JIAS
JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

Growing older with HIV in the Treat-All Era

Guest Editors: Reena Rajasuriar, Heidi M. Crane, Aggrey S. Semeere
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Volume 25, Supplement 4, September 2022

WILEY

Acknowledgements

Reena Rajasuriar, Heidi M. Crane and Aggrey S. Semeere, the guest editors, wish to express their appreciation to all the authors who prepared, submitted, revised manuscripts in response to this supplement request, even those that were not included. They would also like to thank all the reviewers who invested their time to review and respond, providing feedback on each of the manuscripts. This work would have been impossible without the multitude of participants who were involved in the various studies in this supplement and we recognize their immense contributions. As more people grow older with HIV, models of HIV care need to evolve. We hope the research represented here highlights these needs and contributes to lessening the burden of various related challenges. Lastly, we acknowledge the consistent guidance, support and fortitude the editors and staff of the *Journal of the International AIDS Society* have accorded to us during the preparation of this supplement.

Support

This supplement was organized by IAS – the International AIDS Society with financial support through a supplement to a grant from the US National Institutes of Health - National Institutes on Aging (NIH-NIA R33AG067069). The content of this supplement is solely the responsibility of the authors and does not necessarily represent the official views of the NIH-NIA.

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Contents

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JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

Rajasuriar R et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25997
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25997/full | https://doi.org/10.1002/jia2.25997

EDITORIAL

Growing older with HIV in the Treat-All Era

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Keywords: HIV; ageing; comorbidity; lifespan; healthspan; treat-all

Received 4 August 2022; **Accepted** 4 August 2022

One of the most impactful global public health interventions of modern times has been antiretroviral therapy (ART). This has led to reduced HIV transmission; reduced morbidity from opportunistic infections; and dramatically reduced mortality [1–3], resulting in many people with HIV (PWH) surviving into middle and old age. However, even as the lifespan of PWH has increased and begun to more closely approach those without HIV, PWH continue to experience high rates of comorbidities and functional decline, with many comorbidities occurring at higher rates and/or at younger ages than those without HIV. In addition, geriatric syndromes, such as frailty and falls, are becoming more prevalent in PWH. Thus, there is an urgent need to focus on the healthspan of PWH rather than just mortality.

Healthspan, in contrast to lifespan, is defined as the time someone is healthy, not just alive [4]. As the population of older PWH increases, more studies are needed that address the myriad of unprecedented and unique challenges that ensue. This supplement presents a range of studies utilizing varied methodologies examining questions along the spectrum of growing older while living with HIV, ranging from resilience and suicidal risk among young adult PWH to comorbidities, cognition and mental health disorders among older PWH, including unmet needs for optimizing care for older adults with HIV. Included studies are focused on two thematic areas. The first encompasses outcomes across the lifespan, including among younger and older PWH, and their comorbidities, mental health and the UNAIDS 90-90-90 targets for global HIV control (90% of PWH knowing their HIV status, 90% on ART and 90% virally suppressed) [5]. The second thematic area focuses on studies examining priorities for and approaches to improving how health systems care for and support PWH as they age.

Young adults with perinatally acquired HIV (YAPHIV) face unique challenges as they grow older with HIV. They are at increased risk of mental health comorbidities, such as depression, anxiety and substance use, as they transit to adulthood. This transition coincides with increased self-awareness, establishing an identity and doing so within the setting of HIV-associated stigma. Mental health issues can precipitate suicidal ideation, as has been reported among youth with other chronic illnesses [6, 7].

Kreniske et al. examine attempted suicide among YAPHIV and those perinatally exposed to but not living with HIV in the Child and Adolescent Self-Awareness and Health study in New York City [8]. They studied the unique roles of sociodemographic, contextual and psychosocial factors on mental health risks, such as how the impacts of pregnancy, substance use and HIV stigma differ. Worryingly, a quarter of YAPHIV in their study reported ever attempting suicide. Suicide attempts were associated with disorders of mood, anxiety and behaviour. They also were associated with higher occurrence of HIV stigma and pregnancy. These findings highlight the need to evaluate for suicidal risk among YAPHIV in care and of efforts to understand the magnitude and associated factors of all mental health challenges in relation to their peers.

Sirois et al. assessed the achievement of key early life milestones by YAPHIV in the US Perinatal HIV/AIDS Cohort national cohort [9]. Previous studies have suggested that YAPHIV have increased the risk of abnormal neurological development [10–12]. Their work expands on prior studies by focusing on evidence of achievement by YAPHIV, including high school diploma or graduate equivalency degree, post-secondary education, or employment, as well as factors associated with these milestones. While compelling, these potentially reassuring results warrant additional evaluations in different contexts to confirm outcomes and better understand other influences.

This supplement includes studies on renal disease, diabetes, mental health and sarcopenia to better understand comorbidities among ageing adult PWH. While questions abound regarding the relative impact of HIV and inflammation; ART medication, including drug–drug interactions and polypharmacy; behavioural factors, such as diet, smoking, substance use and physical activity; and environmental or genetic factors; it is clear that multiple causes contribute to the higher rates of comorbidities among PWH compared to those without HIV [13–18].

Studying participants with and without HIV in the African Cohort Study, Chang et al. examined the prevalence and risk factors of renal insufficiency, elevated blood pressure, diabetes and dysglycemia [19]. Overall, older PWH were at higher risk for the comorbidities studied compared to PWH <50 years. Interestingly, while the overall prevalence of the

comorbidities studied was high, it was not associated with HIV status. This is one of few studies from sub-Saharan Africa comparing comorbidity risk between older PWH and community-dwelling individuals without HIV. This study also raises questions regarding differences in the populations of those with and without HIV, and the need for better characterization of behavioural risks related to diet, physical activity, smoking and substance use.

Aurpibul et al. evaluated the prevalence and determinants of neurocognitive impairment (NCI) specifically amnestic mild cognitive impairment and dementia among older PWH from Northern Thailand who had a long history of HIV and ART [20]. The overall burden of NCI was substantial (87%), with 20% meeting their definition of dementia. While the prevalence of NCI in this study might be higher than has sometimes been seen in other studies [21], this raises questions regarding whether these differences are due to the population, the measures used or other factors.

Other co-morbidity studies also demonstrate the need for more detailed and comparable research across social and cultural contexts. Luk et al. compared definitions of sarcopenia from the Asia Working Group of Sarcopenia, including consistency between criteria and construct validity as measured by associations with mobility and physical functioning among older PWH in Hong Kong [22]. This study is an example of the use of contextually applicable definitions to advance the field. Mwangala et al. present their study on the prevalence and predictors of symptoms for depression and generalized anxiety disorder among older PWH and those without HIV from Kenya with psychosocial factors, such as HIV stigma, household HIV burden and loneliness, all serving as risk indicators among PWH [23]. These findings reflect the value of longitudinal assessments of cognitive, physical and mental health to understand their impact on the trajectory of age-associated decline among PWH.

These four studies on specific comorbidities among older PWH provide updates on the magnitude and burden of multimorbidity in the current ART era, including associated factors and modes of assessment in understudied regions. While higher prevalence rates for comorbidities were found in some but not all studies, risk factors differed among those with and without HIV, emphasizing the importance of considering comorbidities individually and careful evaluation among PWH to best improve clinical care and outcomes.

Farley et al. [24] provide a contemporaneous evaluation of the achievement of the UNAIDS 90-90-90 targets among older versus younger PWH in 13 African countries [5, 24]. In comparison to younger PWH, older PWH have previously been shown to have suboptimal HIV care and treatment outcomes, especially with regard to immunological and virological responses [25, 26]. Using representative Population-based HIV Impact Assessments data, they found that older PWH achieved the second and third 90 (i.e. initiate ART and are virally suppressed). However, the first 90 on awareness of HIV status remains a challenge. Only 80% of older PWH in the study were aware of their HIV status, emphasizing the need for targeted interventions to enhance HIV prevention and testing in this population.

The pace of health transformation in low- and middle-income countries (LMICs) most affected by the HIV epidemic needs to increase to provide chronic care for more PWH who are surviving longer and growing older. The article by Godfrey et al. describes how US PEPFAR-supported countries now have the largest absolute numbers of older PWH, larger still than all of the older PWH in North America and Western Europe, combined [27]. This burden will only continue to increase in the coming years until an HIV cure is achieved. It is clear that innovative and differentiated service delivery (DSD) models will need to be employed in order to meet the non-HIV health needs of older PWH in these resource-constrained settings. Godfrey et al. outline lessons learned from PEPFAR programmes and suggest adaptations that may be considered. They argue that older PWH generally achieve good HIV treatment outcomes with high rates of adherence and viral suppression, but instead have other specific unmet needs, which include depression, cognitive impairment and frailty. PEPFAR-supported HIV programmes have promoted implementing "simplified algorithms/therapies, task-shifting and decentralize," and suggest these principles to guide the development of DSD for older PWH. These models should incorporate the full extent of care from maximizing opportunities for diagnosis with locally validated tools to securing drug procurement and provision pipelines, as well as strengthening existing monitoring and evaluation. LMICs may leverage PEPFAR-developed capacity-building frameworks established to facilitate task-shifting of HIV treatment and extend this to the management of other chronic comorbidities.

Linkage of health systems to the broader community for social support will be imperative for any model of care for an ageing population, especially given the increased reliance on formal support networks among older PWH. In their papers, Murzin et al. [28] and Reynolds et al. [29] use qualitative methods to better understand the health needs of older PWH in marginalized and rural communities from two diverse economies: Canada and Uganda. Both studies highlighted several similarities with that of the ageing non-HIV population, drawing attention to the common, dominant role poor social and structural determinants of health play in influencing health and wellbeing. In many high-income settings like Canada, support services may be available but poorly accessible by older PWH due to various reasons, as opposed to a complete lack of support services in low-resource settings. Multiple needs—such as maintaining adequate nutrition and housing, mobility and sensory aids, in-home support for daily activities and social/emotional support—were common in both settings and among those ageing without HIV. These studies also highlight how the lived experiences of PWH, including trauma and stigma, play a significant role in contributing to uncertainties about the future, which is an additional source of anxiety for ageing PWH.

Central to the transformation of any health system are the data informing its evolution and adaptation. Marty et al. utilized French national data to show that almost 20% of PWH will be >70 years of age by 2030, and 40% would have been on ART for >30 years [30]. By leveraging multiple research and surveillance resources, their team has provided evidence to guide local health systems to prepare for the levels of ageing-related care these PWH will require. Their findings

alert other contextually similar countries to the growing magnitude of older PWH in their communities.

The papers in this supplement emphasize the need to increase the capacity to design, test and evaluate different models of care for older PWH. This will be critical to inform our understanding of what works in different settings. Moreover, older PWH should be part of the teams designing and evaluating implementation strategies as their lived experiences are an invaluable resource for programmes. Service outcomes should include stigma-reduction indicators and patient-reported outcomes in addition to HIV-related parameters as optimal health outcomes cannot be sustained over the long term without an integral plan to address stigma and quality of life. In addition, research should be dedicated to rigorous language and cultural adaptation and validation of critical tools needed to screen PWH for age-associated and geriatric conditions, such as frailty and cognitive impairment. This is particularly critical given that many of the tools in current use were developed for the general elderly population (65+ years) in high-income settings, and may not be well suited for younger PWH (50+ years) experiencing overlapping pathologies related to general ageing and HIV, nor for those in LMICs where there are far fewer screening and referral services.

In this supplement, studies show how research can be used to guide policy, care and treatment of individuals growing older with HIV. Health systems providing care for PWH need to evolve in response to the available evidence to meet the increasing health needs of both YAPHIV and older PWH beyond that of viral suppression. In many settings, HIV providers are the primary, if not the sole healthcare team overseeing the overall health of PWH, a situation that will invariably extend to managing non-communicable diseases, and social and long-term care as PWH age [31]. Countries will need to adopt integrated care approaches to HIV service provision that can be scalable in countries with a high HIV burden in order to achieve longer and richer healthspans for all those growing older with HIV.

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COMPETING INTERESTS

HMC has received funding for her institution from ViiV Healthcare. The other authors report no competing interests.

AUTHORS' CONTRIBUTIONS

All co-authors drafted and revised the editorial, and approved the final version.

ACKNOWLEDGEMENTS

The authors thank Annette Sohn for her assistance with the editorial.

FUNDING

Authors received funding from the US National Institutes of Health (R33AG067069, U01A1069911, UH3CA202723, U54CA254571), Agency for Healthcare Research and Quality's (AHRQ) and ViiV Health Care.

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Kreniske P et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25984
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25984/full | https://doi.org/10.1002/jia2.25984

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

HIV and suicide risk across adolescence and young adulthood: an examination of socio-demographic, contextual and psychosocial risk factors for attempted suicide in a longitudinal cohort of ageing adolescents affected by HIV living in the New York City Area

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Abstract

Introduction: As children become adolescents and young adults (AYA), their risk for attempting suicide increases dramatically, with chronic health conditions an important risk factor. This study examined correlates of suicidality across development in AYA living with perinatally acquired HIV (AYALPHIV) and those perinatally HIV-exposed but uninfected (AYAPHEU).

Methods: Data come from an ongoing longitudinal New York City-based study (N = 339) with AYALPHIV and AYAPHEU interviewed every 12–18 months from 2003 to 2019 (mean enrolment age = 12 years; current mean age = 27 years). The Diagnostic Interview Schedule for Children (adolescent or young adult version) assessed psychiatric disorders and first-reported suicide attempt. Generalized estimating equations were used to examine associations between first-reported suicide attempt and socio-demographic, contextual and psychosocial correlates measured concurrently across six timepoints.

Results: At enrolment, 51% of participants were female, 72% heterosexual, 60% Black and 50% Latinx. Attempted suicide was significantly higher among AYALPHIV (27%, CI 21–33%) compared to AYAPHEU (16%, CI 10–22%), with an OR of 1.74 (CI 1.04–2.92) in a model adjusting for age. For AYALPHIV, anxiety (OR 2.66, CI 1.46–4.85), mood (OR 3.62, CI 1.49–8.81) and behaviour disorders (OR 5.05, CI 2.15–11.87) and past-year arrest (OR 3.05, CI 1.26–7.4), negative life events (OR 1.27, CI 1.11–1.46), city stress (OR 2.28, CI 1.46–3.57), pregnancy (OR 2.28, CI 1.08–4.81) and HIV stigma (OR 2.46, CI 1.27–4.75) were associated with increased odds of attempted suicide, while identifying as heterosexual (OR 0.27, CI 0.14–0.52), higher personal (OR 0.45, CI 0.26–0.80) and family self-concept (OR 0.36, CI 0.22–0.57) were protective. Interactions by HIV status and age were found: substance use was more strongly associated with attempted suicide among AYAPHEU than AYALPHIV, while negative life events and higher religiosity were more strongly associated with increased odds of attempted suicide among AYA ≥ 19 versus ≤ 18 years.

Conclusions: AYALPHIV compared to AYAPHEU faced unique risks for attempted suicide as they age into adulthood, with the highest risk among AYALPHIV experiencing HIV stigma or pregnancy and the highest risk among AYAPHEU with substance use. Assessing for suicide risk and correlates with attention to ageing can inform preventive interventions tailored to meet AYALPHIV and AYAPHEU needs.

Keywords: HIV; young adults; adolescents; HIV stigma; suicide; cohort studies

Received 2 February 2022; **Accepted** 1 August 2022

1 | INTRODUCTION

Risk of attempting suicide increases dramatically as children become adolescents and young adults (AYA) (10–30 years) [1–5]. During this time, symptoms of mental illness and substance use often emerge [6], increasing the risk for suicidal thoughts and behaviours [7–12]. Social (e.g. racial, gender-based discrimination) [3, 13–18] and contextual (e.g. neighbourhood violence) [19–21] factors may also contribute to increased suicide risk among specific sub-groups of AYA, such

as sexual and racial minorities. Youth with chronic illnesses have shown higher suicidality in some studies [22], including AYA affected by HIV [23], yet, no studies to our knowledge have investigated proximal risk factors for suicidality among AYA affected by HIV as they age across this critical developmental period [24]. Given the staggering numbers globally of young people growing up with HIV or affected by maternal HIV [25, 26], understanding suicidality in this population is critical to informing much-needed evidence-based prevention interventions [27, 28], particularly because the history of attempted suicide is a strong predictor of later death by suicide [29–31].

During adolescence, identity development incorporates sexual, racial and ethnic identity, in the context of lived environments [32–37]. This process includes internalizing values and conceptualizing how identity may impact social experiences and life opportunities [35, 38]. Sexual and racial/ethnic minorities are at increased risk for suicidality because of identity-based discrimination, which has the strongest impact during adolescence and young adulthood [3, 13–18, 39]. For people living with HIV (PLWHIV), establishing an identity can be especially complex as they grapple with a stigmatized, chronic, transmittable infection [40, 41].

A recent systematic review and meta-analysis found that PLWHIV, median age 39 years, had a 100-fold higher risk of dying by suicide than people not living with HIV, with an even higher risk for people living with AIDS [42]. While risk factors for suicide in the general population of AYA are well documented [43–45], few studies have examined suicidality among AYA living with perinatally acquired HIV (AYALPHIV) [24] and those that have showed mixed results [46–50].

To further our understanding of predictors of suicide attempts, we examined longitudinal data (adolescence through young adulthood) from the Child and Adolescent Self-Awareness and Health study (CASAH). CASAH was informed by Social Action Theory (SAT) [51], which considers individual, social and contextual determinants of behavioural health outcomes. The objective of the current analysis was to identify proximal risk and protective socio-demographic, contextual and psychosocial factors associated with suicide attempts in AYALPHIV and AYA who were perinatally HIV-exposed but uninfected (AYAPHEU).

2 | METHODS

2.1 | Study population

CASAH is an ongoing longitudinal cohort study, now in its 19th year, that includes AYALPHIV (n = 207) and AYAPHEU (n = 133) recruited from four New York City (NYC) medical centres between 2003 and 2008 when participants were ages 9–16 years (mean = 12). One AYAPHEU was excluded from the current analyses because they seroconverted during the study. Detailed methods have been described elsewhere [52, 53]. In brief, inclusion criteria were perinatal HIV exposure; cognitive capacity to complete interviews; English or Spanish-speaking; and caregiver with the legal capacity to sign consent for adolescent participation (AYA < 18 provided assent; those ≥ 18 years informed consent). Providers referred eligible clinical patients to the study; 93% of all participants approached enrolled. The current analyses include data collected until 2019 from participants' psychosocial battery at six timepoints, with participants aged 21–32 years (mean = 27) at the most recent visit. Interviews were administered by trained research assistants and participants were compensated for time and travel expenses. The study was approved by the New York State Psychiatric Institute Institutional Review Board.

2.2 | Study measures

We selected risk and protective factors informed by SAT and identified by studies on adolescent suicide, HIV and mental health [7, 9–12, 22–24, 29, 47, 49, 54–67]. Unless otherwise indicated, variables for the following age-appropriate measures that had been used in other studies of PLWHIV and racially and ethnically diverse US populations were assessed at all timepoints. When applicable, we provide Chronbach's alpha as a measure of reliability (Table 1) [68, 69]. We then examined data on potential correlates of the first reported suicide attempt collected from the same timepoint as the report for those who endorsed a suicide attempt.

2.2.1 | Suicidality

Suicidality was assessed at each visit using one item from the well-validated Diagnostic Interview Schedule for Children (DISC) [70] "Have you ever in your whole life tried to kill yourself or make a suicide attempt? (yes/no)." All participants who reported any suicidality, including intentions were evaluated for active suicidal ideation; no participants required being taken to the emergency room, although mental health treatment referrals were routinely made.

2.2.2 | Socio-demographic factors

Socio-demographic variables at enrolment included sex (female/male), age, sexual orientation (heterosexual/not), perinatal HIV status (positive/negative), race and ethnicity, and history of pregnancy in self or partner.

2.2.3 | Contextual factors

Negative life events (measured at enrolment-FU3). This measure consists of 18 negative events (e.g. parents divorced and death of family member) typically considered adverse childhood experiences [71], developed by one of the authors (CAM) and providers at a family-based HIV mental health programme for the target population [72, 73], with higher scores indicating more adverse life events. A total score was created and has been used in multiple papers [74–76].

City Stress Inventory. The 16-item City Stress Inventory assesses perceived neighbourhood stress, specifically urban stressors (e.g. witnessing drug deals and gang violence) appropriate for AYA with an eight grade reading level [77]. AYA reported how frequently they experienced these neighbourhood stressors in the past year using a 4-point scale [0 = never; 4 = often]. Higher scores indicated a higher level of neighbourhood stress.

Recent arrest or incarceration (measured FU2-5). A dichotomous variable was created based on AYA self-report of an arrest, spent time in jail or incarceration in the past year, with

Table 1. Description of measures and timepoints collected in the longitudinal cohort of adolescents and young adults affected by HIV living in the New York City Area

Measure	Scale name	Measure age group	Cronbach's α	Enrol	FU1	FU2	FU3	FU4	FU5
First attempted suicide	The Diagnostic Interview Schedule for Children (adolescent or young adult version) (DISC) [70]	Administered by age (< 18 years received the child version, > 18 years received a slightly modified young adult version)	NA	X	X	X	X	X	X
Age, race/ethnicity, HIV status, sexual orientation, past year pregnancy	N/A	All ages	NA	X	X	X	X	X	X
Recent arrest or incarceration	Monitoring the Future [78]	All ages	NA			X	X	X	X
Young adult negative life events	Children's Life Events Inventory [72]; Life Events Questionnaire [75]	Developed with children ages 8–15 years [72], but items are appropriate for young adults and have been used in other studies of youth living with HIV [75]	NA[a]	X	X	X	X		X
City stress	City Stress Inventory (CSI) [77]	Appropriate for those with an approximate eight-grade reading level [77]	NA[a]	X	X	X	X	X	X
Religiosity	Adapted from Monitoring the Future [78]	All ages	0.77	X	X	X	X	X	X
Self-concept	Tennessee Self-Concept Scale [81]	All ages	Personal: 0.72 Family: 0.78 Social: 0.53	X	X	X	X		
Psychiatric disorder	Diagnostic Interview Schedule for Children (DISC) [70]	Administered by age (< 18 years received the child version, > 18 years received a slightly modified young adult version)	NA	X	X	X	X	X	X
HIV stigma	Social Impact Scale [82], HIV Stigma Scale [147] (FU5)	Appropriate for all ages. Before FU5, Social Impact Scale was only asked to PHIV who's caregivers disclosed youth knew about PHIV status.	0.84	X	X	X	X	X	X

Abbreviation: FU, follow up.
[a]Chronbach's alpha computed at enrolment. The city stress index and life events scale both consist of items that are combined into an index following a formative measurement framework, in which the items are the cause of the construct rather than the effect, and therefore, do not follow a reflective measurement framework. Therefore, Chronbach's alpha is not appropriate for these measures [68,69].

items from Monitoring the Future, a well-validated measure of adolescent risk behaviour [78].

