407–2413.
27. Tucker JS, Burnam MA, Sherbourne CD *et al.* Substance use and mental health correlates of nonadherence to antiretroviral medications in a sample of patients with human immunodeficiency virus infection. *Am J Med* 2003; **114**: 573–580.
28. Choi KW, Sikkema KJ, Velloza J *et al.* Maladaptive coping mediates the influence of childhood trauma on depression and PTSD among pregnant women in South Africa. *Arch Womens Ment Health* 2015; **18**: 731–738.
29. Myer L, Smit J, Roux LL *et al.* Common mental disorders among HIV-infected individuals in South Africa: prevalence, predictors, and validation of brief psychiatric rating scales. *AIDS Patient Care STDS* 2008; **22**: 147–158.
30. Olley BO, Seedat S, Stein DJ. Persistence of psychiatric disorders in a cohort of HIV/AIDS patients in South Africa: a 6-month follow-up study. *J Psychosom Res* 2006; **61**: 479–484.
31. Atwoli L, Stein DJ, Williams DR *et al.* Trauma and posttraumatic stress disorder in South Africa: analysis from the South African Stress and Health Study. *BMC Psychiatry* 2013; **13**: 182.
32. Koenen KC, Ratanatharathorn A, Ng L *et al.* Posttraumatic stress disorder in the World Mental Health Surveys. *Psychol Med* 2017; **47**: 2260–2274.
33. Delahanty DL, Bogart LM, Figler JL. Posttraumatic stress disorder symptoms, salivary cortisol, medication adherence, and CD4 levels in HIV-positive individuals. *AIDS Care* 2004; **16**: 247–260.
34. Nel A, Kagee A. Common mental health problems and antiretroviral therapy adherence. *AIDS Care* 2011; **23**: 1360–1365.
35. Els CBW, Scott, C, Strydom, W, Joubert, G, van der Ryst, E. Psychiatric co-morbidity in South African HIV/AIDS Patients. *S Afr Med J* 1999; **89**: 992–995.
36. Adewuya AO, Afolabi MO, Ola BA *et al.* Psychiatric disorders among the HIV-positive population in Nigeria: a control study. *J Psychosom Res* 2007; **63**: 203–206.
37. Merikangas KR, Jin R, He JP *et al.* Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. *Arch Gen Psychiatry* 2011; **68**: 241–251.
38. Nachega JB, Mutamba B, Basangwa D *et al.* Severe mental illness at ART initiation is associated with worse retention in care among HIV-infected Ugandan adults. *Trop Med Int Health* 2013; **18**: 53–57.
39. Meade CS, Bevilacqua LA, Key MD. Bipolar disorder is associated with HIV transmission risk behavior among patients in treatment for HIV. *AIDS Behav* 2012; **16**: 2267–2271.
40. Moore DJ, Posada C, Parikh M *et al.* HIV-infected individuals with co-occurring bipolar disorder evidence poor antiretroviral and psychiatric medication adherence. *AIDS Behav* 2012; **16**: 2257–2266.
41. Gaynes BN, Pence BW, Eron JJ, Jr, Miller WC. Prevalence and comorbidity of psychiatric diagnoses based on reference standard in an HIV+ patient population. *Psychosom Med* 2008; **70**: 505–511.
42. Gaynes BN, O'Donnell J, Nelson E *et al.* Psychiatric comorbidity in depressed HIV-infected individuals: common and clinically consequential. *Gen Hosp Psychiatry* 2015; **37**: 277–282.
43. Goulet JL, Fultz SL, Rimland D *et al.* Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? *Clin Infect Dis* 2007; **45**: 1593–1601.
44. Wagner GJ, Slaughter M, Ghosh-Dastidar B. Depression at treatment initiation predicts HIV antiretroviral adherence in Uganda. *J Int Assoc Provid AIDS Care* 2017; **16**: 91–97.
45. Safren SA, Bedoya CA, O'Cleirigh C *et al.* Cognitive behavioural therapy for adherence and depression in patients with HIV: a three-arm randomised controlled trial. *Lancet HIV* 2016; **3**: e529–e538.
46. UNAIDS. 90–90–90. *An ambitious treatment target to help end the AIDS epidemic*. 2017. Available at: [www.unaids.org/en/resources/documents/2017/90-90-90](http://www.unaids.org/en/resources/documents/2017/90-90-90) (accessed October 2018).
47. Patel V, Flisher AJ, Hetrick S, McGorry P. Mental health of young people: a global public-health challenge. *Lancet* 2007; **369**: 1302–1313.
48. Mellins CA, Malee KM. Understanding the mental health of youth living with perinatal HIV infection: lessons learned and current challenges. *J Int AIDS Soc* 2013; **16**: 18593.
49. Vreeman RC, McCoy BM, Lee S. Mental health challenges among adolescents living with HIV. *J Int AIDS Soc* 2017; **20**: 100–109.
50. Kamau JW, Kuria W, Mathai M *et al.* Psychiatric morbidity among HIV-infected children and adolescents in a resource-poor Kenyan urban community. *AIDS Care* 2012; **24**: 836–842.
51. Kim MH, Mazenga AC, Devandra A *et al.* Prevalence of depression and validation of the Beck Depression Inventory-II and the Children's Depression Inventory-Short amongst HIV-positive adolescents in Malawi. *J Int AIDS Soc* 2014; **17**: 18965.
52. Binagwaho A, Fawzi MCS, Agbonyitor M *et al.* Validating the Children's Depression Inventory in the context of Rwanda. *BMC Pediatr* 2016; **16**: 29.
53. Betancourt T, Scorza P, Kanyanganzi F *et al.* HIV and child mental health: a case-control study in Rwanda. *Pediatrics* 2014; **134**: e464–472.
54. Gadow KD, Angelidou K, Chernoff M *et al.* Longitudinal study of emerging mental health concerns in youth perinatally infected with HIV and peer comparisons. *J Dev Behav Pediatr* 2012; **33**: 456–468.
55. Nachega JB, Uthman OA, Anderson J *et al.* Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. *Aids* 2012; **26**: 2039–2052.
56. Kapetanovic S, Christensen S, Karim R *et al.* Correlates of perinatal depression in HIV-infected women. *AIDS Patient Care STDS* 2009; **23**: 101–108.
57. Yotebieng KA, Fokong K, Yotebieng M. Depression, retention in care, and uptake of PMTCT service in Kinshasa, the Democratic Republic of Congo: a prospective cohort. *AIDS Care* 2017; **29**: 285–289.
58. Mfusi SK, Mahabeer M. Psychosocial adjustment of pregnant women infected with HIV/AIDS in South Africa. *J Psychol Afr* 2000; **10**: 122–145.
59. Clements-Nolle K, Marx R, Guzman R, Katz M. HIV prevalence, risk behaviors, health care use, and mental health status of transgender persons: implications for public health intervention. *Am J Public Health* 2001; **91**: 915–921.
60. Hightow-Weidman L, LeGrand S, Choi SK *et al.* Exploring the HIV continuum of care among young black MSM. *PLoS One* 2017; **12**: e0179688.
61. Rael CT, Davis A. Depression and key associated factors in female sex workers and women living with HIV/AIDS in the Dominican Republic. *Int J STD AIDS* 2017; **28**: 433–440.
62. Delany-Moretlwe S, Cowan FM, Busza J *et al.* Providing comprehensive health services for young key populations: needs, barriers and gaps. *J Int AIDS Soc* 2015; **18**: 19833.
63. Kaaya S, Eustache E, Lapidus-Salaiz I *et al.* Grand challenges: Improving HIV treatment outcomes by integrating interventions for co-morbid mental illness. *PLoS Med* 2013; **10**: e1001447.
64. Parcesepe AM, Mugglin C, Nalugoda F *et al.* Screening and management of mental health and substance use disorders in HIV treatment settings in low- and middle-income countries within the global IeDEA consortium. *J Int AIDS Soc* 2018; **21**: e25101.
65. Akena D, Stein DJ, Joska J. Does screening HIV-positive individuals in Uganda for major depressive disorder improve case detection rates and antidepressant prescription? *AIDS Behav* 2013; **17**: 2802–2807.
66. Bigna JJ, Plottel CS, Koulla-Shiro S. Challenges in initiating antiretroviral therapy for all HIV-infected people regardless of CD4 cell count. *Infect Dis Poverty* 2016; **5**: 85.
67. World Health Organization. *mhGAP intervention guide for mental, neurological and substance use disorders in non-specialized health settings. Version 2.0*. 2016. Available at: [www.who.int/mental\\_health/mhgap/mhGAP\\_intervention\\_guide\\_02/en](http://www.who.int/mental_health/mhgap/mhGAP_intervention_guide_02/en) (accessed October 2018).
68. Gureje O, Abdulmalik J, Kola L *et al.* Integrating mental health into primary care in Nigeria: report of a demonstration project using the mental health gap action programme intervention guide. *BMC Health Serv Res* 2015; **15**: 242.