2.2.4 | *Psychosocial factors*

Psychiatric disorders. We assessed psychiatric disorders with the DISC, which has well-validated adolescent (< 18 years) and young adult (> 18 years) versions [79]. Symptoms experienced in the past year for the most common psychiatric diagnoses were assessed, adhering to the Diagnostic and Statistical Manual of Mental Disorders [80] diagnostic criteria. The following broad diagnostic categories were examined: mood disorders, anxiety disorders, behaviour disorders and substance use disorders.

Religiosity. Participants reported their religious affiliation, and, using 4-point Likert scales, past year frequency of participation in religious activities, belief in a higher power and the importance of religion or spirituality in their life appropriate for AYA [78]. A total religiosity score was created ranging from 0 to 18, with higher scores indicating higher religiosity (Cronbach's $\alpha = 0.77$).

Self-concept (enrolment-FU3). Self-concept was measured using the Tennessee Self-Concept Scale:2 (TSCS:2), appropriate for AYA [81]. The TSCS:2 is composed of self-descriptive items, each answered on a 5-point Likert Scale (0 = not at all; 5 = very much); higher scores reflect better self-concept. We used three sub-scales: personal self-concept (e.g. "I'm a cheerful person" Cronbach's $\alpha = 0.72$), family self-concept (e.g. "I am a member of a happy family" Cronbach's $\alpha = 0.78$) and social self-concept (e.g. "I am a friendly person" Cronbach's $\alpha = 0.53$).

HIV stigma. Among AYALPHIV, HIV stigma was assessed with the Social Impact Scale appropriate for AYA [82]. Using 18 items from a 4-point Likert-type scale, participants reported how much they agreed with statements concerning social rejection, isolation and internalized shame related to HIV (e.g. "I feel I need to keep my HIV a secret"), with higher scores indicating higher levels of HIV-related stigma (Cronbach's $\alpha = 0.84$).

2.3 | Statistical analysis

Data were set in a long format with participants contributing multiple observations over time. Descriptive statistics were calculated and AYALPHIV and AYAPHEU participants were compared on enrolment socio-demographic and psychosocial variables. *T*-tests and chi-squared tests were used for continuous and categorical variables, respectively. Additionally, we plotted the cumulative incidence (1-Kaplan–Meier) of the time to first suicide attempt with age as the x-axis.

Given the rare outcome of suicide attempt and the use of repeated measures over time, we used logistic regression with generalized estimating equations (GEE) to individually estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between each socio-demographic, contextual and psychosocial factor and having the first report of attempted suicide (binary outcome), adjusting for age at each survey round [83, 84]. Repeated observations were modelled using an independent working correlation matrix, but empirical standard errors were reported, which are robust to the misspecification of the correlation structure. We examined these associations in the overall sample which included both AYALPHIV and AYAPHEU, and among AYALPHIV and AYAPHEU sub-groups. Overall sample models were additionally adjusted for HIV status (PHIV or PHEU), and HIV stigma was only examined among AYALPHIV. Similar to the way, censoring is handled in grouped proportional hazards model [85–87], for participants who ever reported a lifetime suicide attempt, observations were included in the model up until (and including) the observation in which a lifetime suicide attempt was first reported. We explored potential interactions by developmental stage by including an interaction term for ages 9–18 and 19 and older, and by PHIV-status by including a PHIV-status interaction term in analyses with the overall sample. Analyses were completed using SAS version 9.4 [88].

3 | RESULTS

At enrolment, 51% of participants were female ($n = 172$), 72% heterosexual ($n = 227$), 60% Black ($n = 203$) and 50% Latinx ($n = 170$); 11% were Black and Latinx ($n = 36$) and two participants were neither Black nor Latinx) with no significant differences between AYALPHIV and AYAPHEU (Table 2). Participants were followed for a mean of 8.5 years (minimum = 0 years [only enrolment], maximum = 15.9 years). The number of participants reporting attempted suicide increased from 15 (8 females and 7 males) at enrolment to 76 (37 females and 39 males) at the most recent visit. Participants were on average 19 years old (standard deviation = 4.4) at first reported suicide attempt.

Attempted suicide prevalence was significantly higher among AYALPHIV (27%, 95% CI 21–33%) compared to AYAPHEU (16%, 95% CI 10–22%, $p = 0.02$) (Table 2). In the age-adjusted logistic marginal model accounting for participants' repeated observations, AYALPHIV had 1.74 times higher odds than AYAPHEU of ever attempting suicide (95% CI 1.04–2.92) (Table 3). Figure 1 shows the Kaplan–Meier cumulative incidence estimates of first suicide attempt among AYALPHIV and AYAPHEU in our sample. Based on these estimates, by the time a child reached 17 (the median age of all observations), the cumulative incidence of suicide attempt was 6% for AYAPHEU and 10% for AYALPHIV.

3.1 | Socio-demographic factors

In the age-adjusted and HIV status-adjusted logistic marginal models accounting for repeated observations, for the overall and AYALPHIV populations, those who identified as heterosexual had lower odds of attempted suicide compared to those who did not identify as heterosexual (Overall: OR = 0.3, 95% CI, 0.17–0.51; AYALPHIV: OR = 0.27, 95% CI 0.14–0.52). Frequencies of specific non-heterosexual identities were too small to examine separately.

3.2 | Contextual factors

For the overall sample and AYALPHIV group, contextual factors significantly associated with increased odds of attempted suicide were city stress (Overall: OR = 2.07, 95% CI 1.4–3.06; AYALPHIV: OR = 2.28, 95% CI 1.46–3.57; negative life events

Table 2. Description of the overall cohort and AYA living with perinatally acquired HIV (AYALPHIV) and AYA who were perinatally HIV-exposed but uninfected (AYAPHEU) subgroups at enrolment

Variable	Overall sample (N = 339)[b]		AYALPHIV (n = 206)		AYAPHEU (n = 133)		Diff between groups
	n	Mean (SD) or %[b]	*n*	Mean (SD) or %[b]	*n*	Mean (SD) or %[b]	*p*-value
Attempted suicide[a]	76	22% (18%, 27%)	55	27% (21%, 33%)	21	16% (10%, 22%)	**0.02**
Socio-demographic factors							
Sex							0.91
Male	167	49%	102	50%	65	49%	
Female	172	51%	104	50%	68	51%	
Identifies as straight/heterosexual	227	72%	130	69%	97	77%	0.11
Black/African-American	203	60%	131	63.59%	72	54.14%	0.08
Latinx	170	50%	99	48.06%	71	53.38%	0.34
Black and Latinx							
Age	339	12.58 (2.25)	206	12.70 (2.16)	133	12.38 (2.37)	0.19

Abbreviations: AYALPHIV, adolescents and young adults living with perinatally acquired HIV; AYAPHEU, adolescents and young adults perinatally HIV-exposed but uninfected.
Bold indicates $p < 0.05$.
[a]Attempted suicide considers all survey rounds.
[b]*N*s may not sum to total due to missing data. Percentages are of those with non-missing data. Percentages may not sum to 100 due to rounding.

(Overall: OR = 1.23, 95% CI 1.09–1.39; AYALPHIV: OR = 1.27, 95% CI 1.11–1.46); and having been arrested or spent time in jail in the past year (Overall: OR = 2.56, 95% CI 1.16–5.67; AYALPHIV: OR = 3.05, 95% CI 1.26–7.40).

3.3 | Psychosocial factors

Among the overall and AYALPHIV populations, higher personal self-concept (Overall: OR = 0.51, 95% CI 0.32–0.83; AYALPHIV: OR = 0.45, 95% CI 0.26–0.80) and family self-concept (Overall: OR = 0.39, 95% CI 0.26–0.59; AYALPHIV: OR = 0.36, 95% CI 0.22–0.57) were protective against attempted suicide. Overall, psychosocial factors associated with increased odds of attempted suicide included having any anxiety disorder (Overall: OR = 2.88, 95% CI 1.76–4.7); AYALPHIV: OR = 2.66, 95% CI 1.46–4.85; AYAPHEU: OR = 3.43, 95% CI 1.46–8.07); any mood disorder (Overall: OR = 4.39, 95% CI 2.29–8.41); AYALPHIV: OR = 3.62, 95% CI 1.49–8.81; AYAPHEU: OR = 5.88, 95% CI 2.33–14.88); or any behaviour disorder (Overall: OR = 4.70, 95% CI 2.39–9.23; AYALPHIV: OR = 5.05, 95% CI 2.15–11.87; AYAPHEU: OR = 4.06, 95% CI 1.35–12.17). For the overall and AYAPHEU populations, substance use disorder was associated with higher odds of attempted suicide and we found evidence of interaction by PHIV-status (p = 0.04) with substance use as a greater risk factor for attempted suicide in the AYAPHEU group (Overall: OR = 2.60, 95% CI 1.49–4.73; AYAPHEU: OR = 5.83, 95% CI 2.23–15.29). No significant association was found in the AYALPHIV group.

Among AYALPHIV only, pregnancy and HIV stigma were associated with increased odds of attempted suicide. A unit increase in HIV stigma was associated with 2.46 times higher odds of attempted suicide (95% CI: 1.27–4.75). AYALPHIV who experienced pregnancy had 2.28 times higher odds of attempted suicide compared to those who never experienced pregnancy (95% CI: 1.08–4.81). A gender-by-pregnancy interaction term was tested, as it was hypothesized that associations between pregnancy and attempted suicide would be higher for females; the interaction term was not significant (p = 0.90).

3.4 | Interaction by PHIV status and developmental stage

Among older AYA (≥ 19 years), each negative life event increased the odds of attempted suicide by a factor of 1.42 (95% CI: 1.15–1.76) with no significant association among younger AYA (OR = 1.13, 95% CI: 0.97–1.33) (interaction p-value = 0.09). Among older AYA, each unit increase in religiosity score increased the odds of attempted suicide by a factor of 1.60 (95% CI: 1.11–2.31), with no significant association among younger AYA (OR = 0.83, 95% CI: 0.54–1.28) (interaction p-value = 0.03).

4 | DISCUSSION

Adolescence and young adulthood is a high-risk period for attempting suicide [1–4], with AYALPHIV a particularly vulnerable group [49, 50]. The current findings extend the field, not only by providing additional evidence that AYALPHIV are at greater risk for suicide attempts across adolescence and into young adulthood than AYAPHEU peers [23, 49, 50], but also by showing proximal risk and protective factors for both groups as they age through this developmental period. For AYALPHIV, stigma and pregnancy were associated with attempted suicide and for AYAPHEU, substance use was a risk factor. Although our data suggest shared findings with other populations of AYA [67, 89–91], differences were identified

Table 3. Associations between first report of attempted suicide and socio-demographic, structural and psychosocial factors for the overall cohort and within AYA living with perinatally acquired HIV (AYALPHIV) and AYA who were perinatally HIV-exposed but uninfected (AYAPHEU) subgroups

Variable	Odds ratio (95% CI)[a]		
	Overall	AYALPHIV	AYAPHEU
HIV status			
Positive	**1.74 (1.04, 2.92)**		
Negative (ref)			
Socio-demographic factors			
Sex			
Male	0.8 (0.5, 1.28)	0.74 (0.42, 1.3)	1.00 (0.4, 2.45)
Female (ref)			
Identifies as straight/heterosexual			
Yes	**0.30 (0.17, 0.51)**	**0.27 (0.14, 0.52)**	0.37 (0.13, 1.04)
No (ref)			
Race			
Black/African-American	1.12 (0.68, 1.82)	1.28 (0.7, 2.32)	0.79 (0.33, 1.89)
Not Black/African-American (ref)			
Ethnicity			
Latinx	1.38 (0.86, 2.22)	1.21 (0.69, 2.12)	2.02 (0.8, 5.07)
Not Latinx (ref)			
Ever experienced pregnancy			
Yes	1.84 (0.98, 3.45)	**2.28 (1.08, 4.81)**	1.13 (0.35, 3.67)
No (ref)			
Structural factors			
Arrested/spent time in jail past year			
Yes	**2.56 (1.16, 5.67)**	**3.05 (1.26, 7.4)**	1.20 (0.14, 10.13)
No (ref)			
Negative life events	**1.23 (1.09, 1.39)**	**1.27 (1.11, 1.46)**	1.08 (0.85, 1.36)
City Stress Inventory	**2.07 (1.4, 3.06)**	**2.28 (1.46, 3.57)**	1.62 (0.74, 3.53)
Psychosocial factors			
Religiosity	1.23 (0.93, 1.64)	1.14 (0.82, 1.58)	1.52 (0.85, 2.72)
Personal self-concept	**0.51 (0.32, 0.83)**	**0.45 (0.26, 0.8)**	0.68 (0.28, 1.64)
Family self-concept	**0.39 (0.26, 0.59)**	**0.36 (0.22, 0.57)**	0.51 (0.24, 1.09)
Social self-concept	1.10 (0.71, 1.72)	1.19 (0.68, 2.07)	0.87 (0.45, 1.68)
DISC anxiety disorder			
Yes	**2.88 (1.76, 4.7)**	**2.66 (1.46, 4.85)**	**3.43 (1.46, 8.07)**
No (ref)			
DISC mood disorder			
Yes	**4.39 (2.29, 8.41)**	**3.62 (1.49, 8.81)**	**5.88 (2.33, 14.88)**
No (ref)			
DISC behaviour disorder			
Yes	**4.70 (2.39, 9.23)**	**5.05 (2.15, 11.87)**	**4.06 (1.35, 12.17)**
No (ref)			
DISC substance disorder			
Yes	**2.60 (1.49, 4.73)**[b]	1.83 (0.89, 3.78)[b]	**5.83 (2.23, 15.29)**[b]
No (ref)			
HIV-specific factors			
HIV stigma		**2.46 (1.27, 4.75)**	

Abbreviations: AYALPHIV, adolescents and young adults living with perinatally acquired HIV; AYAPHEU, adolescents and young adults perinatally HIV-exposed but uninfected; DISC, Diagnostic Interview Schedule for Children [70].
[a]OR greater than 1 indicates a greater likelihood of attempted suicide. OR adjusted for age at each survey round and overall models were adjusted for PHIV status.
[b]Interaction by PHIV status was significant ($p = 0.041$).
Bold indicates $p < 0.05$.

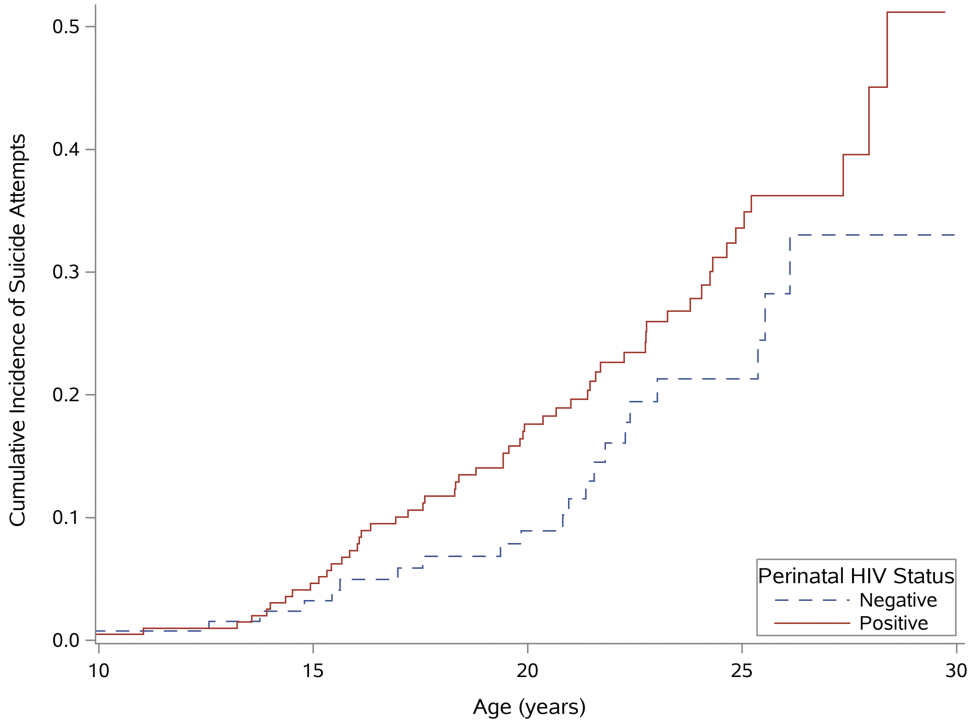

Figure 1. Kaplan–Meier cumulative incidence estimates of first suicide attempt among AYA living with perinatally acquired HIV (AYALPHIV) and AYA who were perinatally HIV-exposed but uninfected (AYAPHEU).

that suggest strategies for suicide prevention tailored for AYA affected by HIV.

The association between pregnancy (self or partner) and attempted suicide among AYALPHIV in our study is an important finding for preventive interventions. Prior studies suggest younger age among HIV-negative pregnant females is a risk factor for suicidality [91–95]. Adult women living with HIV have reported concerns regarding vertical HIV transmission, providing for a child while living with HIV, or fears of mortality [96–98], which may also be relevant to AYALPHIV of all genders. Future studies should examine the timing of pregnancy in this population and mental health effects, including suicidality.

Similar to studies with the general population, we found that non-heterosexual identity was significantly associated with attempted suicide in both AYALPHIV and AYAPHEU [3, 18]. Extensive research has demonstrated associations between sexual identity discrimination and poor mental health outcomes, with AYA sexual minorities being at the greatest risk for suicidality [3, 17, 18]. Further research could inform interventions by exploring how anti-LGBT discrimination might interact with feelings about growing up with HIV and negatively impact AYA social and emotional development.

We identified associations between attempted suicide and contextual factors, including recent arrests, city stress and negative life events in the full cohort, with negative life events having a stronger association with attempted suicide among those who were 19 or older. Interventions for older AYA may be able to stem the harm from exposure to negative life events [99, 100], yet to date, no programmes exist specifically tailored to AYA affected by HIV [27, 28]. Further, these contextual factors may be more salient for Black and Latinx AYA given that they are more likely [53] than White AYA to live in low-income neighbourhoods where negative life events (e.g. family member death, neighbourhood violence and recent arrest) have been associated with attempted suicide [19, 20, 101] and are more common as compared to higher-income neighbourhoods [21, 102–106]. Neighbourhood discrepancies by race and ethnicity are likely the result of systemic racism affecting housing and policing policies, the detrimental impact of which has been documented [64, 107–111]. Unfortunately, we could not examine racial differences as our participants were predominantly Black and Latinx. Additional research among ethnic and racial minorities affected by HIV and suicidality is needed.

Prior study of suicidality among AYA affected by HIV has found mixed results. Three cross-sectional studies (from England, Thailand and South Africa) found no differences in suicide risk between AYALPHIV versus those without HIV [46–48]. Conversely, our current and prior work in the United States [50] and a study in Rwanda [49] both found an increased risk of suicidality among AYALPHIV compared to AYA without HIV. Differences in the HIV epidemic and affected populations across nations [112–114], as well as cross-cultural differences, such as the impact of systemic discrimination on people with intersectional identities, including racial and ethnic minorities living with HIV in the United States, could explain the previously noted mixed findings internationally regarding HIV-status and adolescent suicidality [115–117].

As found in our study, stressful events can also lead to other negative developmental outcomes [21, 102–105], including mental illness, a known correlate of attempted suicide among AYA [7–12, 118]. Self-concept, related to mental health, is an important psychosocial factor that changes during adolescence and young adulthood. Although positive self-concept appears protective against suicidality in other populations, it has not been previously examined over time among AYALPHIV and AYAPHEU. We examined self-concept across different domains [81]. Consistent with international and US studies that suggest family processes influence suicidality among PLWHIV [58, 119], and among adolescents not affected by HIV [12, 66, 67, 120], higher levels of family self-concept were protective against attempted suicide among the overall sample and AYALPHIV. In addition, personal self-concept among the overall sample and AYALPHIV was protective, aligning with prior findings among HIV-negative youth [121, 122].

There were also psychosocial risk factors unique to AYAPHEU and AYALPHIV. Substance use was a risk factor for attempted suicide only among AYAPHEU, supporting prior studies that highlight AYAPHEU as a vulnerable group with unique risks that may require tailored interventions [41, 123, 124]. For AYALPHIV, HIV stigma was a risk factor for attempted suicide. Interestingly, as in our prior work among this cohort, we did not find significant associations between HIV stigma and suicide attempts [50]. Early data from our cohort suggested few participants told others about their HIV which might have limited exposure to stigma. This changed as young people aged, perhaps because of increased sexual behaviour, potentially resulting in more opportunities for stigmatizing experiences [37].

Notably, higher religiosity was associated with higher odds of attempted suicide among AYA over 18 years of age, yet in previous CASAH analyses, we found that religiosity was protective against attempted suicide in earlier adolescence. The changing direction of this association warrants further study and suggests that as our cohort ages, religiosity may shift from a neutral or protective factor to a risk factor for attempted suicide. This changing dynamic between religiosity and attempted suicide as our cohort ages may reflect changes in sexuality, stigmatizing experiences or family dynamics, and corresponds with prior mixed findings from studies of suicide and religiosity in the general population [125, 126].

The longitudinal design of the current study was a strength, allowing us to examine our aims as our cohort transitioned into adolescence and young adulthood. Our use of standardized and validated measures, including the DISC, to assess mental health and attempted suicide was another strength [70, 127, 128].