69. Lund C, Tomlinson M, De Silva M *et al.* PRIME: a programme to reduce the treatment gap for mental disorders in five low- and middle-income countries. *PLoS Med* 2012; **9**: e1001359.
70. Wagner GJ, Ngo V, Goutam P *et al.* A structured protocol model of depression care versus clinical acumen: a cluster randomized trial of the effects on depression screening, diagnostic evaluation, and treatment uptake in Ugandan HIV clinics. *PLoS One* 2016; **11**: e0153132.
71. Pence BW, Gaynes BN, Atashili J *et al.* Feasibility, safety, acceptability, and preliminary efficacy of measurement-based care depression treatment for HIV patients in Bamenda, Cameroon. *AIDS Behav* 2014; **18**: 1142–1151.
72. Chibanda D, Weiss HA, Verhey R *et al.* Effect of a primary care-based psychological intervention on symptoms of common mental disorders in Zimbabwe: a randomized clinical trial. *J Am Med Assoc* 2016; **316**: 2618–2626.
73. Chibanda D, Bowers T, Verhey R *et al.* The Friendship Bench programme: a cluster randomised controlled trial of a brief psychological intervention for common mental disorders delivered by lay health workers in Zimbabwe. *Int J Ment Health Syst* 2015; **9**: 21.
74. Chibanda D, Mesu P, Kajawu L *et al.* Problem-solving therapy for depression and common mental disorders in Zimbabwe: piloting a task-shifting primary mental health care intervention in a population with a high prevalence of people living with HIV. *BMC Public Health* 2011; **11**: 828.
75. Chibanda D, Cowan F, Verhey R *et al.* Lay health workers' experience of delivering a problem solving therapy intervention for common mental disorders among people living with HIV: a qualitative study from Zimbabwe. *Community Ment Health J* 2017; **53**: 143–153.
76. Gaynes BN, Pence BW, Atashili J *et al.* Changes in HIV outcomes following depression care in a resource-limited setting: results from a pilot study in Bamenda, Cameroon. *PLoS One* 2015; **10**: e0140001.
77. Bass J, Neugebauer R, Clougherty KF *et al.* Group interpersonal psychotherapy for depression in rural Uganda: 6-month outcomes: randomised controlled trial. *Br J Psychiatry* 2006; **188**: 567–573.
78. Bolton P, Bass J, Neugebauer R *et al.* Group interpersonal psychotherapy for depression in rural Uganda: a randomized controlled trial. *J Am Med Assoc* 2003; **289**: 3117–3124.
79. Nakimuli-Mpungu E, Wamala K, Okello J *et al.* Group support psychotherapy for depression treatment in people with HIV/AIDS in northern Uganda: a single-centre randomised controlled trial. *Lancet HIV* 2015; **2**: e190–199.
80. Chibanda D, Cowan FM, Healy JL *et al.* Psychological interventions for common mental disorders for people living with HIV in low- and middle-income countries: systematic review. *Trop Med Int Health* 2015; **20**: 830–839.
81. Vitiello B, Burnam MA, Bing EG *et al.* Use of psychotropic medications among HIV-infected patients in the United States. *Am J Psychiatry* 2003; **160**: 547–554.
82. Verhey R, Chibanda D, Brakarsh J, Seedat S. Psychological interventions for post-traumatic stress disorder in people living with HIV in Resource poor settings: a systematic review. *Trop Med Int Health* 2016; **21**: 1198–1208.
83. Bhana A, Mellins CA, Petersen I *et al.* The VUKA family program: piloting a family-based psychosocial intervention to promote health and mental health among HIV infected early adolescents in South Africa. *AIDS Care* 2014; **26**: 1–11.
84. Kaaya SF, Blander J, Antelman G *et al.* Randomized controlled trial evaluating the effect of an interactive group counseling intervention for HIV-positive women on prenatal depression and disclosure of HIV status. *AIDS Care* 2013; **25**: 854–862.
85. Safren SA, O'Cleirigh CM, Bullis JR *et al.* Cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected injection drug users: a randomized controlled trial. *J Consult Clin Psychol* 2012; **80**: 404–415.
86. Hanlon C, Luitel NP, Kathree T *et al.* Challenges and opportunities for implementing integrated mental health care: a district level situation analysis from five low- and middle-income countries. *PLoS One* 2014; **9**: e88437.

87. Bekker LG, Alleyne G, Baral S *et al.* Advancing global health and strengthening the HIV response in the era of the Sustainable Development Goals: the International AIDS Society–Lancet Commission. *Lancet* 2018; **392**: 312–358.

## Appendix. Funding and acknowledgements

The authors wish to thank the leDEA Mental Health Working Group for their support in development of this manuscript.

### Asia-Pacific

The TREAT Asia HIV Observational Database and pediatric Observational Database are initiatives of TREAT Asia, a programme of amfAR, The Foundation for AIDS Research, with support from the US National Institutes of Health's National Institute of Allergy and Infectious Diseases, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Cancer Institute, the National Institute of Mental Health, and the National Institute on Drug Abuse, as part of the International Epidemiology Databases to Evaluate AIDS (leDEA; U01AI069907). The Kirby Institute is funded by the Australian Government Department of Health and Ageing, and is affiliated with the Faculty of Medicine, UNSW Sydney. The content of this publication is solely the responsibility of the authors and does not necessarily represent the official views of any of the governments or institutions mentioned above.

Adult site investigators and study teams:

PS Ly\* and V Khol, National Center for HIV/AIDS, Dermatology & STDs, Phnom Penh, Cambodia; FJ Zhang\* ‡, HX Zhao and N Han, Beijing Ditan Hospital, Capital Medical University, Beijing, China; MP Lee\*, PCK Li, W Lam and YT Chan, Queen Elizabeth Hospital, Hong Kong, China; N Kumarasamy\*, S Saghayam and C Ezhilarasi, Chennai Antiviral Research and Treatment Clinical Research Site (CART CRS), YRGCARE Medical Centre, VHS, Chennai, India; S Pujari\*, K Joshi, S Gaikwad and A Chitalikar, Institute of Infectious Diseases, Pune, India; TP Merati\*, DN Wirawan and F Yuliana, Faculty of Medicine Udayana University & Sanglah Hospital, Bali, Indonesia; E Yunihastuti\*, D Imran and A Widhani, Faculty of Medicine Universitas Indonesia - Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia; J Tanuma\*, S Oka and T Nishijima, National Center for Global Health and Medicine, Tokyo, Japan; JY Choi\*, Na S and JM Kim, Division of Infectious Diseases, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea; BLH Sim\*, YM Gani, and R David, Hospital Sungai Buloh, Sungai Buloh, Malaysia; A Kamarulzaman\*, SF Syed Omar, S Ponnampalavanar and I Azwa, University Malaya Medical Centre, Kuala Lumpur, Malaysia; R Ditangco\*, E Uy and R Bantique, Research Institute for Tropical Medicine, Manila, Philippines; WW Wong\* †, WW Ku and PC Wu, Taipei Veterans General Hospital, Taipei, Taiwan; OT Ng\*, PL Lim, LS Lee and Z Ferdous, Tan Tock Seng Hospital, Singapore; A Avihingsanon\*, S Gatechompol, P Phanuphak and C Phadungphon, HIV-NAT/Thai Red Cross AIDS Research Centre, Bangkok, Thailand; S Kiertiburanakul\*, A Phuphuakrat, L Chumla and N Sanmeema, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; R Chaiwarith\*, T Sirisanthana, W Kotarathitum and J Preparattanapan, Research Institute for Health Sciences, Chiang Mai, Thailand; P Kantipong\* and P Kambua, Chiangrai Prachanukroh Hospital, Chiang Rai, Thailand; KV Nguyen\*, HV Bui, DTH Nguyen and DT Nguyen, National Hospital for Tropical Diseases, Hanoi, Vietnam; DD Cuong\*, NV An and NT Luan, Bach Mai Hospital, Hanoi, Vietnam; AH Sohn\*, JL Ross\* and B Petersen, TREAT Asia, amfAR - The Foundation for AIDS Research, Bangkok, Thailand; MG Law\*, A Jiamsakul\* and R Bijker, The Kirby Institute, UNSW Australia, Sydney, Australia.

\* TAHOD Steering Committee member; † Steering Committee Chair; ‡ co-Chair.

Paediatric site investigators and cohorts:

PS Ly\*, and V Khol, National Centre for HIV/AIDS, Dermatology and STDs, Phnom Penh, Cambodia; J Tucker, New Hope for Cambodian Children, Phnom Penh, Cambodia; N Kumarasamy\*, and E Chandrasekaran, YRGCARE Medical Centre, CART CRS, Chennai, India; DK Wati\*, D Vedaswari, and IB Ramajaya, Sanglah Hospital, Udayana University, Bali, Indonesia; N Kurniati\*, and D Muktiarti, Cipto Mangunkusumo - Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia; SM Fong\*, M Lim, and F Daut, Hospital Likas, Kota Kinabalu, Malaysia; NK Nik Yusoff\*‡, and P Mohamad, Hospital Raja Perempuan Zainab II, Kelantan, Malaysia; TJ Mohamed\* and MR Drawis, Pediatric Institute, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia; R Nallusamy\*, and KC Chan, Penang Hospital, Penang, Malaysia; T Sudjaritruk\*, V Sirisanthana, and L Aурpibul, Department of Pediatrics, Faculty of Medicine, and Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand; R Hansudewechakul\*, P Ounchanum, S Denjanta, and A Kongphonoi, Chiangrai Prachanukroh Hospital, Chiang Rai, Thailand; P Lumbiganon\*†, P Kosalaraksa, P Tharnprisan, and T Udomphanit, Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand; G Jourdain, PHPT-IRD UMI 174 (Institut de recherche pour le développement and Chiang Mai University), Chiang Mai, Thailand; T Puthanakit\*, S Anugulruengkit, W Jantarabenjakul and R Nadsasarn, Department of Pediatrics, Faculty of Medicine and Research Unit in Pediatric and Infectious Diseases, Chulalongkorn University, Bangkok, Thailand; K Chokephaibulkit\*, K Lapphra, W Phongsamart, and S Siricharoenchai, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; KH Truong\*, QT Du, and CH Nguyen, Children's Hospital 1, Ho Chi Minh City, Vietnam; VC Do\*, TM Ha, and VT An Children's Hospital 2, Ho Chi Minh City, Vietnam; LV Nguyen\*, DTK Khu, AN Pham, and LT Nguyen, National Hospital of Pediatrics, Hanoi, Vietnam; ON Le, Worldwide Orphans Foundation, Ho Chi Minh City, Vietnam; AH Sohn\*, JL Ross, and C Sethaputra, TREAT Asia/amfAR - The Foundation for AIDS Research, Bangkok, Thailand; MG Law\* and A Kariminia, The Kirby Institute, UNSW Australia, Sydney, Australia; (\*Steering Committee members; † Current Steering Committee Chair; ‡ co-Chair).