There were also limitations. Larger samples, including participants in other countries, would be helpful in detecting more nuanced group differences and moderators of our findings, particularly larger samples of AYAPHEU. Additionally, our study did not include an HIV-unexposed cohort, thus, limiting the ability to examine the impact of perinatal HIV exposure or familial HIV on suicidality. Over a lifetime, approximately 4.6% of US adults attempt suicide [129], although according to a systematic review, the proportion may be as high as 3.1–8.8% among adolescents in the United States [130], with an international study including 90 countries noting a range of 10–15% [131]. Both AYAPHEU and AYALPHIV appear to have an elevated risk of attempted suicide compared to HIV-unaffected populations. Furthermore, as has been noted in previous work, AYALPHIV have had better access to mental health services through their ongoing HIV care systems than AYAPHEU [53, 132], potentially minimizing group differences. In addition, our findings may not be generalizable to AYALPHIV and AYAPHEU living outside NYC. However, NYC is one of the epicentres of the United States. HIV epidemic among women and children, with 22% of US paediatric HIV cases from NYC; moreover, the demographics of CASAH participants are similar to those reported in national studies of AYAPHIV and AYAPHEU [53, 133–135]. Further, our results align with prior studies in sub-Saharan Africa that suggest the importance of mental health in understanding suicidality among youth affected by HIV [24, 47, 49, 60].

5 | CONCLUSIONS

Adolescence and young adulthood is a critical period when the risk for attempted suicide rises precipitously [1–4]. We found that as our cohort aged, several socio-demographic, contextual and psychosocial factors placed AYA at increased risk for suicidality and that only a higher self-concept was protective. More negative life events and religiosity appeared to increase the risk of attempted suicide for participants over 18 years. Specific risks for attempted suicide for AYALPHIV were HIV stigma and pregnancy, with substance use a risk for attempted suicide among AYAPHEU. There is an urgent need to meet the needs of AYA affected by HIV and highlighting these risks for healthcare providers could be a needed first step towards preventive interventions [27, 28].

In the context of the COVID-19 pandemic, we suspect the risk of suicidality for this cohort and other AYA affected by HIV may increase. Even before COVID, the multifaceted impact of HIV, poverty and racism contributed to high rates of behavioural health problems, health disparities and among AYALPHIV, low rates of viral suppression [136–139], with few available evidence-based interventions to support behavioural health or HIV treatment adherence [27, 28]. The disproportionate burden of COVID-19 on Black and Latinx communities in the United States, and global COVID-related barriers to treatment among PLWHIV, may exacerbate behavioural health problems and limit access to services for chronic health conditions, such as HIV and psychiatric disorders, thus potentially contributing to increased risk for suicidality among AYA affected by HIV [111, 140–146].

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COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

CM, LL, LK, CAM and CD performed the research. CAM, EJA, AW and CD designed the research study. CD managed the data. PWF contributed essential diagnostic tools and expertise. AL analysed the data. AW and EJA assisted in recruiting participants. PK, CM and BHS wrote a first draft of the manuscript. RNR, NN, CAM, EJA, AW and PWF wrote key sections of the manuscript and provided critical comments and insights. All authors contributed to interpreting the final results, reviewing and revising, and all authors have approved the final manuscript.

ACKNOWLEDGEMENTS

We would like to thank the CASAH participants for their time, thoughts and wisdom.

FUNDING

This research was supported by the National Institute of Mental Health (R01MH06913 PI Mellins and P30MH43520 PI Remien). Kreniske was also supported by K01MH122319 (PI Kreniske) and a New York State Office of Mental Health Policy Scholar Award. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

DATA AVAILABILITY STATEMENT

Due to privacy and ethical concerns the data cannot be made available because of the sensitivity of the HIV data, and the relatively small sample and ease of identifying people if a few demographics are known.

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Sirois PA et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25982
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25982/full | https://doi.org/10.1002/jia2.25982

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Ageing with HIV: a longitudinal study of markers of resilience in young adults with perinatal exposure to HIV, with or without perinatally acquired HIV

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Abstract

Introduction: Medical challenges, including perinatally acquired HIV (PHIV), can be considered adversity with the potential to compromise individuals' ability to meet societal expectations across the lifespan. Studies suggest that resilience, defined as positive adaptation in the context of adversity, helps individuals overcome challenges and improve their quality of life. Few longitudinal studies have examined resilience in young adults with perinatally acquired HIV (YAPHIV) or perinatal HIV exposure, uninfected (YAPHEU). We examined three young adult milestones, which can affect the life-long quality of life, as markers of resilience: high school graduation, postsecondary education and current employment.

Methods: Analyses included YAPHIV and YAPHEU, ages 19–27 years, followed in longitudinal cohort studies: Pediatric HIV/AIDS Cohort Study Adolescent Master Protocol (AMP) (7–17 years) and AMP Up (≥18 years). Factors known to influence the attainment of milestones (outcomes) were examined: executive function, cognitive efficiency (working memory and processing speed), behavioural/social-emotional functioning, parent/caregiver mental/physical health and cumulative risk. HIV disease markers for YAPHIV were examined. The most recent AMP assessment was used for each factor; outcomes were measured at AMP Up 1-year follow-up. Separate robust Poisson regression models were used to assess associations of each factor with each outcome; PHIV status was explored as an effect modifier of each association.

Results: Participants (N = 315; YAPHIV = 228): 58% female, 67% Black and 27% Hispanic. Compared to YAPHEU, YAPHIV were older and from families with higher median income and fewer symptoms of parent/caregiver mental health/substance use disorders. Proportions of YAPHIV and YAPHEU, respectively, who achieved each milestone were comparable: 82% versus 78% for high school graduation (p = 0.49), 45% versus 51% for postsecondary education (p = 0.35) and 48% versus 54% for current employment (p = 0.32). Higher cognitive efficiency was positively associated with postsecondary education and current employment. Higher executive function, age-appropriate behavioural/social-emotional functioning and lower cumulative risk were associated with academic milestones. Among YAPHIV, positive associations were: higher current CD4 with postsecondary education and lower nadir CD4 with current employment. PHIV status did not modify any association.

Conclusions: YAPHIV and YAPHEU demonstrated resilience, attaining at least one young adult milestone. Cognitive, behavioural and social resources to support resilience in childhood and adolescence may provide the foundation for continued achievement throughout adulthood.

Keywords: resilience; young adults; perinatal HIV-exposed uninfected; perinatal HIV infection; milestones; lifespan development

Received 18 January 2022; **Accepted** 1 August 2022

1 | INTRODUCTION

Resilience, defined as positive adaptation in the context of risk or adversity [1, 2], is instrumental to the quality of life and attainment of goals in young adulthood, particularly in the areas of work and vocational or higher education. Quality-of-life indicators in adulthood, such as financial stability, physical and mental health, and life expectancy, are improved with the attainment of high school and postsecondary education [3]. There is little information about high school graduation and higher education in the population with perinatal HIV exposure or perinatally acquired infection in the United States.

Therefore, we examined the attainment of three societal milestones known to contribute to the life-long quality of life: high school graduation, postsecondary education and employment.

Perinatal HIV exposure, with or without perinatally acquired HIV, can confer risks to development and wellbeing in childhood [4–10] and subsequently to quality of life in adulthood. Results from the Pediatric HIV/AIDS Cohort Study (PHACS) documented lowered performance in children and adolescents with perinatal HIV exposure compared to nationally representative test standardization samples on measures of key developmental domains. These include intellectual ability and academic achievement [11–13], language [14, 15], learning, memory, executive function [16–19] and adaptive behaviour [11, 18]. Children and adolescents with perinatally acquired HIV (PHIV) or with perinatal HIV exposure who are uninfected (PHEU) demonstrated higher rates of behavioural or emotional problems than their peers in the general population. These rates were not attributed solely to PHIV because children with PHEU showed similar or even higher rates of mental health problems [20–22]. Youth with PHIV or PHEU are often from vulnerable communities affected by poverty, racism and discrimination, familial stressors and health disparities that can affect development across multiple domains [7, 23–27]. Thus, it is critical to determine factors that might influence the attainment of young adult milestones as youth transition through the lifespan. This knowledge could form the basis for evidence-based interventions to benefit this population.

Many factors are known to influence adaptation to adversity: relationships with parents/caregivers and other adults; friends and romantic partners; intelligence and problem-solving skills; self-control, emotional regulation and planning; and self-efficacy and motivation [2]. Risks to optimal development include maternal education less than high school, parental divorce or death, single-parent family, perceived individual and structural racism and witnessing violence [2, 28]. Family socio-economic status (SES) is related to physical health and achievement of societal milestones, such as high school graduation, postsecondary education and sustained employment; thus, poverty and low SES, whether chronic or of recent onset, confer risks to development and are considered major stressors for children, adolescents and families [23, 29–32]. Medical illnesses present additional stressors related to disease and treatment. Regardless of the source of stress, increases in the cumulative number of stressors have been associated with increases in child maladaptation [2, 25–27]; Rutter [33] found child psychiatric problems increased substantially when any combination of four or more stressors was present in the family. Despite this knowledge base, there is a paucity of information about HIV and its effect on goal attainment as youth with PHIV or PHEU age into young adulthood.

This study draws from research in the fields of resilience and paediatric HIV to examine, from a lifespan developmental perspective, the influence of youth and parent/caregiver characteristics on the attainment of young adult milestones of high school graduation, enrolment in postsecondary education and entry into the workforce. These outcomes reflect the attainment of societal expectations for older adolescents and young adults in the United States [3]. The hypotheses were: (1) compared to young adults with PHEU (YAPHEU), a lower proportion of young adults with PHIV (YAPHIV) will earn a high school diploma or graduate equivalency degree (GED), enrol in postsecondary education, or become employed; (2) regardless of PHIV status, difficulties in youth cognitive and behavioural development and parent/caregiver mental and physical health will adversely affect the attainment of milestones; (3) regardless of PHIV status, higher cumulative risk, that is a greater number of individual, familial and life event risks, will adversely affect the attainment of these milestones; and (4) YAPHIV with better immune function will be more likely to attain one or more milestones than those with poorer immune function.

2 | METHODS

2.1 | Participants

The PHACS Adolescent Master Protocol (AMP) and PHACS AMP Up are prospective cohort studies of children, adolescents and young adults with PHIV or PHEU followed for long-term evaluation of cognitive, behavioural, social-emotional and physical health outcomes. In 2006, AMP began enrolling children and adolescents, age 7–15 years, at 15 sites in the United States and Puerto Rico, following them until their 18th birthday. AMP follow-up ended in 2021. In 2014, AMP Up began enrolment at 14 AMP sites for follow-up of AMP participants and other eligible YAPHIV age 18 and older. All YAPHIV and YAPHEU age 19 and older, who were previously followed in AMP and had completed the 1-year follow-up visit in AMP Up, were eligible for this analysis. Semi-annual and annual study visits in AMP included face-to-face testing with participants, interviews with participants and parents/caregivers and medical chart abstraction. Annual study visits in AMP Up include interviews with participants, web-based surveys and medical chart abstraction. Informed consent and assent were obtained from parents/caregivers and participants at the time of enrolment into AMP and from participants at enrolment into AMP Up. Both protocols were reviewed and approved by Institutional Review Boards at all participating sites and Harvard T.H. Chan School of Public Health.

2.2 | Milestone outcomes

Attainment of education and employment milestones was assessed by a web-based survey administered 1 year after entry into AMP Up. High school graduation was defined as receipt of a high school diploma or GED; participants reporting enrolment in postsecondary education without reporting receipt of a high school diploma or GED were counted as high school graduates. Postsecondary education included vocational or technical schools, 2-year associate degree or certification programmes, 4-year college bachelor programmes and graduate education. Employment was defined as current part-time or full-time work.

2.3 | Potential predictors

Several domains of functioning were evaluated as potentially associated with the attainment of the three outcomes

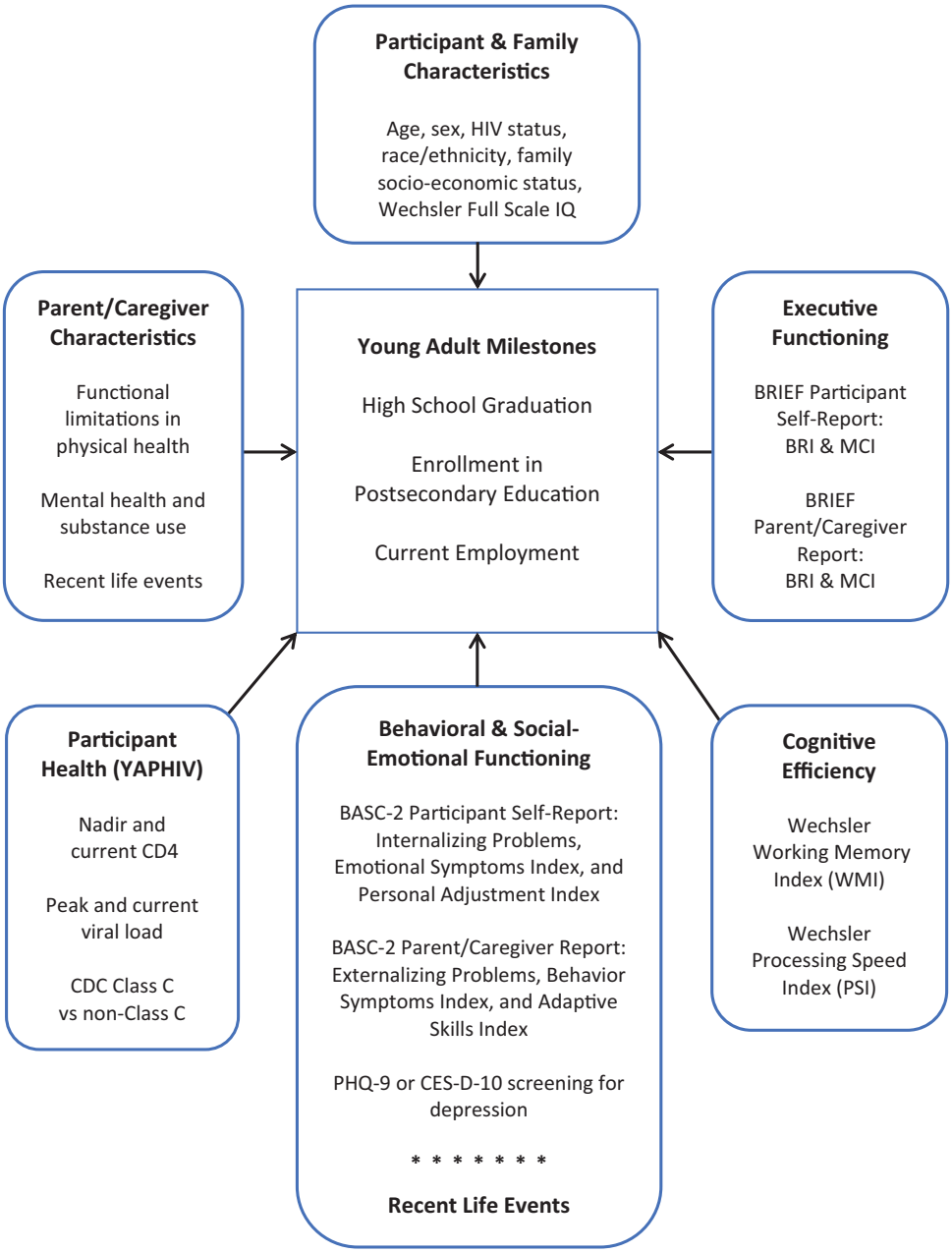

Figure 1. Compensatory (main effects) model of resilience in the AMP Up cohort of the Pediatric HIV/AIDS Cohort Study. Resilience was defined by participants' attainment of one or more young adult milestones. A measure of cumulative risk developed for this study assessed the total number of risks present across all domains. All measures were collected during AMP except for the PHQ-9 and CES-D-10 collected at entry into AMP Up. AMP, Adolescent Master Protocol; AMP Up, long-term follow-up of participants age 18 and older; BASC-2, Behavior Assessment System for Children, Second Ed. [37]; BRIEF, Behavior Rating Inventory of Executive Function [36]; BRI, Behavioral Regulation Index; CDC, Centers for Disease Control and Prevention; CES-D-10, Center for Epidemiological Studies Depression Scale [42]; MCI, Metacognition Index; PHQ-9, Patient Health Questionnaire [41]; Wechsler, Wechsler Intelligence Scale for Children, Fourth Ed. [34] or Wechsler Adult Intelligence Scale, Fourth Ed. [35]; YAPHIV, young adults with perinatally acquired HIV.

(Figure 1). Measures of each domain were administered on a regular schedule during AMP follow-up; not all measures were scheduled for the same visit. Measures selected for this analysis (Table 1) were obtained at the last AMP visit at which each measure was administered. Only those considered valid by internal test validity indices and/or examiner judgement were included. Data from AMP were used as predictors; AMP Up 1-year follow-up data were used for outcomes. Each measure was assessed individually to identify associations between predictors and outcomes. The measures were also combined

Table 1. Potential predictors measured during AMP and included in the analysis

Domain	Measure	Selected index/subtest score
Executive functioning	Behavior Rating Inventory of Executive Function (BRIEF) [36], participant self-report and parent/caregiver report; administered as interviews	Behavioral Regulation Index (BRI) and Metacognition Index (MCI)
Cognitive efficiency	Wechsler intelligence scales, child or adult version as appropriate for age [34, 35]; face-to-face testing with participant, using standardized administration procedures	Working Memory Index (WMI) and Processing Speed Index (PSI)
Behavioural and social-emotional functioning[a]	Behavior Assessment System for Children, Second Edition (BASC-2) [37], participant self-report and parent/caregiver report; administered as interviews	Internalizing Problems, Emotional Symptoms and Personal Adjustment indices from the participant self-report; Externalizing Problems, Behavioral Symptoms and Adaptive Skills indices from the parent/caregiver report
Life events	Life Events Checklist [38], participant self-report of potentially traumatic events; administered as interview	Average life events reported during AMP follow-up[b]
HIV disease severity (YAPHIV only)	a) CD4 count (cells/mm^3) b) Viral load (copies/ml) c) Centers for Disease Control and Prevention (CDC) classification [39]; data obtained through medical chart abstraction	a) Nadir and most recent b) Peak and most recent c) Class C (AIDS-defining diagnoses) versus non-Class C
Parent/caregiver characteristics	a) Client Diagnostic Questionnaire (CDQ) [40][c]; administered as interview b) Caregiver health interview[d] c) Caregiver quality of life interview[d]	a) Number of positive screens for mental health and substance use disorders b) Number of functional limitations in physical health c) Number of potentially traumatic life events during 12 months prior to interview

Abbreviations: AMP, Adolescent Master Protocol; PHACS, Pediatric HIV/AIDS Cohort Study.
[a]Depending on time of entry into AMP Up, symptoms of depression were measured with one of two depression screening instruments: the Patient Health Questionnaire (PHQ-9) [41] or the Center for Epidemiological Studies Depression Scale (CES-D-10) [42]. Results are reported only for descriptive purposes. Total score ≥10 on either measure indicated a positive screen for symptoms of depression, not a diagnosis. Referrals for further clinical evaluation were provided as needed.
[b]A participant-reported screening measure for potentially traumatic life experiences (e.g. illness/death in family, witnessing violence and change in residence) during the 12 months prior to the interview. The average life events score (total events reported over AMP follow-up divided by total number of interviews completed in AMP) was used in the analysis to allow examination of chronic stress rather than recent stress.
[c]Parent/caregiver self-report of symptoms of their own mental health and substance use. Positive scores indicated positive screens for disorders, not diagnoses.
[d]Parent/caregiver self-reports developed for the Pediatric AIDS Clinical Trials Group and subsequently used in PHACS.

into a study-specific cumulative risk index, based on research indicating that cumulative stress is positively associated with adverse outcomes [2, 25–27, 33]. The index score reflected the total number of risks present across all domains. Risks were defined as follows: (1) performance greater than 1.0 standard deviation below the mean for age on the Wechsler [34, 35] Working Memory Index (WMI) and Processing Speed Index (PSI) or above cutoffs indicating clinically relevant concern on indices of the Behavior Rating Inventory of Executive Function (BRIEF) [36] and Behavior Assessment System for Children, Second Edition (BASC-2) [37] (Table 1); (2) number of parent/caregiver-reported symptoms of their own mental health, substance use and physical health problems >1; (3) average number of participant-reported life events >3; and (4) number of parent/caregiver-reported life events >3. The total score ranged from 0 to 13, determined by calculating the presence (1) or absence (0) of each risk.

Based upon prior research [2, 28–33], the following participant and family characteristics were included in the multivariable models as confounding variables: participant age at the time of measurement of each potential predictor, sex, race/ethnicity, Wechsler [34, 35] Full-Scale Intelligence Quotient (FSIQ) and family SES, using annual household income and household density.

2.4 | Statistical analysis

Using chi-square or Fisher's exact test, as appropriate, the proportions of participants who attained each of the three milestones were compared by PHIV status and age at outcome measurement. Each of the potential predictors, as well as proportions of participants who attained zero, one, two or all three milestones, were compared by PHIV status. Separate univariable and multivariable robust Poisson regression models were fit to evaluate the association of each measure with each milestone. Inverse probability of censoring weighting was used to adjust for potential selection bias due to loss to follow-up (censoring) of AMP participants who did not enrol into AMP Up. Weights were generated by fitting logistic regression models for 669 AMP participants (excluding five deaths and four with no visits after enrolment into AMP), with censoring as the outcome. Variables included as predictors of censoring were age, FSIQ and education at the most recent AMP visit, sex, race/ethnicity and research site, as well as the potential predictors of the milestone outcomes. The model for YAPHIV also included CD4 and viral load at the most recent AMP visit. The weights were then incorporated into the Poisson regression models. To evaluate whether any of the associations differed by PHIV status (effect modification), an interaction term between PHIV status and each measure was added to the univariable and multivariable models.

The multiple imputation approach was used to account for missing predictor and covariate measures. Fully conditional specification with discriminant function was used to impute missing data for categorical variables; the predictive mean matching method was used to impute missing data for continuous variables. Sensitivity analyses were conducted using the complete case analysis approach, excluding participants with missing data on any measure from the multivariable models. Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

3 | RESULTS

3.1 | Participant and parent/caregiver characteristics

AMP enrolled 678 participants. As of 1 January 2020, there were 712 participants enrolled in AMP Up, 411 of whom were previously enrolled in AMP (61%). Of the 411, 315 (228 YAPHIV and 87 YAPHEU) had completed the AMP Up Year 1 web-based survey and were included in the analysis. Table 2 summarizes participant and parent/caregiver characteristics for YAPHIV and YAPHEU and disease severity for YAPHIV. Compared to YAPHEU, YAPHIV were older (mean age 20.2 vs. 20.8 years, respectively, $p = 0.002$; range 19–27 years), more often from families with greater financial resources per person supported ($p < 0.001$) and with parents/caregivers less likely to screen positive for mental health or substance use disorders ($p < 0.001$ and $p = 0.03$, respectively). Measures of HIV disease severity indicated that 39% of YAPHIV had nadir CD4 <200 cells/mm^3 and 28% had received a CDC Class C classification [39] at some time in their lives. For the majority of YAPHIV, the most recent CD4 count was ≥500 cells/mm^3 (63%), and the most recent viral load was <400 copies/ml (64%). Primary caregivers included biological parents (43% YAPHIV vs. 77% YAPHEU); biological family members (24% vs. 14%, respectively); and non-biological family, such as adoptive and foster parents (32% vs. 9%, respectively). These data are presented for descriptive purposes and were not included in the analysis. A majority of parents/caregivers (68–72%) had a high school education or higher; 48–59% reported at least one limitation in physical health.