### Central Africa (CA-leDEA)

Research reported in this publication was supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Number U01AI096299 (PI: Anastos and Nash). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Site investigators and cohorts:

Nimbona Pélagie, ANSS, Burundi; Patrick Gateretse, Jeanine Munezero, Valentin Nitereka, Théodore Niyongabo, Christelle Twizere, Centre National de Reference en Matiere de VIH/SIDA, Burundi; Hélène Bukuru, Thierry Nahimana, CHUK, Burundi; Jérémie Biziragusenyuka, Risase Scholastique Manyundo, HPRC, Burundi; Tabeyang Mbuh, Kinge Thompson Njje, Edmond Tchasse, Kien-Atsu Tsi, Bamenda Hospital, Cameroon; Rogers Ajeh, Mark Benwi, Anastase Dzudie, Akindeh Mbuh, Marc Lionel Ngamani, Victorine Nkome, CRENC & Douala General Hospital, Cameroon; Djenabou Amadou, Eric Ngassam, Eric Walter Pefura Yone, Jamot Hospital, Cameroon; Alice Ndelle Ewanoge, Norbert Fuhngwa, Chris Moki, Denis Nsame Nforniwe, Limbe Regional Hospital, Cameroon; Catherine Akele, Faustin Kitetele, Patricia Lelo, Martine Tabala, Kalembelembe Pediatric Hospital, Democratic Republic of Congo; Emile Wemakoy Okitolonda, Landry Wenzu,

Kinshasa School of Public Health, Democratic Republic of Congo; Merlin Diafouka, Martin Herbas Ekati, Dominique Mahambou Nsonde, CTA Brazzaville, Republic of Congo; Adolphe Mafou, CTA Pointe-Noire, Republic of Congo; Fidele Ntarambirwa, Bethsaida Hospital, Rwanda; Yvonne Tuyishimire, Busanza Health Center, Rwanda; Theogene Hakizimana, Gahanga Health Center, Rwanda; Josephine Ayinkamiye, Gikondo Health Center, Rwanda; Sandrine Mukantwali, Kabuga Health Center, Rwanda; Henriette Kayitesi, Olive Uwamahoro, Kicukiro Health Center, Rwanda; Viateur Habumuremyi, Jules Ndumuhire, Masaka Health Center, Rwanda; Joyce Mukamana, Yvette Ndoli, Oliver Uwamahoro, Nyarugunga Health Center, Rwanda; Gallican Kubwimana, Pacifique Mugenzi, Benjamin Muhoza, Athanase Munyaneza, Emmanuel Ndahiro, Diane Nyiransabimana, Jean d'Amour Sinayobye, Vincent Sugira, Rwanda Military Hospital, Rwanda; Chantal Benekigeri, Gilbert Mbaraga, WE-ACTx Health Center, Rwanda.

Coordinating and data centres:

Adebola Adedimeji, Kathryn Anastos, Madeline Dilorenzo, Lynn Murchison, Jonathan Ross, Albert Einstein College of Medicine, USA; Diane Addison, Margaret Baker, Ellen Brazier, Heidi Jones, Elizabeth Kelvin, Sarah Kulkarni, Grace Liu, Denis Nash, Matthew Romo, Olga Tymeczyk, Institute for Implementation Science in Population Health, Graduate School of Public Health and Health Policy, City University of New York (CUNY), USA; Batya Elul, Columbia University, USA; Xiatao Cai, Don Hoover, Hae-Young Kim, Chunshan Li, Qiuhi Shi, Data Solutions, USA; Robert Agler, Kathryn Lancaster, Marcel Yotebieng, Ohio State University, USA; Mark Kuniholm, University at Albany, State University of New York, USA; Andrew Edmonds, Angela Parcesepe, University of North Carolina at Chapel Hill, USA; Olivia Keiser, University of Geneva; Stephany Duda; Vanderbilt University School of Medicine, USA; April Kimmel, Virginia Commonwealth University School of Medicine, USA; Margaret McNairy, Weill Cornell Medical Center.