3.2 | Milestone outcomes

The proportions of YAPHIV and YAPHEU, respectively, who achieved each of the milestones were comparable: 82% versus 78% for high school graduation ($p = 0.49$), 45% versus 51% for postsecondary education ($p = 0.35$) and 48% versus 54% for current employment ($p = 0.32$). The proportions of YAPHIV and YAPHEU, respectively, who attained zero (11% vs. 16%), one (27% vs. 16%), two (37% vs. 37%) or all three milestones (24% vs. 31%) were also similar ($p = 0.14$). A small number of participants ($n = 40$; 13%) did not achieve any milestones (Table 3). This finding was associated with lower family SES and lower participant FSIQ, as well as lower cognitive efficiency and executive functioning (data not shown), which may be related to FSIQ. Among the 19-year-olds ($n = 151$), 72% had graduated high school by the AMP Up Year 1 follow-up visit; high school graduation rates were 93% for those age 22 and older ($n = 59$) (Table 3). There was greater variability across ages in the attainment of the other two milestones.

3.3 | Comparisons by PHIV status

3.3.1 | Executive functioning

On average, YAPHIV and YAPHEU were within age expectations on the Behavioral Regulation Index (BRI) and Metacognition Index (MCI) of the BRIEF, with no significant differences between the groups (Table 4).

3.3.2 | Cognitive efficiency

Compared to same-age peers in the Wechsler standardization samples, on average, YAPHIV and YAPHEU were within the Wechsler Low Average to Average range for age on the WMI and PSI and did not differ statistically from one another (Table 4). However, 9–10% of participants in both groups showed impairment in working memory (WMI <70); 6–7% showed impairment in processing speed (PSI <70).

3.3.3 | Behavioural and social-emotional functioning

According to the BASC-2 parent/caregiver reports, YAPHEU were more likely to show symptoms of externalizing behaviour problems than YAPHIV, although results for both groups, on average, were within age expectations. According to participant self-reports, there were no differences between the groups on any BASC-2 measures of behavioural and social-emotional functioning (Table 5); on average, both groups were within age expectations. Participants (18%) in both groups screened positive for symptoms of depression on the Patient Health Questionnaire (PHQ-9) [41] or Center for Epidemiological Studies Depression Scale (CES-D-10) [42] completed at AMP Up entry.

Table 2. Participant and parent/caregiver characteristics measured during AMP

		Perinatal HIV status		
		YAPHIV (*n* = 228)	YAPHEU (*n* = 87)	*p*-value
Participant characteristics				
Age (years) at AMP Up Year 1 follow-up visit	Mean (SD)	20.8 (1.6)	20.2 (1.5)	0.002[a]
Sex	M	93 (41%)	39 (45%)	0.52[b]
	F	135 (59%)	48 (55%)	
Race/Ethnicity	Black, non-Hispanic	160 (70%)	50 (57%)	0.13[b]
	White/other, non-Hispanic	12 (5%)	5 (6%)	
	Hispanic	55 (24%)	30 (34%)	
	Unknown	1 (0%)	2 (2%)	
Family SES	Annual income per person supported, Mdn (Q1, Q3)	$8000 ($5000, $15,000)	$5000 ($3333, $7500)	<0.001[a]
Wechsler FSIQ	Mean (SD)	84.2 (16.3)	86.3 (15.4)	0.30[a]
Nadir CD4 count, cells/mm^3	≥500	40 (18%)	n/a	
	200–499	100 (44%)	n/a	
	<200	88 (39%)	n/a	
Most recent CD4 count, cells/mm^3	≥500	144 (63%)	n/a	
	200–499	65 (29%)	n/a	
	<200	19 (8%)	n/a	
Peak viral load, copies/ml	≤20,000	13 (6%)	n/a	
	>20,000 to <100,000	35 (15%)	n/a	
	≥100,000	180 (79%)	n/a	
Most recent viral load, cells/mm^3	<400	145 (64%)	n/a	
	400 to <1000	14 (6%)	n/a	
	≥1000	69 (30%)	n/a	
CDC Class C	Yes	63 (28%)	n/a	
	No	165 (72%)	n/a	
Parent/caregiver characteristics				
Education	High school or greater	164 (72%)	59 (68%)	0.49[b]
	Less than high school	62 (27%)	27 (31%)	
	Unknown	2 (1%)	1 (1%)	
Limitations in physical health	Yes	109 (48%)	51 (59%)	0.12[b]
	No	106 (46%)	33 (38%)	
Positive screen for mental health disorder	Yes	46 (20%)	38 (44%)	<0.001[b]
	No	150 (66%)	45 (52%)	
	Unknown	32 (14%)	4 (5%)	
Positive screen for substance use disorder	Yes	11 (5%)	11 (13%)	0.03[b]
	No	185 (81%)	72 (83%)	
	Unknown	32 (14%)	4 (5%)	
Life events in past year	0–3	168 (74%)	70 (80%)	0.63[b]
	> 3	24 (11%)	12 (14%)	
	Unknown	36 (16%)	5 (6%)	

Abbreviations: AMP, Adolescent Master Protocol; AMP Up, Adolescent Master Protocol for Participants 18 Years of Age and Older; CDC, Centers for Disease Control and Prevention [39]; n/a, not applicable; SES, socio-economic status; Wechsler FSIQ, Wechsler Intelligence Scale for Children, Fourth Ed. [34] (ages 6–16) or Wechsler Adult Intelligence Scale, Fourth Ed. [35] (ages 17 and older) Full-Scale Intelligence Quotient; YAPHEU, young adults with perinatal HIV exposure, uninfected; YAPHIV, young adults with perinatally acquired HIV.
[a]*T*-test with equal variance.
[b]Chi-square test.

Table 3. Distribution of milestones by age at AMP Up Year 1 follow-up visit

Milestone		Total (*N* = 315)	Age (years) at AMP Up Year 1 follow-up visit				*p*-value[a]
			19 (*n* = 151)	20 (*n* = 53)	21 (*n* = 52)	≥22 (*n* = 59)	
High school graduation	Yes	254 (81%)	109 (72%)	43 (81%)	47 (90%)	55 (93%)	0.001
	No	61 (19%)	42 (28%)	10 (19%)	5 (10%)	4 (7%)	
Enrolment in postsecondary education	Yes	146 (46%)	67 (44%)	32 (60%)	20 (38%)	27 (46%)	0.12
	No	169 (54%)	84 (56%)	21 (40%)	32 (62%)	32 (54%)	
Current employment	Yes	156 (50%)	63 (42%)	30 (57%)	27 (52%)	36 (61%)	0.05
	No	159 (50%)	88 (58%)	23 (43%)	25 (48%)	23 (39%)	
Number of milestones attained	0	40 (13%)	29 (19%)	4 (8%)	4 (8%)	3 (5%)	0.02
	1	76 (24%)	36 (24%)	14 (26%)	13 (25%)	13 (22%)	
	2	117 (37%)	55 (36%)	14 (26%)	24 (46%)	24 (41%)	
	3	82 (26%)	31 (21%)	21 (40%)	11 (21%)	19 (32%)	

Abbreviation: AMP Up, Adolescent Master Protocol for Participants 18 Years of Age and Older.
High school graduation, high school diploma or graduate equivalency degree.
Enrolment in postsecondary education, enrolment in technical and trade schools, college (freshman to senior year), associate and bachelor degrees and graduate school.
Current employment, part-time or full-time employment at the time of the AMP Up Year 1 follow-up visit.
[a]Chi-square test.

3.3.4 | *Cumulative risk*

The average score on the cumulative risk index (Table 6) did not differ between YAPHIV and YAPHEU (3.1 vs. 3.2, respectively, $p = 0.81$), but the frequency of individual risks in several domains was greater than expected. In executive functioning, 20% of YAPHIV demonstrated risk on BRI, and 26% demonstrated risk on MCI, according to parent/caregiver reports. In cognitive efficiency, 22–44% of participants met the criteria for the definition of risk in WMI or PSI. In behavioural and social/emotional functioning, according to parent/caregiver reports, 21–23% of YAPHEU demonstrated behavioural problems, while 28–30% of both groups demonstrated lower-than-expected adaptive skills. Approximately 50% of YAPHIV and YAPHEU averaged more than three potentially traumatic life events per year during the course of AMP, meeting one of the definitions of risk. Parents/caregivers of YAPHIV and YAPHEU (17% vs. 31%, respectively) reported one or more difficulties in their own mental health, physical health or substance use. Parents/caregivers in both groups (11–14%) reported three or more potentially traumatic life events occurring within the 12 months prior to the interview.

3.4 | Predictors of attainment of young adult milestones

Higher cognitive efficiency was positively associated with enrolment into postsecondary education and current employment (Figure 2a). Higher executive function, per parent/caregiver report, and lower cumulative risk were associated with a greater likelihood of attaining both academic milestones (Figures 2a and b). Age-appropriate behaviour (BASC-2 parent/caregiver report) was positively associated with high school graduation, while age-appropriate adaptive skills (BASC-2 participant self-report and parent/caregiver report) and perceived lack of difficulty in emotional functioning (BASC-2 participant self-report Internalizing Problems and Emotional Symptoms indices) were positively associated with enrolment in postsecondary education. Lack of functional limitations in caregiver physical health was associated with a lower likelihood of employment (Figure 2b). For YAPHIV, positive associations were: higher current CD4 with postsecondary education and lower nadir CD4 with current employment (Figure 3). PHIV status did not modify any associations. The results of the complete case analysis approach were similar to those of the multiple imputation approach for missing data.

4 | DISCUSSION

Resilience among YAPHIV and YAPHEU participants was demonstrated by their attainment of one or more young adult milestones. Although PHIV is an important aspect of participants' lives, it was not determinative of success in milestone attainment. Rather, success was influenced more by participants' development during childhood and adolescence across the cognitive, behavioural and social/emotional domains examined.

Despite well-documented early and sometimes ongoing risks for individuals affected by HIV, the proportions of young adults who attained each milestone did not differ by PHIV status, contrary to Hypothesis 1. Attainment of milestones was positively associated with higher participant executive functioning, cognitive efficiency and behavioural/social-emotional functioning, as well as fewer parent/caregiver risks and lower cumulative risk, supporting Hypotheses 2 and 3. For YAPHIV, higher current CD4 was positively associated with postsecondary education; the current viral load was not associated with any of the outcomes. Thus, Hypothesis 4 was partially supported. The finding that lower nadir CD4 was positively associated with current employment is counterintuitive; it is possible that residual or unmeasured confounding contributed to the observed association.

Table 4. Measures of executive functioning and cognitive efficiency collected during AMP

Domain and measures			Perinatal HIV status		*p*-value
			YAPHIV (*n* = 228)	YAPHEU (*n* = 87)	
Executive functioning					
BRIEF[a] Participant Self-Report					
Behavioral Regulation Index (BRI)	Mean (SD)		50.3 (12.1)	50.4 (11.4)	0.95[c]
	T ≥ 65:	Yes	29 (13%)	8 (9%)	0.42[d]
		No	170 (75%)	66 (76%)	
		Unknown	29 (13%)	13 (15%)	
Metacognition Index (MCI)	Mean (SD)		51.4 (11.4)	49.5 (11.4)	0.23[c]
	T ≥ 65:	Yes	29 (13%)	8 (9%)	0.42[d]
		No	170 (75%)	66 (76%)	
		Unknown	29 (13%)	13 (15%)	
BRIEF Parent/Caregiver Report					
Behavioral Regulation Index (BRI)	Mean (SD)		52.4 (11.6)	54.9 (12.9)	0.13[c]
	T ≥ 65:	Yes	23 (10%)	12 (14%)	0.32[d]
		No	169 (74%)	60 (69%)	
		Unknown	36 (16%)	15 (17%)	
Metacognition Index (MCI)	Mean (SD)		55.6 (12.5)	53.1 (12.1)	0.14[c]
	T ≥ 65:	Yes	46 (20%)	16 (18%)	0.77[d]
		No	146 (64%)	56 (64%)	
		Unknown	36 (16%)	15 (17%)	
Cognitive efficiency					
Wechsler[b] Working Memory Index (WMI)	Mean (SD)		86.8 (15.0)	90.2 (14.6)	0.08[c]
	WMI > 115		7 (3%)	4 (5%)	0.34[d]
	WMI = 85–115		113 (50%)	53 (61%)	
	WMI = 70–84		77 (34%)	22 (25%)	
	WMI < 70		23 (10%)	8 (9%)	
Wechsler[b] Processing Speed Index (PSI)	Mean (SD)		90.6 (16.4)	94.2 (14.7)	0.07[c]
	PSI > 115		16 (7%)	7 (8%)	0.34[d]
	PSI = 85–115		133 (58%)	61 (70%)	
	PSI = 70–84		55 (24%)	14 (16%)	
	PSI < 70		16 (7%)	5 (6%)	

Abbreviations: AMP, Adolescent Master Protocol; YAPHEU, young adults with perinatal HIV exposure, uninfected; YAPHIV, young adults with perinatally acquired HIV.
[a]BRIEF, Behavior Rating Inventory of Executive Function [36], reported as T-scores with Mean = 50, SD = 10. T ≥ 65 is considered clinically significant.
[b]Wechsler, Wechsler Intelligence Scale for Children, Fourth Ed. [34] (ages 6–16) or Wechsler Adult Intelligence Scale, Fourth Ed. [35] (ages 17 and older), reported as standard scores with Mean = 100, SD = 15. WMI/PSI < 70 indicates impaired performance.
[c]*T*-test with equal variance.
[d]Chi-square test.

The National Center for Education Statistics (NCES) [43] reports public high school graduation rates for young adults who complete high school within 4 years of entering ninth grade. In 2019, the rates were 86% for the United States general population and 80%, 82% and 89% for Black, Hispanic and White students, respectively. In our study, 81% of the total sample (*N* = 315) met the high school graduation/GED milestone, and graduation rates increased steadily from 72% for 19-year-olds to 93% for those age 22 and older. The comparison between NCES data and the present study is not equal because the NCES report does not reference student age, only timely graduation, and our sample of graduates included participants who attained a GED, while the NCES sample does not. While the total high school graduation rate in our sample is consistent with NCES data for Black and Hispanic students, the relatively low proportion among 19-year-olds (72%) indicates the presence of difficulties that may have impeded their academic progress. Developmental delays and subsequent difficulties in cognition, executive functioning and language [8, 9, 11–19], and possibly school absences due to medical complications, were present throughout the lives of many PHACS participants and may contribute to the slower-than-expected graduation rate.

Regarding mental health, 18% of 19-year-olds in each group screened positive for depression, comparable to a sample of 18- to 29-year-olds in the general population who

Table 5. Measures of behavioural and social-emotional functioning collected during AMP

Measure		Perinatal HIV status		*p*-value
		YAPHIV (*n* = 228)	YAPHEU (*n* = 87)	
BASC-2[a] Participant Self-Report				
Internalizing Problems	Mean (SD)	48.4 (10.3)	47.0 (10.5)	0.28[c]
Clinically significant	T ≥ 70	8 (4%)	3 (3%)	0.92[d]
At risk	T = 60–69	21 (9%)	7 (8%)	
Average	T < 60	189 (83%)	76 (87%)	
	Unknown	10 (4%)	1 (1%)	
Emotional Symptoms Index	Mean (SD)	48.4 (10.4)	47.1 (10.1)	0.30[c]
Clinically significant	T ≥ 70	10 (4%)	2 (2%)	0.46[d]
At risk	T = 60–69	16 (7%)	9 (10%)	
Average	T < 60	192 (84%)	75 (86%)	
	Unknown	10 (4%)	1 (1%)	
Personal Adjustment	Mean (SD)	50.5 (9.7)	51.2 (9.8)	0.59[c]
Clinically significant	T ≤ 30	8 (4%)	2 (2%)	0.75[d]
At risk	T = 31–40	21 (9%)	10 (11%)	
Average	T ≥ 41	189 (83%)	74 (85%)	
	Unknown	10 (4%)	1 (1%)	
BASC-2 Parent/Caregiver Report				
Externalizing Problems	Mean (SD)	48.6 (10.1)	52.4 (10.5)	0.003[c]
Clinically significant	T ≥ 70	9 (4%)	9 (10%)	0.07[d]
At risk	T = 60–69	17 (7%)	9 (10%)	
Average	T < 60	194 (85%)	69 (79%)	
	Unknown	8 (4%)	0 (0%)	
Behavioral Symptoms Index	Mean (SD)	49.5 (10.7)	52.3 (10.5)	0.04[c]
Clinically significant	T ≥ 70	13 (6%)	7 (8%)	0.29[d]
At risk	T = 60–69	21 (9%)	13 (15%)	
Average	T < 60	186 (82%)	67 (77%)	
	Unknown	8 (4%)	0 (0%)	
Adaptive Skills	Mean (SD)	47.8 (11.4)	47.9 (11.1)	0.94[c]
Clinically significant	T ≤ 30	15 (7%)	7 (8%)	0.63[d]
At risk	T = 31–40	54 (24%)	17 (20%)	
Average	T ≥ 41	151 (66%)	63 (72%)	
	Unknown	8 (4%)	0 (0%)	
PHQ-9[b] or CES-D-10[b], Total ≥ 10	Yes	42 (18%)	16 (18%)	0.96[d]
	No	183 (80%)	71 (82%)	
	Unknown	3 (1%)	0 (0%)	

Abbreviations: AMP, Adolescent Master Protocol; YAPHEU, young adults with perinatal HIV exposure, uninfected; YAPHIV, young adults with perinatally acquired HIV.
[a]BASC-2, Behavior Assessment System for Children, Second Ed. [37], reported as T-scores, Mean = 50, SD = 10.
[b]PHQ-9, Patient Health Questionnaire [41]; CES-D-10, Center for Epidemiological Studies Depression Scale [42]. Depending on time of entry into AMP Up, symptoms of depression were measured with one of two depression screening instruments. Results are reported only for descriptive purposes. Total score ≥ 10 on either measure indicated a positive screen for symptoms of depression, not a diagnosis. Referrals for further clinical evaluation were provided as needed.
[c]*T*-test with equal variance.
[d]Chi-square test.

completed a similar screener [44]. In addition, participants in our sample reported symptoms of depression and anxiety at a level commensurate with their peers in a national standardization sample [37].

To our knowledge, there are only two reports examining similar milestones in longitudinal studies of YAPHIV and YAPHEU. In the Bellevue pediatric cohort study (birth years 1977–1978) conducted in New York City, 57% of YAPHIV, age 19 and older, had graduated high school or earned a GED [45]; YAPHEU were not included, thus limiting comparisons with the present study. Investigators with the Child and Adolescent Self-Awareness and Health Study (CASAH; enrolment in 2003–2008) [46] reported on the attainment of young adult milestones among YAPHIV and YAPHEU, age

Table 6. Risk index: frequency of participant and parent/caregiver risks by perinatal HIV status

	Perinatal HIV status		
	YAPHIV (*n* = 228)	YAPHEU (*n* = 87)	
	Risk present (*n*, %)		
Participant risks			
Performance discrepant from age expectations[a] on measures of:			
Executive functioning (BRIEF)[b]			
Participant or parent/caregiver report, BRI ≥ 65	45 (20%)	19 (22%)	
Participant or parent/caregiver report, MCI ≥ 65	60 (26%)	20 (22%)	
Cognitive efficiency (Wechsler)			
WMI < 85	100 (44%)	30 (34%)	
PSI < 85	71 (31%)	19 (22%)	
Behavioral/social-emotional functioning (BASC-2)			
Participant self-report, Internalizing Problems > 60	29 (13%)	10 (11%)	
Participant self-report, Emotional Symptoms > 60	26 (11%)	11 (13%)	
Participant self-report, Personal Adjustment < 40	29 (13%)	12 (14%)	
Parent/caregiver report, Externalizing Problems > 60	26 (11%)	18 (21%)	
Parent/caregiver report, Behavioral Symptoms Index > 60	34 (15%)	20 (23%)	
Parent/caregiver report, Adaptive Skills Index < 40	69 (30%)	24 (28%)	
Number of participant-reported life events > 3, averaged over all life event interviews completed in AMP	110 (48%)	47 (54%)	
Parent/caregiver risks			
Number of parent/caregiver mental health, substance use and physical health problems > 1[c]	38 (17%)	27 (31%)	
Number of parent/caregiver-reported life events > 3 in 12 months prior to interview	24 (11%)	12 (14%)	
Mean Index Score[d]	3.1 (2.6)	3.2 (2.9)	$p = 0.81$[d]

Abbreviations: AMP, Adolescent Master Protocol of the Pediatric HIV/AIDS Cohort Study (PHACS); BASC-2, Behavior Assessment System for Children, Second Ed. [37]; BRIEF, Behavior Rating Inventory of Executive Function [36]; BRI, Behavioral Regulation Index; MCI, Metacognition Index; PSI, Processing Speed Index; Wechsler, Wechsler Intelligence Scale for Children, Fourth Ed. [34] (ages 6–16) or Wechsler Adult Intelligence Scale, Fourth Ed. [35] (ages 17 and older); WMI, Working Memory Index; YAPHEU, young adults with perinatal HIV exposure, uninfected; YAPHIV, young adults with perinatally acquired HIV.
[a]Defined as T-scores or standard scores greater than 1.0 standard deviation from the population mean.
[b]For the BRIEF, when the participant self-report and parent/caregiver report were both available (*n* = 225), the report with the higher score (indicating greater difficulty) was used in the analysis.
[c]Only parents/caregivers with available data for all three measures were included in the calculation.
[d]Each variable was assigned a score of 0 or 1 depending on the absence (0) or presence (1) of the variable. The total score for each participant ranged from 0 to 13; higher scores indicated greater total adversity.

18–28 years, living in New York City: 67% graduated high school or earned a GED, 19% were in college, 42% were employed; 38% were neither in school nor working. Milestone attainment was higher in AMP Up than in CASAH, but both studies found no differences in attainment between YAPHIV and YAPHEU. Important differences between the study samples might have contributed to discrepancies in results. CASAH was recruited from four sites in New York City versus 14 sites across the United States, and participants in CASAH were older than those in AMP Up at the time milestone attainment was assessed.

Attainment of academic and employment milestones is not the only way to define resilience; however, these milestones are important in United States society and predictive of success in adulthood [3]. Understanding of HIV disease and appropriate treatment has improved substantially since the early days of the epidemic, resulting in reduced morbidity and mortality. Because of these advances, our participants were likely better able to participate in social and educational activities available to their peers, possibly contributing to the attainment of young adult milestones. It is important to note that data included in this analysis were obtained prior to the COVID-19 pandemic. Results of future studies may differ for youth who missed social, educational and psychotherapeutic opportunities or access to comprehensive medical care due to pandemic-related restrictions in 2020–2022.

This study has several strengths, including a large number of participants, longitudinal follow-up through childhood and into young adulthood, and the use of standardized, well-researched measures of functioning. Some limitations were noted. The sample might not be representative of the general population of YAPHIV or YAPHEU since all participants

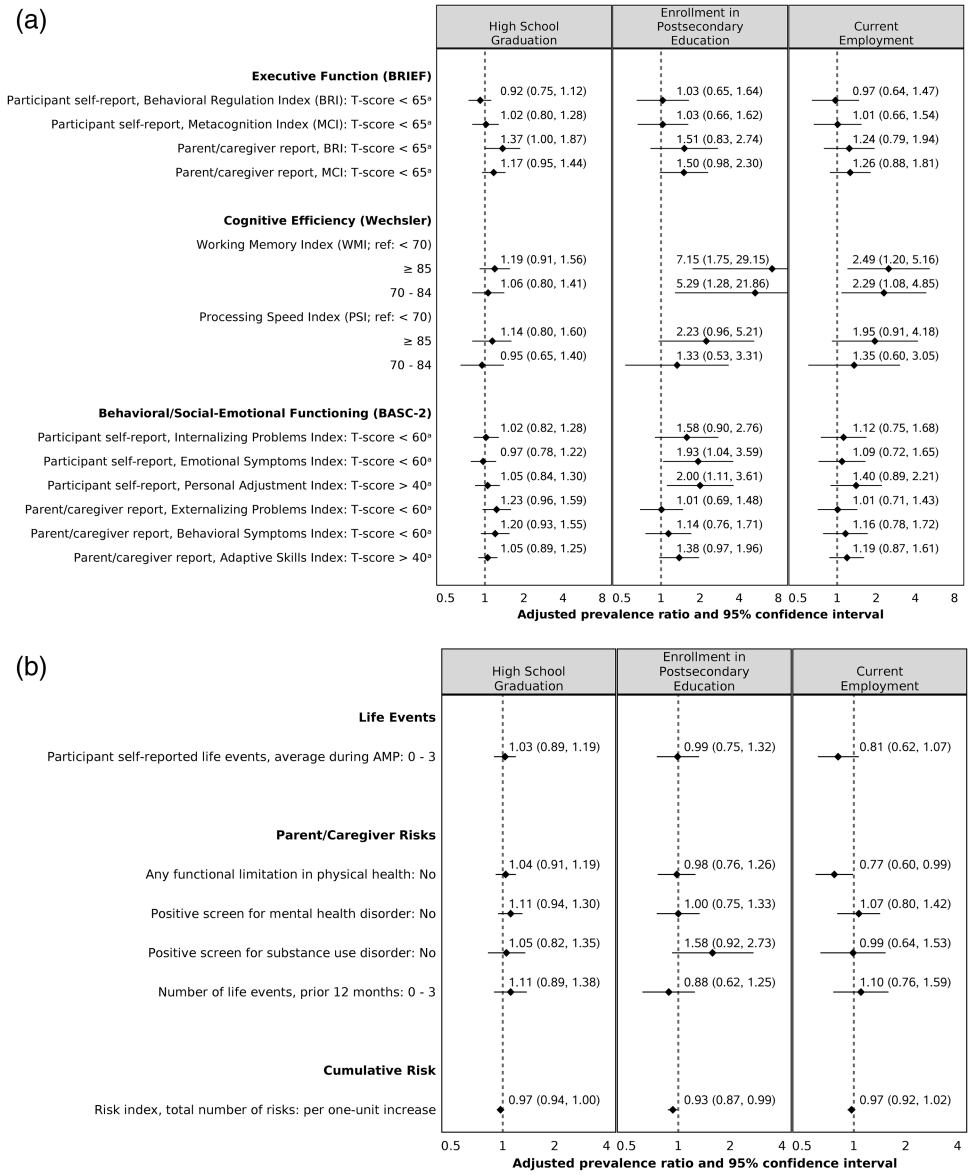

Figure 2. (a) Adjusted associations between predictors and attainment of young adult milestones. The association between each predictor and outcome is presented as follows: the solid diamond represents the prevalence ratio, and the horizontal line represents the 95% confidence interval. In addition, the dotted vertical line represents the null value (prevalence ratio = 1.0). The adjusted prevalence ratio for the attainment of a specific milestone compared participants with a specific predictor versus a reference group. Each model adjusted for sex, race/ethnicity, Wechsler FSIQ (except the model for cognitive efficiency due to potential overcorrection), family socio-economic status (an index including annual income and household density) and age at the time of measurement of each predictor. [a]Indicates lower frequency or intensity of problems. (b) Adjusted associations between predictors and attainment of young adult milestones. The association between each predictor and outcome is presented as follows: the solid diamond represents the prevalence ratio, and the horizontal line represents the 95% confidence interval. In addition, the dotted vertical line represents the null value (prevalence ratio = 1.0). The adjusted prevalence ratio for the attainment of a specific milestone compared participants with a specific predictor versus a reference group. Each model adjusted for sex, race/ethnicity, Wechsler FSIQ, family socio-economic status (an index including annual income and household density), and age at the time of measurement of each predictor. BASC-2, Behavior Assessment System for Children, Second Ed. [37]; BRIEF, Behavior Rating Inventory of Executive Function [36]; Risk index, a study-specific summary of risks; Wechsler FSIQ, Wechsler Intelligence Scale for Children, Fourth Ed. [34] or Wechsler Adult Intelligence Scale, Fourth Ed. [35] Full-Scale Intelligence Quotient.

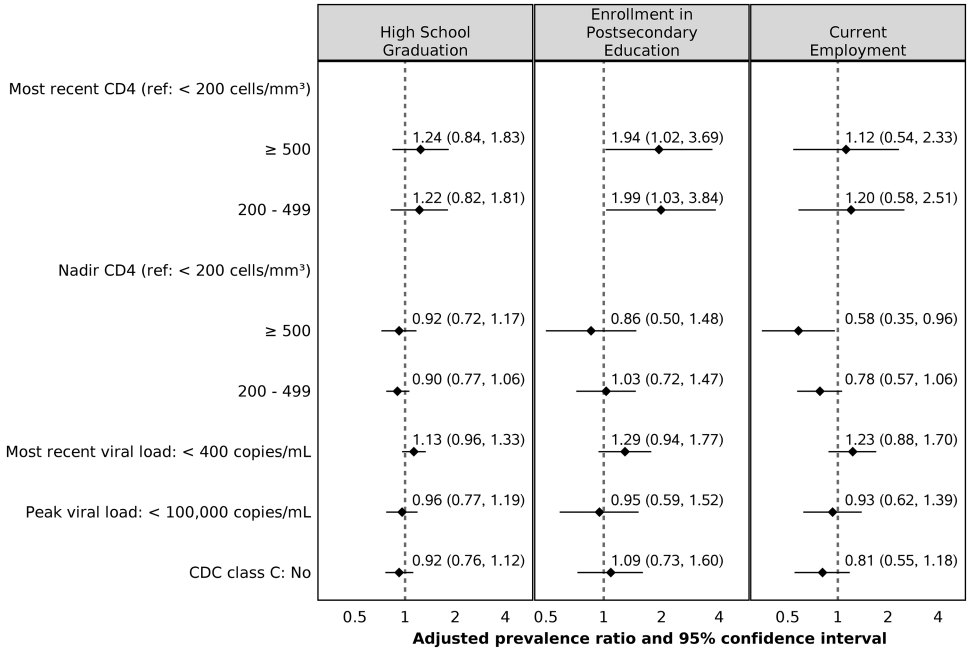

Figure 3. Adjusted associations between measures of HIV disease severity and attainment of young adult milestones in YAPHIV. The association between each predictor and outcome is presented as follows: the solid diamond represents the prevalence ratio, and the horizontal line represents the 95% confidence interval. In addition, the dotted vertical line represents the null value (prevalence ratio = 1.0). The adjusted prevalence ratio for the attainment of a specific milestone compared YAPHIV participants with a specific measure of HIV disease severity (predictor) versus a reference group. Each model adjusted for sex, race/ethnicity, Wechsler FSIQ (except the models for nadir CD4 and peak viral load), family socio-economic status (an index including annual income and household density) and age at the time of measurement of each predictor. Wechsler FSIQ, Wechsler Intelligence Scale for Children, Fourth Ed. [34] or Wechsler Adult Intelligence Scale, Fourth Ed. [35] Full-Scale Intelligence Quotient; YAPHIV, young adults with perinatally acquired HIV.

were involved in medical follow-up and chose to stay engaged in longitudinal research conducted at selected sites in the United States. We cannot say how youth who remained on study differed in the attainment of young adult milestones from those who opted to discontinue participation. However, results from unweighted models were largely consistent with those from models weighted to reduce selection bias, suggesting minimal bias in the association of predictors with the milestones. A comparison group of non-HIV-affected children was not included. In longitudinal paediatric research, several challenges make the inclusion of an appropriate comparison group particularly difficult: (1) enrolling a sufficiently large, representative sample who do not experience the medical condition(s) under study and who may not receive potential study-related benefits and (2) minimizing attrition among participants who are in generally good health. Our cohort is a unique one, and it was important to compare the participants' performance to that of their age-mates in the United States general population. The standardization samples from each instrument included in the analyses are representative of United States children and youth at various ages, providing appropriate comparison groups and allowing us to determine how well our cohort of young adults was achieving the goals expected of them in United States society. Although self-report measures can be perceived as potentially biased, the measures included in this study were psychometrically sound and contained internal validity indices to account for response patterns. The study did not include measures of social determinants of health, structural racism or various forms of discrimination; findings from such measures could further our understanding of factors influencing the attainment of young adult milestones by YAPHIV and YAPHEU in the United States.

Due to advances in HIV medicine, the current generation of young adults with PHIV is living in comparatively good health. However, the older generation of adults over 50 living with HIV are experiencing high rates of age-related comorbidities, including heart disease, hypertension, liver and bone disease, and neurocognitive impairment; these difficulties are occurring approximately 16 years earlier than in adults without HIV [47]. As the younger generation ages, they may become increasingly vulnerable to the medical comorbidities that the older generation is experiencing; there is already evidence of a higher risk for cardiovascular disease in youth with PHIV [48]. In our study, early difficulties did not define the participants' ultimate ability to demonstrate resilience by achieving societal expectations, and these achievements may offer personal and societal benefits that buffer young adults from the effects of future complications. These findings highlight the need for early identification of emerging difficulties and provision of ongoing culturally relevant, community-oriented services throughout the lifespan to support further education, sustained employment, social-emotional wellbeing and retention in medical care for younger and older adults living with HIV.

5 | CONCLUSIONS

Future studies of resilience in youth with PHIV and PHEU should examine additional milestones typically involved in the transition to adulthood, such as sustained employment, financial independence, romantic and committed partner/marital relationships and parenthood. Our findings suggest it is important to maintain developmental surveillance and interventions, including access to medical care and age-appropriate multidisciplinary supports, throughout the lifespan. With targeted and timely support, we can strengthen cognitive and behavioural/social-emotional functioning to promote resilience and thereby increase rates of education, employment and medical wellbeing among YAPHIV and YAPHEU.

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COMPETING INTERESTS

The authors have no competing interests to disclose.

AUTHORS' CONTRIBUTIONS

PAS and MLN conceived the idea for the study and wrote the first draft of the manuscript. YH and KT designed the statistical method and analysed the data. PAS, YH, MLN, PAG, LLH, KM, RMcE, CAM, SLN, RS and KT contributed to the study design, provided critical reviews and edited the manuscript for content. All authors read and approved the final manuscript.

ACKNOWLEDGEMENTS

We thank the participants, caregivers and families for their participation in the Pediatric HIV/AIDS Cohort Study (PHACS) and the individuals and institutions involved in the conduct of PHACS. We also thank Latricia Conley and Brandon Montanez, members of the PHACS Peers United Group, for their contributions to this project. This research was presented as a Science Spotlight presentation at the *virtual* Conference on Retroviruses and Opportunistic Infections (*v*CROI), March 6–10, 2021.

The following institutions, clinical site investigators and staff participated in conducting PHACS AMP and AMP Up in 2019, in alphabetical order: Ann & Robert H. Lurie Children's Hospital of Chicago: Ellen Chadwick, Margaret Ann Sanders, Kathleen Malee, Yoonsun Pyun; Baylor College of Medicine: Mary Paul, Shelley Buschur, Chivon McMullen-Jackson, Lynnette Harris; Bronx Lebanon Hospital Center: Murli Purswani, Mahboobullah Mirza Baig, Alma Villegas; Children's Diagnostic & Treatment Center: Lisa- Gaye Robinson, Sandra Navarro, Patricia A. Garvie; Boston Children's Hospital: Sandra K. Burchett, Rebecca Pinsky, Adam R. Cassidy; Jacobi Medical Center: Andrew Wiznia, Marlene Burey, Ray Shaw, Molly L. Nozyce; Rutgers–New Jersey Medical School: Arry Dieudonne, Linda Bettica, Juliette Johnson, Karen Surowiec; St. Christopher's Hospital for Children: Janet S. Chen, Taesha White, Mitzie Grant; St. Jude Children's Research Hospital: Katherine Knapp, Jamie Russell-Bell, Megan Wilkins, Erick Odero; San Juan Hospital Research Unit/Department of Pediatrics, San Juan, Puerto Rico: Midnela Acevedo-Flores, Heida Rios, Vivian Olivera; Tulane University School of Medicine: Margarita Silio, Medea Gabriel, Patricia Sirois; University of California, San Diego: Stephen A. Spector, Megan Loughran, Veronica Figueroa, Sharon Nichols; University of Colorado Denver Health Sciences Center: Elizabeth McFarland, Carrie Chambers, Emily Barr, Mary Glidden; University of Miami: Gwendolyn Scott, Grace Alvarez, Juan Caffroni, Anai Cuadra.

FUNDING

The study was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development with co-funding from the National Institute on Drug Abuse, the National Institute of Allergy and Infectious Diseases, the National Institute of Mental Health, the National Institute of Neurological Disorders and Stroke, the National Institute on Deafness and Other Communication Disorders, the National Institute of Dental and Craniofacial Research, the National Cancer Institute, the National Institute on Alcohol Abuse and Alcoholism, the Office of AIDS Research and the National Heart, Lung, and Blood Institute through cooperative agreements with the Harvard T.H. Chan School of Public Health (HD052102) (Principal Investigator: George R. Seage III; Programme Director: Liz Salomon) and the Tulane University School of Medicine (HD052104) (Principal Investigator: Russell Van Dyke; Co-Principal Investigator: Ellen Chadwick; Project Director: Patrick Davis). Data management services were provided by Frontier Science and Technology Research Foundation (PI: Suzanne Siminski), and regulatory services and logistical support were provided by Westat, Inc (PI: Julie Davidson).

DISCLAIMER

The conclusions and opinions expressed in this article are those of the authors and do not necessarily reflect those of the National Institutes of Health or the U.S. Department of Health and Human Services.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

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JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

SHORT REPORT

Non-communicable diseases by age strata in people living with and without HIV in four African countries

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Abstract

Introduction: Non-communicable diseases (NCDs) are an important driver of morbidity among ageing people living with HIV (PLWH). We examined the composite role of age and HIV status on NCDs in people living with and without HIV.

Methods: The African Cohort Study (AFRICOS) prospectively enrols participants aged ≥15 years with and without HIV at 12 sites in Kenya, Tanzania, Uganda and Nigeria. From 21 January 2013 to 1 September 2021, we assessed participants for renal insufficiency (estimated glomerular filtration rate <60 ml/minute/1.73 m^2), elevated blood pressure (BP) (any systolic BP >139 mmHg or diastolic BP >89 mmHg), obesity (body mass index >30 kg/m^2), diabetes mellitus (DM) (fasting glucose ≥126 mg/dl or antidiabetic medication) and dysglycemia (fasting glucose ≥99 mg/dl or non-fasting ≥199 mg/dl). Multivariable logistic regression with generalized estimating equations was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for factors associated with each NCD. The main exposure of interest was a composite of HIV status and age dichotomized around 50 years. All models were adjusted for study site and sex. The renal insufficiency model was additionally adjusted for elevated BP and dysglycemia.

Results and discussion: Of 3761 participants with age data, 557 (14.8%) were age ≥50, 2188 (58.2%) were females and 3099 (82.4%) were PLWH. At enrolment, the prevalence of elevated BP, dysglycemia, renal insufficiency and obesity were n = 128 (26.9%), n = 75 (15.8%), n = 8 (1.7%) and n = 40 (8.4%), respectively, for PLWH ≥50. Compared to people without HIV age <50, PLWH age ≥50 had increased adjusted odds of having DM (OR: 2.78, 95% CI: 1.49–5.16), dysglycemia (OR: 1.98, 95% CI: 1.51–2.61) and renal insufficiency (OR: 6.20, 95% CI: 2.31–16.66). There were significant differences by study site, specifically, participants from Nigeria had the highest odds of elevated BP, dysglycemia and renal insufficiency as compared to Uganda.

Conclusions: There was a high burden of NCDs in this African cohort with differences by geographic region. In order to promote healthy ageing with HIV, screening and treatment for common NCDs should be incorporated into routine HIV care with attention paid to geographic heterogeneity to better allocate resources.

Keywords: Africa; LMIC; HIV epidemiology; quality of life; cohort studies; HIV care continuum

Received 26 January 2022; **Accepted** 1 August 2022

1 | INTRODUCTION

People living with HIV (PLWH) are experiencing increased life expectancy in both high- and low-income countries with some life expectancy nearing that of people living without HIV (PLWoH) [1–5]. As the access to antiretroviral therapy (ART) is scaled up and progress is made in reaching UNAIDS 95-95-95 targets, the median age of PLWH is expected to increase. Recent data demonstrate that one-third of PLWH in the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) programmes are age >50 [6]. As the PLWH population ages, it is important to understand the effect of HIV and age to promote healthy ageing.

Non-communicable diseases (NCDs), such as diabetes and cardiovascular disease, have been associated with HIV and are important drivers of morbidity and mortality [7–9]. Studies show that PLWH in sub-Saharan Africa have a high prevalence of NCDs, such as hypertension [10]. PLWH appear to have a higher prevalence of NCDs, such as hyperglycaemia and diabetes, as compared to PLWoH [11, 12]. Previous work from the African Cohort Study (AFRICOS) showed that PLWH on ART have an increased risk of NCDs compared to PLWH not

on ART [13]. We investigated the prevalence and factors associated with NCDs in AFRICOS, focusing on age and HIV status.

2 | METHODS

2.1 | Study setting and population

AFRICOS is an ongoing prospective cohort enrolling at 12 clinics across five programmes supported by PEPFAR: Kayunga, Uganda; South Rift Valley, Kenya; Kisumu West, Kenya; Mbeya, Tanzania; and Lagos and Abuja, Nigeria [13]. PLWH were recruited from randomized lists of current PEPFAR clinic patients and those with new HIV diagnoses. Enrolees were encouraged to bring partners in for testing and recruitment. PLWoH were also recruited from community members accessing HIV testing, a small subset of participants was recruited from prior research studies. Participants were included if they were age ≥15 years, intended to be a long-term area resident, willing to provide contact information, consented to data/specimen collection and storage for future use, and understood English or the local language. Individuals were excluded if they were pregnant at enrolment.

The study was approved by institutional review boards of the Walter Reed Army Institute of Research and all collaborating institutions. All participants provided written informed consent.

2.2 | Procedures

At enrollment, all participants were administered a medical history, physical exam, demographic questionnaire and underwent phlebotomy. PLWH underwent confirmatory HIV rapid diagnostic testing, CD4 T-lymphocyte count and HIV Viral Load (VL) [14]. Study visits occurred every 6 months and participants provided medical history, completed a physical examination and underwent laboratory assessments. Study clinicians performed medical record reviews and extracted ART start date and regimen at every visit. HIV rapid tests were performed at each visit for PLWoH and CD4 counts and VL were performed at every visit for PLWH. All participants had an assessment of serum creatinine and blood glucose performed annually. Study-specific laboratory assessments included tests that were not part of routine care at study sites; test results were shared with care providers. All assessments were performed in laboratories that were accredited by the College of American Pathologists or had successfully completed external quality assurance.

2.3 | Data collection and definitions

Demographic variables, including sex, age, education level, HIV status and clinical care site, are reported for the enrolment visit. For PLWH, ART use and VL stratum were combined into the following categories: not on ART, on ART and VL <1000 copies/ml, and on ART and VL ≥1000 copies/ml. CD4 nadir was categorized as <200, 200–349, 350–499 and ≥500 cells/mm^3. All data were recorded on paper case report forms and double entered into the ClinPlus platform (DZS Software Solutions, Bound Brock, NJ).

Elevated blood pressure (BP) was defined as systolic blood pressure of >139 mmHg, diastolic blood pressure >89 mmHg or receipt of antihypertensive medications. Abnormal BPs were repeated for confirmation. Dysglycemia was defined as fasting glucose ≥99 mg/dl, non-fasting glucose ≥199 mg/dl or receipt of hypoglycaemic medications. Diabetes mellitus (DM) was defined as fasting glucose ≥126 mg/dl or receipt of hypoglycaemic medications. Renal insufficiency was defined as the estimated glomerular filtration rate <60 ml/minute/1.73 m^2 calculated using the Modification of Diet in Renal Disease equation [15]. Obesity was defined as a body mass index (BMI) of >30 kg/m^2.