#### **Caribbean, Central and South America network for HIV epidemiology (CCASAnet)**

This work was supported by the NIH-funded Caribbean, Central and South America network for HIV epidemiology (CCASAnet), a member cohort of the International Epidemiology Databases to Evaluate AIDS (IeDEA) (U01AI069923). This award is funded by the following institutes: Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Cancer Institute (NCI), National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Mental Health (NIMH), and the Office of the Director, National Institutes of Health (OD).

Acknowledgements list

Fundación Huésped, Argentina: Pedro Cahn, Carina Cesar, Valeria Fink, Omar Sued, Emanuel Dell'Isola, Hector Perez, Jose Valiente, Cleyton Yamamoto

Instituto Nacional de Infectologia-Fiocruz, Brazil: Beatriz Grin-sztejn, Valdilea Veloso, Paula Luz, Raquel de Boni, Sandra Cardoso Wagner, Ruth Friedman, Ronaldo Moreira.

Universidade Federal de Minas Gerais, Brazil: Jorge Pinto, Flavia Ferreira, Marcelle Maia.

Universidade Federal de São Paulo, Brazil: Regina Célia de Menezes Succi, Daisy Maria Machado, Aida de Fátima Barbosa Gouvêa

Fundación Arriarán, Chile: Marcelo Wolff, Claudia Cortes, Maria Fernanda Rodriguez, Gladys Allendes Les Centres GHESKIO, Haiti: Jean William Pape, Vanessa Rouzier, Adias Marcelin, Christian Perodin. Hospital Escuela Universitario, Honduras: Marco Tulio Luque.

Instituto Hondureño de Seguridad Social, Honduras: Denis Padgett.

Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico: Juan Sierra Madero, Brenda Crabtree Ramirez, Paco Belaunzaran, Yanink Caro Vega.

Instituto de Medicina Tropical Alexander von Humboldt, Peru: Eduardo Gotuzzo, Fernando Mejia, Gabriela Carriquiry.

Vanderbilt University Medical Center, USA: Catherine C McGowan, Bryan E Shepherd, Timothy Sterling, Karu Jayathilake, Anna K Person, Peter F Rebeiro, Mark Giganti, Jessica Castilho, Stephany N Duda, Fernanda Maruri, Hilary Vansell.

#### **East Africa IeDEA**

Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute Of Child Health & Human Development (NICHD), National Institute On Drug Abuse (NIDA), National Cancer Institute (NCI), and the National Institute of Mental Health (NIMH), in accordance with the regulatory requirements of the National Institutes of Health under Award Number U01AI069911 East Africa IeDEA Consortium. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Site investigators and cohorts

Diero L, Ayaya S, Sang E, MOI University, AMPATH Plus, Eldoret, Kenya; Bukusi E, Charles Karue Kibaara, Elisheba Mutegi, KEMRI (Kenya Medical Research Institute), Kisumu, Kenya; John Ssali, Mathew Ssemakadde, Masaka Regional Referral Hospital, Masaka, Uganda; Mwebesa Bosco Bwana, Michael Kanyesigye, Mbarara University of Science and Technology (MUST), Mbarara, Uganda; Barbara Castelnovo; John Michael Matovu, Infectious Diseases Institute (IDI), Mulago, Uganda; Fred Nalugoda, Francis X. Wasswa, Rakai Health Sciences Program, Kalisizo, Uganda; G.R. Somi, Joseph Nondi,

NACP (National AIDS Control Program) Dar es Salaam, Tanzania; Rita Elias Lyamuya, Francis Mayanga, Morogoro Regional Hospital, Morogoro, Tanzania; Kapella Ngonyani, Jerome Lwali, Tumbi Regional Hospital, Pwani, Tanzania; Mark Urassa, Denna Michael, Richard Machecha, National Institute for Medical Research (NIMR), Kisesa HDSS, Mwanza, Tanzania; Kara Wools-Kaloustian, Constantin Yiannoutsos, Rachel Vreeman, Beverly Musick, Indiana University School of Medicine, Indiana University, Indianapolis, IN, USA; Batya Elul, Columbia University, New York City, NY, USA; Jennifer Syvertsen, Ohio State University, Columbus, OH, USA; Rami Kantor, Brown University/Miriam Hospital, Providence, RI, USA; Jeffrey Martin, Megan Wenger, Craig Cohen, Jayne Kulzer, University of California, San Francisco, CA, USA; Paula Braitstein, University of Toronto, Toronto, Canada

#### **NA-ACCORD**

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This work was supported by National Institutes of Health grants U01AI069918, F31DA037788, G12MD007583, K01AI093197, K23EY013707, K24AI065298, K24AI118591, K24DA000432, KL2TR000421, M01RR000052, N01CP01004, N02CP055504, N02CP91027, P30AI027757, P30AI027763, P30AI027767, P30AI036219, P30AI050410, P30AI094189, P30AI110527, P30MH62246, R01AA016893, R01CA165937, R01DA011602, R01DA012568, R01AG053100, R24AI067039, U01AA013566, U01AA020790, U01AI031834, U01AI034989, U01AI034993, U01AI034994, U01AI035004, U01AI035039, U01AI035040, U01AI035041, U01AI035042, U01AI037613, U01AI037984, U01AI038855, U01AI038858, U01AI042590, U01AI068634, U01AI068636, U01AI069432, U01AI069434, U01AI103390, U01AI103397, U01AI103401, U01AI103408,

U01DA03629, U01DA036935, U01HD032632, U10EY008057, U10EY008052, U10EY008067, U24AA020794, U54MD007587, UL1RR024131, UL1TR000004, UL1TR000083, UL1TR000454, UM1AI035043, Z01CP010214 and Z01CP010176; contracts CDC-200-2006-18797 and CDC-200-2015-63931 from the Centers for Disease Control and Prevention, USA; contract 90047713 from the Agency for Healthcare Research and Quality, USA; contract 90051652 from the Health Resources and Services Administration, USA; grants CBR-86906, CBR-94036, HCP-97105 and TGF-96118 from the Canadian Institutes of Health Research, Canada; Ontario Ministry of Health and Long Term Care; and the Government of Alberta, Canada. Additional support was provided by the National Cancer Institute, National Institute for Mental Health and National Institute on Drug Abuse.

#### Site investigators and cohorts:

Constance A. Benson and Ronald J. Bosch, AIDS Clinical Trials Group Longitudinal Linked Randomized Trials; Gregory D. Kirk, AIDS Link to the IntraVenous Experience; Stephen Boswell, Kenneth H. Mayer and Chris Grasso, Fenway Health HIV Cohort; Robert S. Hogg,

P. Richard Harrigan, Julio SG Montaner, Angela Cescon and Karyn Gabler; HAART Observational Medical Evaluation and Research; Kate Buchacz and John T. Brooks, HIV Outpatient Study; Kelly A. Gebo and Richard D. Moore, HIV Research Network; Richard D. Moore, Johns Hopkins HIV Clinical Cohort; Benigno Rodriguez, John T. Carey Special Immunology Unit Patient Care and Research Database, Case Western; Benigno Rodriguez, Reserve University; Michael A. Horberg, Kaiser Permanente Mid-Atlantic States; Michael J. Silverberg; Kaiser Permanente Northern California; Jennifer E. Thorne, Longitudinal Study of Ocular Complications of AIDS; Charles Rabkin, Multicenter Hemophilia Cohort Study-II; Lisa

P. Jacobson and Gypsyamber D'Souza, Multicenter AIDS Cohort Study; Marina B. Klein, Montreal Chest Institute Immunodeficiency Service Cohort; Sean B. Rourke, Anita R. Rachlis, Jason Gliberman and Madison Kopansky-Giles, Ontario HIV Treatment Network Cohort Study; Robert F. Hunter-Mellado and Angel M. Mayor, Retrovirus Research Center, Bayamon Puerto Rico; M. John Gill, Southern Alberta Clinic Cohort; Steven G. Deeks and Jeffrey N. Martin, Study of the Consequences of the Protease Inhibitor Era; Pragna Patel and John T. Brooks, Study to Understand the Natural History of HIV/AIDS in the Era of Effective Therapy; Michael S. Saag, Michael J. Mugavero and James Willig, University of Alabama at Birmingham 1917 Clinic Cohort; Joseph J. Eron and Sonia Napravnik, University of North Carolina at Chapel Hill HIV Clinic Cohort; Mari M. Kitahata, Heidi M. Crane and Daniel R. Drozd, University of Washington HIV Cohort; Timothy R. Sterling, David Haas, Peter Rebeiro, Megan Turner, Sally Bebawy and Ben Rogers, Vanderbilt Comprehensive Care Clinic HIV Cohort; Amy C. Justice, Robert Dubrow and David Fiellin, Veterans Aging Cohort Study; Stephen J. Gange and Kathryn Anastos, Women's Interagency HIV Study

#### Study administration:

Richard D. Moore, Michael S. Saag, Stephen J. Gange, Mari M. Kitahata, Keri N. Althoff, Rosemary G. McKaig and Aimee M. Freeman, Executive Committee; Richard D. Moore, Aimee M. Freeman and Carol Lent, Administrative Core; Mari M. Kitahata, Stephen E. Van Rompaey, Heidi M. Crane, Daniel R. Drozd, Liz Morton, Justin McReynolds and William B. Lober, Data Management Core; Stephen J. Gange, Keri N. Althoff, Alison G. Abraham, Bryan Lau, Jinbing Zhang, Jerry Jing, Sharada Modur, Cherise Wong, Brenna Hogan, Fidel Desir and Bin Liu and Bin YouHealth,

Family Medicine, University of Cape Town, South Africa, Epidemiology and Biostatistics Core