2.4 | Statistical analyses

The main exposure of interest was a composite of HIV status and age dichotomized around 50 years. Comparisons of demographic characteristics and other parameters across groups of interest were made using Pearson chi-squared test for categorical variables and the Kruskal–Wallis test for continuous variables. Longitudinal analyses involved multivariable logistic regression with generalized estimating equations, clustered by a participant to account for repeated measures, to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for factors associated with each NCD. NCDs were assessed at every follow-up visit and the model was time updated. Once diagnosed with an NCD, a participant would not have additional events of that disease. DM and dysglycemia models were adjusted for potential confounders, including study site and sex. Renal insufficiency models were adjusted for elevated BP and dysglycemia given the known risk factors for disease [16, 17]. Analyses were performed in SAS 9.3 (SAS, Cary, NC) and Stata 16.0 (StataCorp, College Station, TX).

3 | RESULTS AND DISCUSSION

3.1 | Demographics and clinical characteristics

Between 21 January 2013 and 1 September 2021, 3762 participants were enrolled in AFRICOS and 3761 with age data were included in these analyses (Table 1). Data from the enrolment visit are presented in Table 1. Most of the cohort were PLWH, 3099 (82.4%). There were fewer participants aged ≥50, with the least comprised of PLWoH age ≥50 (n = 80, 2.1%). Among PLWH age <50, 1572 (60.0%) had virologic suppression less than 1000 copies/ml. In comparison, a greater proportion of PLWH age ≥50 had virologic suppression less than 1000 copies/ml (n = 351, 73.6%). Thirty-six percent (n = 1135) of participants had a CD4 nadir below 200 cells/mm^3. Thirty-five percent (n = 1099) had an enrolment CD4 above 500 cells/mm^3. Most PLWH were on a non-nucleoside reverse transcriptase inhibitor or an integrase strand transfer inhibitor (INSTI); only 5.5% were on a protease inhibitor based regimen.

3.2 | Prevalence of NCDs

There was a higher prevalence of NCDs in the ≥50 age group for both PLWH and PLWoH at enrolment (Figure 1). In PLWH age ≥50, the most common NCD was elevated BP

Table 1. Demographic and clinical characteristics of study participants stratified by age and HIV status at enrolment

	<50, PLWoH *n* = 582	<50, PLWH *n* = 2622	≥50, PLWoH *n* = 80	≥50, PLWH *n* = 477	Total *N* = 3761	*p*-value
Study site						<0.001
Kayunga, Uganda	95 (16.3%)	478 (18.2%)	18 (22.5%)	72 (15.1%)	663 (17.6%)	
South Rift Valley, Kenya	176 (30.2%)	881 (33.6%)	32 (40.0%)	168 (35.2%)	1257 (33.4%)	
Kisumu West, Kenya	123 (21.1%)	448 (17.1%)	17 (21.3%)	103 (21.6%)	691 (18.4%)	
Mbeya, Tanzania	91 (15.6%)	488 (18.6%)	6 (7.5%)	109 (22.9%)	694 (18.5%)	
Abuja and Lagos Nigeria	97 (16.7%)	327 (12.5%)	7 (8.8%)	25 (5.2%)	456 (12.1%)	
Sex						<0.001
Male	249 (42.8%)	1007 (38.4%)	41 (51.2%)	276 (57.9%)	1573 (41.8%)	
Female	333 (57.2%)	1615 (61.6%)	39 (48.8%)	201 (42.1%)	2188 (58.2%)	
Age (years), median (IQR)	32 (25.3–39)	35.4 (28.4–41.5)	54.8 (52.45–58.75)	54.8 (52.2–58.7)	37 (29.2–45.1)	<0.001
Education						<0.001
Primary or less	266 (45.7%)	1451 (55.3%)	47 (58.8%)	306 (64.2%)	2070 (55.0%)	
Secondary or above	315 (54.1%)	1168 (44.5%)	33 (41.3%)	171 (35.8%)	1687 (44.9%)	
Missing	1 (0.2%)	3 (0.1%)	0 (0.0%)	0 (0.0%)	4 (0.1%)	
BMI 30+						<0.001
No	500 (85.9%)	2456 (93.7%)	66 (82.5%)	436 (91.4%)	3458 (91.9%)	
Yes	81 (13.9%)	161 (6.1%)	14 (17.5%)	40 (8.4%)	296 (7.9%)	
Missing	1 (0.2%)	5 (0.2%)	0 (0.0%)	1 (0.2%)	7 (0.2%)	
Diabetes						<0.001
No	293 (50.3%)	2546 (97.1%)	38 (47.5%)	457 (95.8%)	3334 (88.6%)	
Yes	8 (1.4%)	31 (1.2%)	2 (2.5%)	18 (3.8%)	59 (1.6%)	
Missing	281 (48.3%)	45 (1.7%)	40 (50.0%)	2 (0.4%)	368 (9.8%)	
Dysglycemia						<0.001
No	275 (47.3%)	2360 (90.0%)	33 (41.3%)	400 (83.9%)	3068 (81.6%)	
Yes	26 (4.5%)	217 (8.3%)	7 (8.8%)	75 (15.7%)	325 (8.6%)	
Missing	281 (48.3%)	45 (1.7%)	40 (50.0%)	2 (0.4%)	368 (9.8%)	
Renal insufficiency						0.35
No	296 (50.9%)	2562 (97.7%)	39 (48.8%)	469 (98.3%)	3366 (89.5%)	
Yes	1 (0.2%)	31 (1.2%)	0 (0.0%)	8 (1.7%)	40 (1.1%)	
Missing	285 (49.0%)	29 (1.1%)	41 (51.2%)	0 (0.0%)	355 (9.4%)	
Elevated BP						<0.001
No	503 (86.4%)	2371 (90.4%)	49 (61.3%)	348 (73.0%)	3271 (87.0%)	
Yes	79 (13.6%)	247 (9.4%)	31 (38.8%)	128 (26.8%)	485 (12.9%)	
Missing	0 (0.0%)	4 (0.2%)	0 (0.0%)	1 (0.2%)	5 (0.1%)	
ART type						<0.001
EFV		959 (36.6%)		201 (42.1%)	1160 (37.4%)	
NVP		521 (19.9%)		169 (35.4%)	690 (22.3%)	
DTG		159 (6.1%)		0 (0.0%)	159 (5.1%)	
PI		148 (5.6%)		22 (4.6%)	170 (5.5%)	
ART naïve		827 (31.5%)		82 (17.2%)	909 (29.3%)	
Other		8 (0.3%)		3 (0.6%)	11 (0.4%)	
CD4 count nadir (cells/mm^3)						<0.001
<200		906 (34.6%)		229 (48.0%)	1135 (36.6%)	
200–349		538 (20.5%)		111 (23.3%)	649 (20.9%)	
350–499		259 (9.9%)		37 (7.8%)	296 (9.6%)	
500+		268 (10.2%)		28 (5.9%)	296 (9.6%)	
Missing		651 (24.8%)		72 (15.1%)	723 (23.3%)	

(*Continued*)

Table 1. Continued

	<50, PLWoH *n* = 582	<50, PLWH *n* = 2622	≥50, PLWoH *n* = 80	≥50, PLWH *n* = 477	Total *N* = 3761	*p*-value
CD4 count (cells/mm^3)						0.23
<200		479 (18.3%)		96 (20.1%)	575 (18.6%)	
200–349		600 (22.9%)		123 (25.8%)	723 (23.3%)	
350–499		563 (21.5%)		101 (21.2%)	664 (21.4%)	
500+		947 (36.1%)		152 (31.9%)	1099 (35.5%)	
Missing		33 (1.3%)		5 (1.0%)	38 (1.2%)	
Duration on ART						<0.001
<6 months		379 (14.5%)		52 (10.9%)	431 (13.9%)	
6 months–5 years		797 (30.4%)		166 (34.8%)	963 (31.1%)	
5+ years		602 (23.0%)		173 (36.3%)	775 (25.0%)	
ART naïve		827 (31.5%)		82 (17.2%)	909 (29.3%)	
Missing		17 (0.6%)		4 (0.8%)	21 (0.7%)	
Viral suppression <1000 copies/ml						<0.001
Not suppressed		995 (37.9%)		122 (25.6%)	1117 (36.0%)	
Suppressed		1572 (60.0%)		351 (73.6%)	1923 (62.1%)	
Missing		55 (2.1%)		4 (0.8%)	59 (1.9%)	

Note: Participant characteristics at enrolment, by age and HIV status. Significant differences between the four age/HIV status groups were assessed using Pearson chi-squared tests for categorical variables and Kruskal–Wallis for continuous variables to identify whether the proportion with a particular characteristic is different in one or more groups as compared to the others.
Abbreviations: ART, antiretroviral therapy; DTG, dolutegravir; EFV, efavirenz; NVP, nevirapine; PI, protease inhibitor; PLWH, people living with HIV; PLWoH, people living without HIV.

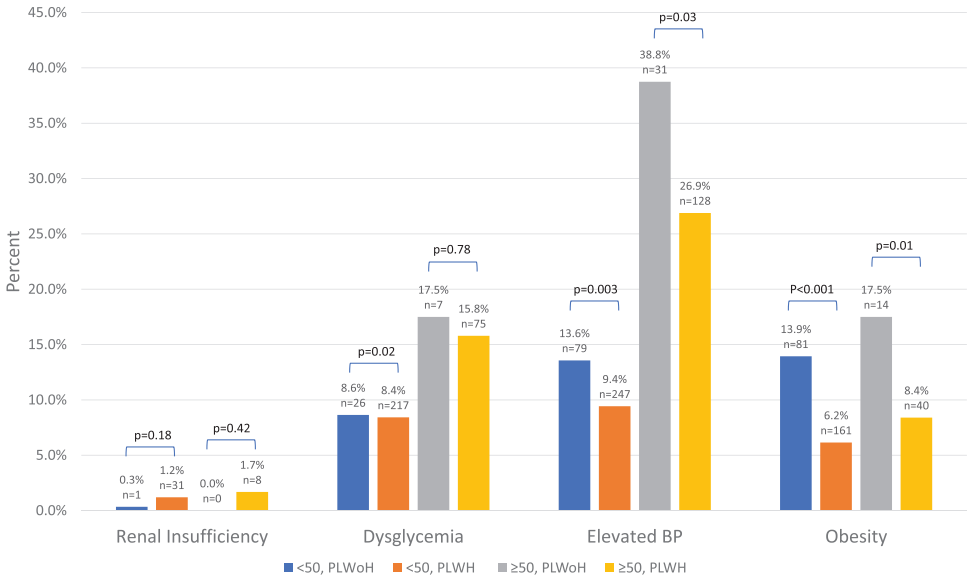

Figure 1. Prevalence of non-communicable diseases at enrolment. The prevalence of NCDs by age and HIV status at enrolment visit. Abbreviations: PLWH, people living with HIV; PLWoH, people living without HIV; BP, blood pressure.

(26.9%), followed by dysglycemia (15.8%), obesity (8.4%) and renal insufficiency (1.7%). PLWoH had a statistically significant increased prevalence of elevated BP and obesity when compared to PLWH in the same age group. There were no significant differences seen between PLWoH and PLWH age ≥50 for renal insufficiency and dysglycemia.

3.3 | Factors associated with NCDs

Participants were followed for a median (IQR) of 4.66 (1.74–6.08) years to evaluate factors associated with NCDs. In the multivariable analysis for factors associated with dysglycemia and diabetes (Table 2), there were significant increases in

Table 2. Adjusted odds of non-communicable diseases

	Dysglycemia				Diabetes				Renal insufficiency			
	no. ppts (n = 3623)	no. obs (n = 15,433)	aOR	95% CI	no. ppts (n = 3623)	no. obs (n = 15,430)	aOR	95% CI	no. ppts (n = 3620)	no. obs (n = 15,406)	aOR	95% CI
Age, HIV status												
<50, PLWoH	66/470	83/1050	–		17/470	20/1049	–		7/469	4/1044	–	
<50, PLWH	640/2607	988/10,878	1.19	0.93–1.54	124/2607	176/10,876	0.88	0.48–1.60	169/2606	154/10,870	3.56	1.35–9.40
≥50, PLWoH	18/70	49/255	2.61	1.70–4.02	9/70	33/255	6.75	3.47–13.14	7/69	7/243	7.64	2.36–24.67
≥50, PLWH	177/476	467/3250	1.98	1.51–2.61	60/476	167/3250	2.78	1.49–5.16	64/476	76/3249	6.20	2.31–16.66
Study site												
Uganda	92/641	150/3052	–		24/641	54/3052	–		25/640	27/3043	–	
SRV, Kenya	369/1210	648/5162	2.40	1.81–3.17	78/1210	171/5161	1.69	0.92–3.12	87/1209	66/5146	1.25	0.66–2.36
Kisumu, Kenya	96/673	117/2869	0.81	0.58–1.13	26/673	29/2869	0.56	0.29–1.09	29/673	32/2870	1.20	0.57–2.54
Tanzania	125/657	215/2382	1.70	1.23–2.35	37/657	74/2381	1.55	0.79–3.00	31/658	36/2383	1.42	0.69–2.89
Nigeria	219/442	457/1968	4.66	3.52–6.17	45/442	68/1967	2.12	1.13–3.99	75/440	80/1964	4.00	2.12–7.53
Sex												
Male	423/1510	776/6389	–		103/1510	192/6389	–		81/1509	87/6378	–	
Female	478/2113	811/9044	0.71	0.62–0.82	107/2113	204/9041	0.75	0.51–1.11	166/2111	154/9028	1.42	0.99–2.04
BMI												
BMI <30	809/3346	1297/13,845	–		174/3346	302/13,843	–					
BMI >30	92/277	290/1588	1.74	1.47–2.06	36/277	94/1587	2.40	1.56–3.68				
Elevated BP												
No									180/3161	167/13,192	–	
Yes									67/459	74/2214	1.91	1.32–2.76
Dysglycemia												
No									209/3275	192/13,838	–	
Yes									38/345	49/1568	1.48	1.00–2.19

Note: Dysglycemia and DM models were adjusted for age/HIV status, study site, sex and BMI. The renal insufficiency model was adjusted for age/HIV status, study site, sex, dysglycemia and elevated BP.

Abbreviations: BMI, body mass index; PLWH, people living with HIV; PLWoH, people living without HIV; no. ppt, number of participants; no obs, number of observations during follow up; SRV, South Rift Valley.

Chang D et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25985
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25985/full | https://doi.org/10.1002/jia2.25985

odds of having both diseases in PLWH and PLWoH age ≥50 when compared to PLWoH age <50. There were no significant differences when comparing PLWH age <50 to PLWoH age <50. Study site differences were seen for dysglycemia and diabetes. Participants in Nigeria had 4.66 (95% CI: 3.52–6.17) and 2.12 (95% CI: 1.13–3.99) odds of having dysglycemia and diabetes, respectively, compared to participants in Uganda. Participants in Kenya and Tanzania also had significantly higher odds of having dysglycemia as compared to participants in Uganda. BMI >30 was significantly associated with dysglycemia and diabetes.

The multivariable analysis for renal insufficiency (Table 2) demonstrated increased odds for PLWH age <50, PLWoH and PLWH age ≥50 of having renal insufficiency when compared to PLWoH age <50. The greatest odds of disease were seen in PLWoH age ≥50 with wide CIs overlapping with the PLWH age ≥50 CI's. Study site differences were again seen with participants in Nigeria having 4.0 (95% CI: 2.12–7.53) odds of having renal insufficiency compared to participants in Uganda. Participants with elevated BP and dysglycemia had increased odds of having renal insufficiency, 1.91 (95% CI: 1.32–2.76) and 1.48 (95% CI: 1.00–2.19), respectively.

4 | DISCUSSION

NCDs are a leading cause of morbidity and mortality in low- and middle-income countries [7, 18]. In this observational cohort in four sub-Saharan African countries, there was a high burden of NCDs. Over a quarter of PLWH age ≥50 had elevated BP and over 15% had dysglycemia. Factors associated with NCDs were consistent with those known to be a risk factor for NCDs, such as obesity increasing the risk for diabetes or diabetes increasing the risk for renal insufficiency [16, 17].

Geographic heterogeneity was seen with NCDs in AFRICOS. Cohort participants in Nigeria had the highest odds of having dysglycemia and renal insufficiency. NCDs account for up to 29% of all deaths in Nigeria [19]. Dietary differences could account for the differences seen in renal insufficiency as Nigerians appear to have higher salt intake than recommended [20]. The study sites in Nigeria were only in urban centres, which may explain dietary and physical activity differences potentially accounting for differences seen in NCDs [21]. Further analyses will be needed to understand the aetiology for the geographic heterogeneity seen and to better guide interventions.

Treatment of HIV with ART has been implicated in the development of certain NCDs by side effects or toxicity. Long-term use of tenofovir disoproxil fumarate (TDF) can result in nephrotoxicity. Dolutegravir raises serum creatinine without changing renal function because it inhibits proximal renal tubular secretion of creatinine by organic cation transporters [22]. In addition, the increased odds of renal insufficiency at a younger age in PLWH may be due to "accelerated ageing" where conditions seen in older persons appear in PLWH at a younger age [8, 23]. In this cohort, there was an association seen with renal insufficiency in the age <50 group with PLWH having increased odds of having disease compared to PLWoH. While this analysis did not focus on aetiology, the risk of renal disease in PLWH can be modified by changing ART regimens. Most participants in this cohort are on TDF and considerations can be made to switch to newer, less nephrotoxic, tenofovir formulations in areas of high renal insufficiency prevalence.

INSTIs, particularly second-generation INSTIs, have been implicated in substantial weight gain [24–26]. While over 70% of PLWH age ≥50 were on an INSTI at the most recent visit, DTG was not programmatically rolled out by PEPFAR until late 2018 [27]. The maximum exposure time of DTG at the time of this analysis would have been 3 years. Even though the prevalence of obesity in PLWH age ≥50 was significantly lower compared to age-matched counterparts without HIV, the prevalence of obesity should be monitored as the duration of DTG increases. If the evidence for DTG association with weight gain becomes stronger, programmatic considerations can be considered weighing the benefits of DTG against other options.

This study has multiple strengths, including a diverse population with extensive data collected since 2013. Limitations are that this is an observational cohort with a low number of participants aged≥50, particularly PLWoH in that age group that limit statistical power. Testing for diabetes, dysglycemia and renal insufficiency was not added to study procedures for PLWoH until 2017 and, therefore, these data are not available for these participants. However, data were included for subsequent visits by these participants after amendment implementation. We attempted to adjust for confounders, including study site, age, HIV status, sex and other diseases, known to increase the risk of NCDs; however, we did not adjust for ART exposure differences given the inclusion of PLWoH. We were unable to adjust for other confounders, such as physical activity and nutrition, as these were not collected as part of the study.

5 | CONCLUSIONS

This study provides NCD prevalence and characteristics in an ageing sub-Saharan African PLWH population. There was a large burden of NCDs in this cohort that varied by geographic region. If left unmitigated, NCDs can lead to downstream effects, such as neurologic and cardiovascular disease, causing significant morbidity and mortality. Treating individuals with multiple comorbidities is complex and models of care will need to be developed to appropriately manage these individuals. The geographic component is important because in areas with high burdens of NCDs it will be important to appropriately allocate resources to promote healthy ageing with HIV.

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COMPETING INTERESTS

The authors have no competing interests to disclose.

AUTHORS' CONTRIBUTIONS

CCG, JAA, JSC, ALE and DC conceived of the presented research idea. EB, MI, HK, JO, JM and VS carried out the data collection, laboratory activities and reviewed the collected data for quality and reliability. ALE designed the model and analysed the data. ND verified underlying data. DC, ALE, JAA, TAC, NFD, CSP, JSC and CCG contributed to the interpretation of the results. ALE and DC took the lead in writing the manuscript. CCG, CSP and JAA were in charge of overall direction and planning. All authors provided critical feedback and helped shape the research, analysis and manuscript. All authors approve of the final submitted manuscript.

ACKNOWLEDGEMENTS

We thank the study participants, local implementing partners and hospital leadership at Kayunga District Hospital, Kericho District Hospital, AC Litein Mission Hospital, Kapkatet District Hospital, Tenwek Mission Hospital, Kapsabet District Hospital, Nandi Hills District Hospital, Kisumu West District Hospital, Mbeya Zonal Referral Hospital, Mbeya Regional Referral Hospital, Defence Headquarters Medical Center and the 68th Nigerian Army Reference Hospital. We would also like to thank the AFRICOS Study Group (https://www.hivresearch.org/pepfar/AFRICOS-study-group).

FUNDING

This work was supported by the President's Emergency Plan for AIDS Relief via a cooperative agreement between the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. and the U.S. Department of Defense.

DISCLAIMER

The views expressed are those of the authors and should not be construed to represent the positions of the US Army, the Department of Defense or the Department of State. The investigators have adhered to the policies for the protection of human subjects as prescribed in Army Regulation 70-25.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analysed during the current study are not publicly available due to privacy protections but are available from the corresponding author on reasonable request. The Henry M. Jackson Foundation for the Advancement of Military Medicine (HJF) and the Water Reed Army Institute of Research (WRAIR) are committed to safeguarding the privacy of research participants. The distribution of data will require compliance with all applicable regulatory and ethical processes, including the establishment and approval of an appropriate data-sharing agreement. To request a minimal dataset, please contact the data coordinating and analysis center (DCAC) at PubRequest@hivresearch.org and indicate the RV329 study along with the name of the manuscript.

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Aurpibul L et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25983
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25983/full | https://doi.org/10.1002/jia2.25983

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Neurocognitive performance and quality of life of older adults with HIV on antiretroviral treatment in Northern Thailand

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Abstract

Introduction: With virologic suppression and longer life expectancy, older adults with HIV (OAHIV) are at risk for neurocognitive impairment (NCI). This study investigated neurocognitive performance, quality of life (QOL) and the association between OAHIV determinants.

Methods: This cross-sectional study was conducted in OAHIV aged ≥ 50 years on antiretroviral treatment at community hospitals in Northern Thailand between September and November 2020. The Montreal Cognitive Assessment Thai Version (MoCA-T) and the Thai-validated Medical Outcomes Study HIV (MOS-HIV) were used. NCI was defined as MoCA-T scores <25: 16–24 for amnestic mild cognitive impairment (aMCI) and <16 for dementia. For QOL, higher scores meant better QOL; a physical health summary T-score ≥50 was defined as good QOL.

Results: Overall, 269 OAHIV were enrolled; 59% were female and 99% had virologic suppression. The current median age was 61.8 years (interquartile range [IQR] 58.9–65.7). The median duration of antiretroviral treatment was 10.5 years (IQR 8.5–13.5). The current median CD4 count (234 tested) was 484 cells/mm^3 (IQR 339–634), and 99% had plasma HIV RNA <40 copies/ml (229 tested). The median MoCA-T score was 20.0 (IQR 16.3–23.0). There were 234 OAHIV (87.3%) with NCI: 182 (67.9%) with aMCI and 52 (19.4%) with dementia. A hundred and ninety (70.6%) had good QOL. Bivariate analysis revealed no correlation between MoCA-T scores and QOL. Multivariable linear regression analysis revealed that MoCA-T score was associated with older age ($r = -0.144$, $p = 0.002$), lower education ($r = 0.629$, $p < 0.001$), lower income ($r = 0.797$, $p = 0.040$) and shorter treatment duration ($r = 0.189$, $p = 0.006$).

Conclusions: The vast majority of OAHIV with virologic suppression had NCI. Approximately two-thirds had a mild impairment and one-fifth had dementia. Neurocognitive performance and QOL were not correlated. Addressing mild NCI would enable more targeted monitoring. Early intervention and support could minimize functional impairment with increased age.

Keywords: neurocognitive; quality of life; older adults with HIV; antiretroviral treatment; Thailand; cohort studies

Received 8 November 2021; **Accepted** 1 August 2022

1 | INTRODUCTION

Due to the widespread use of effective antiretroviral treatment (ART), the median age of people with HIV (PWHIV) has increased [1]. In 2016, an estimated 5.7 million PWHIV globally were over the age of 50 [2] accounting for 30% of adults with HIV in high-income countries, and varying from 6% to 17% in other regions of the world [3]. In Thailand, the national scale-up of HIV care began in 2000 [4]. Many patients on ART have survived into their fifties, and are now considered older adults with HIV (OAHIV). Apart from age-related illnesses, studies have demonstrated an increased risk of chronic non-AIDS-related diseases, including neurocognitive complications in OAHIV, partly related to chronic inflammation [5].

Neurocognitive impairment (NCI) is one among several comorbidities associated with a decline in activities of daily living, cognitive symptoms and functional status in PWHIV [6]. NCI classifications include asymptomatic NCI, mild neurocognitive disorders and HIV-associated dementia [7]. Prior to the widespread availability of ART, the prevalence of NCI in ART-naïve adults with HIV in an Indian study between 2003 and 2004 was 60% [8]. NCI remained prevalent in the initial ART era, though profound HIV-associated neurocognitive disorders were only infrequently seen [9]. A report from a Southeast Asian consortium study in 2006 documented moderate to severe HIV-related NCI in 12% of PWHIV in both ART-naïve and ART treatment groups [10]. The 2NN study in Thailand in 2008 documented NCI in 37.5% of PWHIV at a median age of 41.2 years who had good virologic control

[11]. More recently, a 2015–2017 study in Bangkok reported an NCI prevalence of 59.4% among PWHIV with a median age of 54.3 years [12]. Factors associated with NCI included increased age, being female, low education, depression and low income [13, 14]. It is possible that pre-existing neurological deficits were present prior to ART initiation, or that NCI developed later due to ongoing inflammatory processes associated with chronic HIV infection [15]. The consequences of NCI include poor medical adherence, disruption of daily functioning, decreased quality of life (QOL) and increased risk of mortality [16]. The impact of NCI on health-related QOL of PWHIV in all domains was documented [17]. Meanwhile, a Kenyan study reported worse QOL in PWHIV without significantly different cognitive deficits [18]. There have been several studies of QOL among PWHIV in Thailand. However, an association between QOL and NCI has not been well established [19, 20].

In this study, we hypothesized that even with sustained virologic suppression through ART, OAHIV could remain at increased risk for impaired QOL and early NCI. The study objective was to determine the frequency of NCI among Thai OAHIV residing in communities. We assessed the correlation between neurocognitive performance and QOL and looked for factors associated with NCI in this population.

2 | METHODS

2.1 | Study design and population

A cross-sectional study was conducted at 12 community hospitals in Chiang Mai, Thailand between September and November 2020. The study population was OAHIV in a prospective cohort study, which was started in August 2015. The primary aim of the cohort is to follow the QOL and health outcomes of OAHIV receiving the national standard of HIV care. The national AIDS programme covered antiretroviral medication, CD4 counts and laboratory safety parameter measurements every 6 months, and annual HIV-RNA testing. Treatment for comorbidities and other diseases is covered under the universal healthcare coverage scheme for all Thai citizens. In every community hospital, an HIV clinic had been set up that was separated from the outpatient services for general patients, which afforded greater privacy and confidentiality. For this cohort, 12 hospitals were selected from a total of 23 community hospitals in the province, according to the advice of the Chiang Mai Provincial Public Health office. Specifically, the selected hospitals had been serving larger populations with HIV since the national HIV programme was launched in 2002. In 2015, potential participants were approached and invited to join the cohort study during routine clinical visits. The inclusion criteria were (1) living with HIV, (2) being aged ≥50 years and (3) receiving ART at study enrolment. Each hospital approached its oldest patients first. After enrolment, all participants were continuously followed in HIV clinics for regular care at 2- or 3-month intervals under the Thai national AIDS programme. All participants who attended their annual follow-up visits in 2020 were invited to join this study.

2.2 | Sample size estimation

The prevalence of NCI among PWHIV and non-HIV older adults in other studies were between 59.4% and 71.4% [12, 21]. In our study, the estimated prevalence was 80%. The evaluable number of participants was 246, which would have 80% power at the confidence interval of 95% to assess NCI.

2.3 | Ethics statement

The study was approved by the Ethics Committee at the Research Institute for Health Sciences, Chiang Mai University (Certificate approval number 35/2020). Written informed consent was obtained from each participant. The study staff assessed their literacy prior to the consent process (e.g. through reading out loud). Literate participants gave written consent, while low literacy and illiterate participants provided consent with a thumbprint in presence of an impartial witness.

2.4 | Data collection and tools

A range of demographic characteristics (sex, age, education, monthly income, number of family members and year of HIV diagnosis) were obtained as part of the main study. Clinical data (date of ART initiation, current CD4, HIV RNA and comorbidities) were extracted from hospital records by HIV clinic staff. After consent, the assessment took place in a private space within the hospital. Cognitive performance was assessed by certified investigators (physicians and nurses) using the Thai version of the Montreal Cognitive Assessment (MoCA-T). MoCA-T is a screening measure that covers eight cognitive domains, including attention and concentration, visuospatial/executive function, memory, language, visuoconstructional skills, conceptual thinking, calculations and orientation. MoCA-T has been validated with acceptable reliability for use in screening for amnestic mild cognitive impairment (aMCI) in Thai patients. The internal consistency was demonstrated to have a Cronbach's alpha coefficient of 0.914 [13]. MoCA-T has also been used in studies among PWHIV after ART initiation [12, 14]. When an assessment was completed, all scores were summed out of a total possible score of 30. For individuals with ≤6 years of education, one point was added to their summed score. In this study, NCI was defined as a MoCA-T score <25. Scores 16–24 were defined as aMCI, and scores <16 as dementia. With these cut-offs, the areas under the receiver-operating characteristics (ROC) curve were 0.813 for aMCI and 0.938 for Alzheimer's disease compared to healthy controls in a psychometric properties study [22].

Health-related QOL was assessed using the Thai-validated version of the Medical Outcomes Study HIV (MOS-HIV) [23]. It was developed from the MOS-Short form 20 with additional constructs relevant to PWHIV, and has been used in HIV-related clinical trials as an outcome measure [24]. It consists of 35 close-ended items measuring 11 dimensions of health-related QOL, namely general health perception, physical functioning, role functioning, social functioning, cognitive functioning, pain, mental health, energy fatigue, health distress, QOL and health transition. For each question, participants would provide their responses in 2- to 6-point Likert scales. Some questions were in the positive direction,

and some were reversed. The dimensions are scored ranging from 0 to 100. Higher scores indicate better perceived QOL. The dimensions are then aggregated into the physical health summary (PHS) and mental health summary (MHS) status scores, in which they are linearly transformed to a 0–100 scale using factor-analysis-based or regression-based weights. The standardized scores (T-scores) had a mean of 50 and a standard deviation of 10. The norm-based standardization dimension scores, the PHS and MHS T-scores, were reported. Higher dimension scores meant better QOL. Based on the Norm-Based Scoring, a PHS T-score of ≥50 was defined as a good QOL [25].

2.5 | Statistical analysis

Statistical analysis was performed using SPSS version 22.0 (IBM Corporation, New York). Demographic characteristics were presented by numbers (percentages) for categorical data, means (standard deviation, SD) for continuous data with normal distributions and medians (interquartile range [IQR]) for continuous data with non-normal distributions. A comparison of demographic characteristics between OAHIV with impaired and good QOL was made using the chi-square test or Fisher's exact test, as appropriate for categorical variables, and Mann–Whitney tests for continuous variables. The outcome variables of interest in this study were total MoCA score and domain scores, the proportion of participants with NCI (aMCI and dementia), PHS and MHS T-scores, and itemized scores in 11 dimensions of QOL. Bivariate correlation between each score was analysed. Linear regression was used to identify factors potentially associated with MoCA scores: age, sex, education, time since HIV diagnosis, time from HIV diagnosis to ART initiation, duration on ART, monthly income, CD4 at study entry, current CD4, marital status and presence of comorbidities. In the multivariable regression analysis, factors with statistical significance in univariable analysis or that had a potential role as confounders were included. Statistical significance was defined as $p < 0.05$.

3 | RESULTS

3.1 | Characteristics of study participants

Two hundred and sixty-nine OAHIV were approached. All provided consent and were enrolled in this study. One hundred and fifty-nine (59.33%) were female. QOL assessments were completed in 268, and one PWHIV was excluded due to insufficient literacy. Their median age was 61.8 years (IQR 58.9–65.7), and the median monthly income was 4000 Baht (IQR 2000–10,000; ~125 US Dollars). Two hundred and thirteen (79.5%) received ≤4 years of formal education. The median duration from HIV diagnosis to ART initiation was 15.4 years (IQR 10.6–19.3); 233 (86.6%) started ART (non-nucleoside reverse transcriptase-based regimens) between 1998 and 2013 while they were immunosuppressed, and 36 (13.4%) started ART after 2013 when it became available for all at any CD4 level. The median ART duration at the time of this study was 10.5 years (IQR 8.5–13.5). The current median CD4 cell count was 484 cells/mm^3 (IQR 339–634) of 234 tested, and 99% were virologically suppressed (HIV-RNA <40 copies/ml) of 229 tested. Comorbidities were reported in 119 (44.4%) of the participants and included dyslipidaemia in 101 (37.7%), diabetes in 35 (13.1%) and renal diseases in 5 (1.9%). There was no difference in demographic characteristics between OAHIV with impaired and good QOL (Table 1).

3.2 | Quality of life

The median PHS T-score was 54.97 (IQR 48.07–58.46). There were 190 OAHIV (70.6%) with good QOL (PHS T-score ≥50) and 79 (29.4%) with impaired QOL (PHS T-score <50). The highest physical health dimension scores were role and social functioning, whereas the lowest dimension score was general health. The median mental health dimension (MHS) T-score was 58.40 (54.30–61.74), with the highest score for health distress and the lowest dimension score was health transition. The PHS and MHS T-scores were significantly correlated (Pearson's coefficient 0.522, $p < 0.001$). Those with good QOL also had a significantly higher median MHS T-score (59.54 vs. 54.03 in those with impaired QOL, respectively; $p < 0.001$). When comparing groups, OAHIV with impaired QOL had significantly lower median scores than those with good QOL in all dimensions, except for the health transition domain. Scores were especially divergent in pain scores and in energy & fatigue (vitality) scores (Table 2).

3.3 | Neurocognitive performance

During the assessment, all participants were asked to complete each test consecutively without skipping. The median MoCA score was 20.0 (IQR 16.3–23.0). The median MoCA scores were not different between OAHIV with good and impaired QOL ($z = -0.868$, $p = 0.385$). The three domains with the lowest scores included language, abstraction and delayed recall. There were 234 OAHIV (87.3%) with NCI (score <25). A hundred and eighty-two (67.9%) had aMCI (scores 16–24), whereas 52 (19.4%) had dementia (scores <16) (Table 2).

3.4 | Correlation

The bivariate correlation revealed no relationship between MoCA and PHS T-score ($r = 0.030$, $p = 0.627$), MHS T-score ($r = 0.033$, $p = 0.587$) or cognitive functioning dimension score ($r = 0.006$, $p = 0.925$) (Table 3). Comparison between OAHIV with dementia and those with better neurocognitive performance (MoCA scores <16 vs. ≥16) also revealed no significant differences in PHS T-score ($z = -1.736$, $p = 0.083$) and MHS T-scores ($z = -0.506$, $p = 0.614$), or any QOL dimension scores.

3.5 | Factors associated with NCI

The univariate linear regression revealed that age, education, ART duration and income were associated with MoCA scores, whereas sex, duration of HIV or treatment, CD4 at study entry, current CD4 and comorbidities were not associated. In the multivariable analysis, sex and comorbidities were specifically included as potential determinants of NCI. We found positive association with MoCA scores for years of education

Table 1. Demographic characteristics of all older adults with HIV in this study

Characteristics	Total	OAHIV with impaired QOL	OAHIV with good QOL	*p*-value	Test statistics
Number of OAHIV	269	79 (29.4%)	190 (70.6%)		
Sex					
Female	159 (59.3%)	43 (27.0%)	116 (73.0%)	0.314	−1.004
Male	110 (40.9%)	36 (32.7%)	74 (67.3%)		
Age (years)	61.8 (58.9–65.7)	62.0 (59.0–66.0)	61.0 (59.0–65.3)	0.934	−0.083
Age > 60 years	160 (59.5%)	47 (29.4%)	113 (70.6%)	0.998	−0.003
Formal education					
0–4 years	213 (79.5%)	57 (72.7%)	156 (82.1%)	0.055	−2.260
5–12 years	46 (17.2%)	16 (20.3%)	30 (15.8%)		
> 12 years	10 (3.7%)	6 (7.6%)	4 (2.1%)		
Monthly income (Thai baht)	4000 (2000–10,000)	5000 (3000–10,000)	3800 (2000–9000)	0.056	−1.914
Marital status					
Married or in a relationship	106 (39.4%)	28 (35.4%)	78 (41.1%)	0.391	−0.856
Single/separated/divorced	163 (60.6%)	51 (64.6%)	112 (58.9%)		
Duration since HIV diagnosis (years)	26.2 (23.3–28.8)	26.6 (24.0–29.1)	25.9 (23.2–28.7)	0.522	−0.640
Duration on ART (years)	10.5 (8.5–13.5)	9.9 (8.1–13.1)	10.8 (8.5–13.6)	0.114	−1.581
Current CD4 cell count, cells/mm^3 (n = 234)	484 (339–634)	468 (305–590)	501 (357–666)	0.227	−1.209
Current virologic suppression	227/229 (99.1%)	70/70 (100%)	157/159 (98.7%)	1.000	−0.940
Comorbidities	119 (44.4%)	32 (40.5%)	87 (45.8%)	0.427	0.793
Renal disease	5 (1.9%)	1 (1.3%)	4 (2.1%)	1.000	0.463
Diabetes	35 (13.1%)	11 (13.9%)	24 (12.6%)	0.774	−0.286
Dyslipidaemia	101 (37.7%)	27 (34.2%)	74 (38.9%)	0.462	0.734

Note: Data in median (interquartile range, IQR), mean (standard deviation, SD) or number (%) as appropriate. Impaired QOL was defined as a physical health summary (PHS) T-score < 50, and good QOL was defined as PHS T-score ≥ 50. *p*-value by chi-square, Fisher's exact or Mann–Whitney test.
Abbreviations: ART, antiretroviral treatment; OAHIV, older adults with HIV; QOL, quality of life.

(β = 0.629, $p < 0.001$), ART duration (β = 0.189, $p = 0.006$) and monthly income (β = 0.797, $p = 0.040$), while age was negatively associated (β = −0.144, $p = 0.002$) (Table 4).

4 | DISCUSSION

More than two-thirds of OAHIV in this study had good QOL, while 87.3% of them had NCI, including one-fifth who had dementia. There was no correlation between their neurocognitive performance and QOL. Low MoCA scores were associated with older age, fewer years of formal education, shorter duration on ART and low income.

Recently, the MoCA-T has been increasingly used to identify Thai PWHIV with NCI and is a user-friendly tool for NCI screening in HIV clinics. The median MoCA score of our study participants was 20.0 (IQR 16.3–23.0), which was lower than the median MoCA score of 24 (IQR 21–26) reported in a previous study in Bangkok [12]. The frequency of NCI in their cohort of 340 OAHIV (median age of 54.3 years) with good immune status and virologic suppression was 59.4%, which was lower than in our study. Nearly one-third of their participants had a bachelor-level education or higher, were living with an HIV diagnosis for a median of 18.3 years (IQR 14.9–20.9) and had been taking ART for a median of 16.1 years. With similar immunologic and virologic outcomes, our participants were older, less educated and experienced a median of 15.4 years delay between HIV diagnosis and ART initiation.

A large majority (86.6%) of OAHIV in our study started ART before the test and treat era in 2013. During that period, ART was not prescribed for PWHIV under the National AIDS programme until they developed some degree of immunosuppression. Meanwhile, the Bangkok study enrolled participants from a long-term study cohort in which ART was initiated approximately 2 years after the HIV diagnosis as a part of the clinical trial in 2002. The delayed ART initiation in our participants might explain the higher rate of NCI. Another neurocognitive study was conducted among Thai PWHIV with virologic suppression, at the mean age of 45 years and a median ART duration of 12.1 years, where the frequency of NCI was 43% [14]. Their mean MoCA score of 22.24 ± 3.83 was significantly lower than the HIV-negative comparison group. Within the HIV group, worse performance was observed in those who were older and had lower incomes. No associations with HIV-related characteristics were reported, which is in line with our study findings.

Table 2. Neurocognitive performance and quality of life of OAHIV in this study

Characteristics	Maximum scores	Total	OAHIV with impaired QOL	OAHIV with good QOL	*p*-value	Test statistics
Quality of life (MOS-HIV), n = 269						
Physical health summary T-score		**54.97 (48.07–58.46)**	**41.01 (33.75–46.84)**	**56.93 (54.59–59.43)**	**<0.001**	**−12.914**
General health	100	65.00 (55.00–82.00)	50.00 (35.00–65.00)	70.00 (60.00–80.00)		
Physical functioning	100	91.67 (75.00–100)	66.67 (41.67–75.00)	91.67 (83.33–100)		
Role functioning	100	100 (100–100)	50.00 (0–50.00)	100 (100–100)		
Social functioning	100	100 (100–100)	60.00 (40.00–100)	90.00 (80.00–100)		
Pain	100	77.78 (55.56–100)	44.44 (44.44–66.67)	88.89 (66.67–100)		
Mental health summary T-score		**58.40 (54.30–61.74)**	**54.03 (49.02–58.97)**	**59.54 (56.49–62.75)**	**<0.001**	**−6.790**
Cognitive functioning	100	90.00 (80.00–95.00)	85.00 (75.00–90.00)	90.00 (85.00–95.00)		
Mental health	100	92.00 (80.00–100)	84.00 (76.00–96.00)	96.00 (80.00–100)		
Energy & fatigue (vitality)	100	85.00 (70.00–95.00)	65.00 (50.00–80.00)	90.00 (80.00–100)		
Health distress	100	100 (100–100)	90.00 (75.00–100)	100 (100–100)		
Quality of life	100	75 (75–75)	75.00 (50.00–75.00)	75.00 (50.00–100)		
Health transition	100	50.00 (50.00–75.00)	50.00 (50.00–75.00)	50.00 (50.00–75.00)		
Neurocognitive performance (MoCA), n = 268						
Median scores (IQR)	30	20 (16.3–23.0)	20.0 (16.0–24.0)	20.0 (17.0–22.0)	0.385	−0.868
Mean scores ±SD		19.3 ± 4.7	19.7 (5.0)	19.2 (4.6)	0.418	0.812
Domain scores						
Visuospatial/executive	5	2.9 (1.4)	2.9 (1.4)	2.9 (1.4)	0.810	0.241
Naming	3	2.5 (0.8)	2.5 (0.7)	2.4 (0.8)	0.390	0.862
Attention	6	4.3 (1.4)	4.3 (1.4)	4.3 (1.4)	0.853	0.186
Language	3	0.8 (0.9)	0.9 (0.9)	0.7 (0.8)	0.100	1.649
Abstraction	2	0.6 (0.8)	0.7 (0.8)	0.6 (0.8)	0.447	0.762
Delayed recall	5	1.8 (1.6)	1.9 (1.6)	1.8 (1.6)	0.489	0.693
Orientation	6	5.7 (0.7)	5.8 (0.6)	5.7 (0.8)	0.435	0.782
Neurocognitive impairment, *n* (%)		234 (87.3%)				
aMCI, *n* (%)		182 (67.9%)	48 (60.8%)	134 (70.9%)	0.052	1.499
Dementia, *n* (%)		52 (19.4%)	15 (19.0%)	37 (19.6%)		

Note: MoCA, the Thai version of the Montreal Cognitive Assessment; MOS-HIV, the Thai-validated version of the Medical Outcomes Study HIV; NCI, neurocognitive impairment (scores < 25); aMCI, amnestic mild cognitive impairment (scores 16–24); dementia (scores <16). Bold values highlights that they are summary T-scores, which are significantly different between the two groups.
Abbreviations: IQR, interquartile range; OAHIV, older adults living with HIV; SD, standard deviation.

There was a study conducted in 2020 among older villagers in the rural area of Northern Thailand where the prevalence of aMCI was 71.4% [21]. The mean age of their participants was 68.3 years and 95.1% had formal education of ≤4 years, which was more similar to our participants. Apart from having HIV, the higher prevalence of NCI in our study could be affected by the diversity in geographic, ethnocultural and education factors. Despite having Thai citizenship, some participants were from ethnic minorities (Shan people, Yunnan and hill tribes) who may have had less access to formal education in childhood. In the present study, we found low domain scores in language, abstraction and delayed recall, while in their study, the most common impairments were executive function, attention and delayed recall.