#### leDEA Southern Africa

Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number U01AI069924. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

#### Site investigators and cohorts:

Gary Maartens, Aid for AIDS, South Africa; Michael Vinikoor, Centre for Infectious Disease Research in Zambia (CIDRZ), Zambia; Monique van Lettow, Dignitas, Malawi; Robin Wood, Gugulethu ART Programme, South Africa; Nosisa Sipambo, Harriet Shezi Clinic, South Africa; Frank Tanser, Africa Centre for Health & Population Studies (Hlabisa), South Africa; Andrew Boulle, Khayelitsha ART Programme, South Africa; Geoffrey Fatti, Kheth'Impilo, South Africa; Sam Phiri, Lighthouse Clinic, Malawi; Cleophas Chimbetete, Newlands Clinic, Zimbabwe; Karl Technau, Rahima Moosa Mother and Child Hospital, South Africa; Brian Eley, Red Cross Children's Hospital, South Africa; Josephine Muhairwe, SolidarMed Lesotho; Anna Jores, SolidarMed Mozambique; Cordelia Kunzekwenyika, SolidarMed Zimbabwe, Matthew P Fox, Themba Lethu Clinic, South Africa; Hans Prozesky, Tygerberg Academic Hospital, South Africa.

#### Data centres:

Nina Anderegg, Marie Ballif, Lina Bartels, Julia Bohlius, Frédérique Chammartin, Benedikt Christ, Cam Ha Dao Ostinelli, Matthias Egger, Lukas Fenner, Per von Groote, Andreas Haas, Taghavi Katayoun, Eliane Rohner, Lilian Smith, Adrian Spörri, Gilles Wandeler, Elizabeth Zaniewski, Kathrin Zürcher, Institute of Social and Preventive Medicine, University of Bern, Switzerland; Andrew Boulle, Morna Cornell, Mary-Ann Davies, Victoria Iyun, Leigh Johnson, Mmamapudi Kubjane, Nicola Maxwell, Tshabakwane Nemandona, Patience Nyakato, Ernest Mokotoane, Gem Patten, Michael Schomaker, Priscilla Tsondai, Renee de Waal, School of Public Health and Family Medicine, University of Cape Town, South Africa.

#### West Africa

Research reported in this publication was supported by the US National Institutes of Health (NIAID, NICHD, NCI and NIMH) under Award Number U01AI069919 (PI: Dabis). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

#### Site investigators and cohorts:

Adult cohorts: Marcel Djimon Zannou, CNHU, Cotonou, Benin; Armel Poda, CHU Souro Sanou, Bobo Dioulasso, Burkina Faso; Fred Stephen Sarfo & Komfo Anokye Teaching Hospital, Kumasi, Ghana; Eugene Messou, ACONDA CePReF, Abidjan, Cote d'Ivoire; Henri Chenal, CIRBA, Abidjan, Cote d'Ivoire; Kla Albert Minga, CNTS, Abidjan, Cote d'Ivoire; Emmanuel Bissagnene, & Aristophane Tanon, CHU Treichville, Cote d'Ivoire; Moussa Seydi, CHU de Fann, Dakar, Senegal; Akessiwe Akouda Patassi, CHU Sylvanus Olympio, Lomé, Togo.

Paediatric cohorts: Sikiratou Adouni Koumakpai-Adeothy, CNHU, Cotonou, Benin; Lorna Awo Renner, Korle Bu Hospital, Accra, Ghana; Sylvie Marie N'Gbeche, ACONDA CePReF, Abidjan, Ivory Coast; Clarisse Amani Bosse, ACONDA\_MTCT+, Abidjan, Ivory Coast; Kouadio Kouakou, CIRBA, Abidjan, Cote d'Ivoire; Madeleine Amorissani Folquet, CHU de Cocody, Abidjan, Cote d'Ivoire; François Tanoh Eboua, CHU de Yopougon, Abidjan, Cote d'Ivoire;

Fatoumata Dicko Traore, Hopital Gabriel Toure, Bamako, Mali;  
Elom Takassi, CHU Sylvanus Olympio, Lomé, Togo

Coordinating and data centres:

François Dabis, Elise Arrive, Eric Balestre, Renaud Becquet, Charlotte Bernard, Shino Chassagne Arikawa, Alexandra Doring, Sophie

Desmonde, Patricia Dumazert, Antoine Jaquet, Julie Jesson, Valeriane Leroy, Karen Malateste, Elodie Rabourdin, Thierry Tien-drebeogo, ADERA, Isped & INSERM U1219, Bordeaux, France. Didier Koumavi Ekouevi, Jean-Claude Azani, Patrick Coffie, Abdoulaye Cissé, Guy Gnepa, Apollinaire Horo, Christian Kouadio, Boris Tchounga, PACCI, CHU Treichville, Abidjan, Côte d'Ivoire