Table 3. Bivariate correlation between MoCA and quality of life scores in older adults with HIV (n = 268)

Quality of life dimensions	Correlation coefficients[a]	*p*-value	Median[b]	Test statistic (U)	*p*-value
Physical health summary T-score	0.030	0.627	54.97	7981.0	0.796
General health	0.052	0.395	65.00	8072.5	0.914
Physical functioning	0.098	0.108	91.67	7363.0	0.188
Role functioning	0.007	0.909	100.00	7749.5	0.446
Social functioning	−0.041	0.503	100.00	7629.5	0.257
Pain	0.047	0.444	77.78	7958.0	0.762
Mental health summary T-score	0.033	0.587	58.40	7816.0	0.595
Cognitive functioning	0.006	0.925	90.00	7756.5	0.521
Mental health	−0.014	0.824	92.00	7754.5	0.519
Energy & fatigue (vitality)	0.038	0.539	85.00	8095.0	0.943
Health distress	0.041	0.506	100.00	7986.0	0.778
Quality of life	0.032	0.599	75.00	7824.0	0.580
Health transition	−0.023	0.708	50.00	8008.5	0.806

Note: Data in median (IQR) or number (%).
[a]Pearson correlation estimates.
[b]Comparison between those with dementia (MoCA score < 16) and those with normal or mild impairment (score ≥16).

Table 4. Univariable and multivariable linear regression analysis of factors associated with MoCA scores of OAHIV

Covariate	Univariable			Multivariable*	
	R	β coefficient (95% CI)	*p*-value	β coefficient (95% CI)	*p*-value
Sex	0.079	0.753 (−0.399 to 1.905)	0.199	0.307 (−0.698 to 1.312)	0.547
Age (years)	0.214	−0.187 (−0.291 to −0.084)	<0.001	−0.144 (−0.234 to −0.054)	0.002
Education (years)	0.470	0.678 (0.524–0.831)	<0.001	0.629 (0.475–0.783)	<0.001
Duration from HIV diagnosis	0.004	0.004 (−0.124 to 0.132)	0.951		
Time from HIV diagnosis to ART initiation (years)	0.089	−0.071 (−0.167 to 0.025)	0.146		
Duration on ART (years)	0.148	0.190 (0.036–0.343)	0.015	0.189 (0.056–0.322)	0.006
Current monthly income (Thai baht)	0.236	1.693 (0.852–2.534)	<0.001	0.797 (0.035–1.559)	0.040
CD4 at study entry (year 1)	0.002	0.003 (−0.126 to 0.131)	0.969		
Current CD4 (year 5)	0.036	0.036 (−0.002 to 0.003)	0.586		
Marital status	0.072	0.696 (−0.465 to 1.857)	0.239		
Comorbidities	0.074	−0.700 (−0.167 to 0.025)	0.089	−0.658 (−1.634 to 0.0317)	0.185

Abbreviations: ART, antiretroviral treatment; CI, confidence interval; MoCA, the Montreal cognitive assessment; OAHIV, older adults with HIV.
*Factors with statistical significance or potential role as confounders were included in the multivariable analysis.

The impairment in delayed recall indicates impaired memory and is an early sign of AD, while impaired visuospatial/executive function indicates neurodegenerative change [26]. However, our participants did not perceive their memory problems (the median cognitive function domain score in QOL was 90/100). Moreover, they had a high role and social functioning (median scores 100/100). Low perceived difficulty in their daily activities might have been due to low instrumental activities involved. Our participants lived in communities with relatively low technology environments, where high-level cognitive skills were not required. This may have been why their NCI did not affect their perceived QOL. The investigators who performed NCI assessment in our study reported language and abstraction as the most problematic domains.

Different MoCA score cut-offs were mentioned across studies. In a US study, the frequency of NCI in OAHIV was 67% when a cut-off of ≤26 was used. Their mean score was 25.2±3.0, the mean age of their participants was 58.2 years and the mean duration of HIV infection was 18 years; 98% were on ART and 92% were virologically suppressed [6]. A Malaysian study reported that 64.3% of PWHIV, mean age 44.7 years, had cognitive impairment using a MoCA cut-off score of ≤26 [27]. However, when the adjusted T-scores were applied instead of the standard scores, it resulted in

decreased frequency of cognitive impairment in their study to 23.4%. Another study in Thailand was conducted in a tertiary care hospital among 74 PWHIV with a mean age of 45.6 years, about half were diagnosed with NCI using the Frascati criteria [28]. Their ROC analysis revealed that using a lower MoCA cut-off of ≤23 instead of ≤24 would yield higher specificity of the MoCA in screening for NCI. As using different MoCA cut-off results in varying frequencies of impairment, it is difficult to make direct comparisons between studies, and the results must be interpreted with caution.

Determination of QOL in PWHIV is critical as it allows healthcare providers to better understand their patients' perceptions of their health and life satisfaction [29]. HIV programme assessment based on clinical outcomes alone may not be sufficient to ensure the wellbeing of OAHIV experiencing age-related changes after years on ART. We found that two-thirds of OAHIV in this study had good QOL. Those with good physical health (PHS) also had higher mental health (MHS) T-scores. This was in line with a 2017 study in Northern Thailand which reported that 96.3% of PWHIV aged 20–60 years reported overall QOL at moderate levels, as assessed by the World Health Organization QOL brief assessment tool [30]. They mentioned that CD4 count <200 cells/mm^3 was associated with low QOL. We did not see this association, as our participants had higher median CD4 counts at the time of the study. Another study in 2012 on PWHIV at a tertiary care hospital in Thailand also used the MOS-HIV. Their population's median age was 42 years, the mean duration following HIV diagnosis was 6.8 years and 54% had been on ART for between 1 and 5 years [20]. They reported that age <50 years was a positive predictive factor for PHS while being on ART and having good compliance were positive predictive factors for MHS.

An earlier analysis of our cohort using data from 2015 to 2017 demonstrated that QOL in OAHIV could improve or be maintained over time [19]. Our participants were virologically suppressed, which indicated good ART compliance, and we did not see an age difference between those with good and impaired QOL. A Pakistani study reported that age >50 years, CD4 count >500 cells/mm^3 and a primary/secondary education were associated with better QOL when compared to younger participants with a lower CD4 count, or those with tertiary education [31]. We found no significant difference in education or neurocognitive performance between OAHIV with impaired and good QOL. However, the observed high scores in the role and social functioning dimensions suggested that there might be other determinants of QOL that were stronger contributors (i.e. socio-demographic, social support, geographic or environmental factors). Sex, marital status and physical exercise engagement were predictors of QOL in a study among Thai OAHIV [19]. A Kenyan study documented poorer QOL and mental health in PWHIV with low literacy in relation to the HIV-negative group, despite exhibiting no significant cognitive deficits [18]. Living with the chronic disease might partly explain the low QOL, as we observed the lowest median scores in the pain, role functioning and energy & fatigue (vitality) domains in OAHIV with impaired QOL. Screening for frailty and addressing support needs could be useful interventions in this context.

The low median health transition scores in all study participants regardless of their QOL might have been impacted by the Covid-19 pandemic. At the time of the assessment, the worsening Covid-19 situation in Northern Thailand resulted in many new public health restrictions (e.g. social distancing, face masks and limited travel). Since the health transition question asked about physical health and emotional condition compared to the previous 4 weeks, these restrictions could have been a factor in their responses.

The study had several strengths. To our knowledge, this is the first neurocognitive study of community-dwelling OAHIV in rural Thailand. Our study participants represented the first generation of PWHIV in the country who acquired HIV from heterosexual contact. After they were diagnosed, delays in accessing treatment during that period resulted in immunosuppression. After starting ART, they have continuously been receiving HIV care through the Thai national programme for over a decade. The results revealed the presence of NCI of varying severity, which highlights the need for monitoring, intervention and social support. The findings from this study can help inform policymakers and may encourage more budget allocations to tailor health programmes for OAHIV. Our study limitations include enrolment bias, as only OAHIV who visited the clinics were included, in which case those with profound dementia or extreme QOL might not be included. Second, there were some participants with low literacy for whom MoCA might not be the optimal screening tool. However, we chose this instrument because of its widespread use in Thailand, which allowed us to make comparisons with other studies in Thai OAHIV. Third, we did not include data on all historic or current opportunistic infections and comorbidities, which could have been the cause of chronic inflammation or affected the central nervous system function. Fourth, we did not assess NCI in older adults without HIV of comparable age, sex, education level and geographic location for comparison. This limited our ability to make conclusions regarding the effects of such factors on the study results.

5 | CONCLUSIONS

We documented NCI in a large majority of OAHIV with immune recovery and virologic suppression following delayed ART initiation. Further assessment of functioning to address problems in performing activities of daily living is required in those with low scores. More research to identify potentially modifiable factors affecting neurocognitive performance in ageing populations who started ART both later and sooner after HIV acquisition is warranted. Early detection of NCI among this population would allow healthcare providers to monitor, counsel or intervene appropriately in a more timely manner.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

LA, AT and KS designed the study. LA, WC and SS collected data and performed study assessments. PS and LA did the data analysis. LA and PS prepared the first draft of the manuscript. AT and KS reviewed and edited the main manuscript text. WC and SS composed the table. All authors reviewed the manuscript.

ACKNOWLEDGEMENTS

This study was part of the HIV/AIDS study among People living with HIV/AIDS in Chiang Mai. We thank all community hospital staff and older adults living with HIV/AIDS in rural Chiang Mai Province who contributed to this research.

FUNDING

The study was supported by the Center of Excellence in HIV/AIDS Chiang Mai University Research and the National Research University Project under Thailand's Office of the Higher Education Commission.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Luk FWL et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25988
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25988/full | https://doi.org/10.1002/jia2.25988

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Sarcopenia in people living with HIV in Hong Kong: which definition correlates with health outcomes?

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Abstract

Introduction: Sarcopenia is an important clinical syndrome in older people living with HIV (PLWH). With a change to the Asia sarcopenia definition in 2019, we aimed to determine whether health outcomes were associated with different definitions of sarcopenia among Asian PLWH.

Methods: We performed a prospective cross-sectional study enrolling PLWH aged ≥35 years from January 2018 to November 2021. We defined sarcopenia by the Asia Working Group of Sarcopenia (AWGS) criteria in 2014 and 2019. AWGS-2014 included low muscle mass plus weak handgrip strength and/or slow gait speed. AWGS-2019 included low muscle mass plus low muscle strength or physical performance, while the presence of all defines severe sarcopenia. We measured appendicular skeletal muscle mass using dual-energy X-ray absorptiometry, handgrip strength, usual gait speed, five-time chair stand test and Short Physical Performance Battery. Correlations between each sarcopenia definition and health-related quality of life (using EQ-5D-5L and SF-36) and functional disability were determined.

Results: One hundred and fifty Asian PLWH were enrolled, 132 (88%) were male, mean age was 60±10 years, duration of HIV diagnosis was 13 (IQR 8–18) years and current CD4 count was 574 (IQR 362–762) cells/mm^3, 67 (45%) had multimorbidity, 64 (43%) had polypharmacy. Prevalence of sarcopenia by AWGS-2014, AWGS-2019 and severe sarcopenia was 17.3%, 27.3% and 18.0%, respectively. Age, education and polypharmacy were associated with sarcopenia. Sarcopenia (AWGS-2014) and severe sarcopenia were associated with mobility, physical functioning and physical component score (SF-36). All three criteria were associated with impaired instrumental activities of daily living (IADL). After age and sex adjustment, sarcopenia (AWGS-2014) (adjusted odds ratio/aOR 5.4, 95% confidence interval/CI 2.0–15.1) and severe sarcopenia (aOR 5.1, 95% CI 1.9–14.0) were associated with mobility and physical component score (SF-36) (β coefficients −5.3342, $p = 0.022$ and −5.412, $p = 0.019$). Sarcopenia (AWGS 2014) (aOR 5.2, 95% CI 1.7–16.2), sarcopenia (AWGS-2019) (aOR 4.5, 95% CI 1.5–13.1) and severe sarcopenia (aOR 3.5, 95% CI 1.1–10.9) were associated with impaired IADL in fully adjusted models.

Conclusions: In a sample of Asian PLWH, 17.3%, 27.3% and 18.0% had sarcopenia as defined by AWGS-2014, AWGS-2019 and severe sarcopenia, respectively. Sarcopenia by AWGS-2014 and severe sarcopenia correlated with parameters of poor health outcomes, while sarcopenia by AWGS-2019 correlated with functional disability.

Keywords: HIV; sarcopenia; quality of life; disability; polypharmacy; ageing

Additional information may be found under the Supporting Information tab of this article.

Received 20 January 2022; **Accepted** 1 August 2022

1 | INTRODUCTION

Sarcopenia, deriving from the Greek words *sarx* (meaning "flesh") and *penia* (meaning "loss"), was proposed by Irwin Rosenberg in 1988 to describe an age-related loss of muscle mass and function [1]. Sarcopenia predicted functional decline, disability, hospitalization, mortality and increased health costs in older adults in the general population [2–4]. The prevalence of sarcopenia in the general older adult population ranged from 10% to 30% [2].

Sarcopenia is appreciated to be an important phenomenon among older people living with HIV (PLWH) [5]. The pooled prevalence of sarcopenia among PLWH was 24% in a recent meta-analysis, and PLWH had a six-fold increased risk of sarcopenia compared with matched HIV-uninfected controls [6]. Among PLWH, sarcopenia was associated with demographic

and HIV-related factors, including age, sex, education, employment status, smoking, alcohol use, longer duration of HIV infection, CD4 count and longer exposure to anti-retroviral therapy [6–8]. Among PLWH, sarcopenia was associated with functional impairment, disability and mortality risk [8, 9]. At present, there is a paucity of data evaluating the prevalence and risk factors of sarcopenia among Asian PLWH [6, 8].

Since the development of the first consensus definition of sarcopenia in 2009 [2], definitions of sarcopenia have evolved as new evidence emerged. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP1) defined sarcopenia as low muscle mass together with either low muscle strength or low physical performance [10]. A revised version in 2018 (EWGSOP2) focused on low muscle strength, while confirming the diagnosis by low muscle quantity or quality, and defining severe sarcopenia with the additional presence of poor physical performance [11]. In 2014, the Asia Working Group for Sarcopenia (AWGS-2014) defined sarcopenia as low muscle mass plus either weak handgrip strength or slow gait speed [12]. An updated version in 2019 (AWGS-2019) retained the original definition of "loss of skeletal muscle mass plus loss of muscle strength and/or reduced physical performance" and added the category of "severe sarcopenia," which included all three components [13]. In AWGS-2019, the thresholds for handgrip strength and gait speed were lowered, measures of physical performance were expanded to include a Short Physical Performance Battery (SPPB) and a five-time chair stand test [12, 13].

Currently, there are no data comparing the AWGS-2014 and AWGS-2019 definitions of sarcopenia among PLWH in Asia. It is uncertain which definition of sarcopenia would be more applicable in PLWH. Therefore, we performed this study to determine the prevalence and risk factors of sarcopenia among PLWH living in Hong Kong SAR, China, and the correlation between different definitions of sarcopenia and health outcomes.

2 | METHODS

2.1 | Study design and setting

We performed an observational cross-sectional study involving PLWH recruited from January 2018 to November 2021 at the Prince of Wales Hospital Infectious Diseases clinic in Hong Kong. This clinic received referrals from other HIV clinics for screening or management of chronic comorbidities in PLWH. Inclusion criteria were positive HIV antibody and age of 35 years old or above. The only exclusion criterion was the refusal to consent. The study protocol was approved by the Joint Chinese University of Hong Kong—New Territories East Cluster Clinical Research Ethics Committee.

2.2 | Data collection

We recorded demographic and clinical information for all participants at each study visit. This included date of birth, sex, smoking, alcohol intake, comorbidities included in Charlson's Comorbidity Index, hepatitis B and C co-infection, year of diagnosis of HIV, history of AIDS-defining illness, current and previous anti-retroviral drug regimens, medications other than anti-retroviral drugs, current CD4 count, CD4:CD8 ratio and HIV RNA level. We defined multimorbidity as the presence of two or more chronic comorbidities, and polypharmacy as taking five or more non-anti-retroviral drugs.

During the study visit, we measured handgrip strength, gait speed, chair stand test and SPPB. We measured handgrip strength three times for both hands, using Jamar Hydraulic Hand dynamometer (5030J1, Sammons Preston, Bolingbrook, IL), with the participant sitting with 90° elbow flexion. The best performance of all trials was used for analyses. We calculated gait speed by measuring the average time of two trials taken to walk 6 metres at a normal pace, using a stopwatch. We performed the chair stand test by measuring the time taken to perform five chair stands. We performed SPPB, which included the ability to stand for up to 10 seconds with feet positioned in side-by-side, semi-tandem and tandem positions, usual gait speed and five-time chair stand test [14]. All participants underwent dual-energy X-ray absorptiometry using the Hologic QDR 4500A fan-beam densitometer (Hologic, Inc., Bedford, MA) to measure appendicular skeletal muscle mass, which was adjusted by body height.

2.3 | Definition of sarcopenia

We defined sarcopenia using AWGS-2014 and AWGS-2019 criteria. AWGS-2014 defines sarcopenia as the presence of low muscle mass (height-adjusted muscle mass <7 kg/m^2 in men and <5.4 kg/m^2 in women) plus weak handgrip strength (<25 kg in men and <18 kg in women) and/or slow gait speed (≤0.8 m/second) [12]. AWGS-2019 defines sarcopenia as low muscle mass (cut-offs as above) plus low muscle strength or physical performance, while the presence of all three components defines severe sarcopenia. Low muscle strength is defined as handgrip strength <28 kg for men and <18 kg for women, and low physical performance as gait speed <1 m/second, SPPB score ≤9 or five-time chair stand test ≥12 seconds [13].

2.4 | Outcome measures

We measured the following health outcomes: health-related quality of life (QOL) and functional disability. We measured health-related QOL by the EuroQOL 5-dimensional 5-Level questionnaire (EQ-5D-5L) and 36-item Short Form Health Survey (SF-36). The EQ-5D-5L questionnaire contains five dimensions of QOL: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each of these dimensions is graded as "no problem," "slight problem," "moderate problem," "severe problem" and "extreme problem." Participants with any severity of the problem in a particular dimension were considered as having a problem with that dimension. The EQ-5D-5L index was converted from the EQ-5D-5L health states using an established Hong Kong value set by weighting each participant's self-report health status to a single preference-based health index [15]. The EuroQOL Visual Analogue Scale (EQ-VAS) is the self-reported overall health perception of the participants, recording their self-rated health on a vertical scale from 0 (the worst health) to 100 (the best health) scale.

Participants also completed the Chinese (Hong Kong) version of SF-36 [16], which covers eight health domains, including physical function, role limitations related to physical health, bodily pain, mental health, and role limitations related to emotional health, social functioning, vitality and general health. The eight domain scores were summarized into two summary scores: the physical component summary (PCS) and the mental component summary scores. Higher scores indicate better QOL.

Functional disability was defined as an impairment in any domains of activities of daily living (ADL) or instrumental ADL (IADL) [17]. We measured ADL by means of the Katz Index [18] and IADL by Lawton Instrumental Activities of Daily Living (IADL) [19]. The Katz Index assesses dependence or independence concerning six essential functions of ADL (feeding, continence, bathing, transferring, toileting and dressing). Each domain is scored from 0 (independence) to 6 (total dependence). The Lawton IADL scale measures eight domains of function (ability to use telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medications and the ability to handle finances). Requirement of any assistance in any domain was considered as having impairment in ADL or IADL.

2.5 | Statistical analysis

We presented descriptive statistics as number (percentage), mean ± standard deviation or median (interquartile range/IQR), as appropriate. We determined agreement between the different definitions of sarcopenia and severe sarcopenia using Cohen's kappa test. Kappa was interpreted as poor if value was < 0.20, fair if 0.21–0.4, moderate if 0.41–0.60, good if 0.61–0.80 and very good if 0.81–1.00 [20]. We compared baseline demographic and clinical variables between those with and without sarcopenia or severe sarcopenia according to different definitions using chi-square, Student's *t* and Mann–Whitney U test, as appropriate. Age, sex and variables identified to be associated with each definition of sarcopenia in the above univariate analyses were included in multivariable binary logistic stepwise regression models, to determine the variables that were independently associated with each definition of sarcopenia and severe sarcopenia. For each regression analysis, collinearity was assessed using the variance inflation factor.

Associations between different definitions of sarcopenia or severe sarcopenia and disability and health-related QOL measures were determined using the chi-square test and Student's *t*-test, as appropriate. The logistic regression model for binary outcome measure and linear regression model for continuous outcome measure were used to determine the association between sarcopenia and these outcomes in multivariable models. The associations between each definition of sarcopenia and the outcome measures were determined in two multivariable models: model 1 adjusted for age and sex, and model 2 adjusted for age, sex and variables with significant independent association with each definition of sarcopenia. Correlation between different components included in the definitions of sarcopenia and disability and health-related QOL measures were determined using logistic regression for binary outcome measures and linear regression analyses for continuous outcome measures. Statistical significance was defined as a *p*-value less than 0.05. Statistical analyses were conducted using SPSS (IBM version 26).

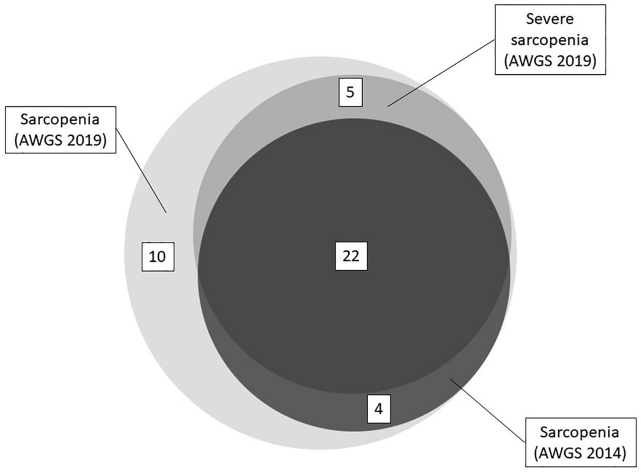

Figure 1. Venn diagram showing the number of participants with sarcopenia and severe sarcopenia diagnosed by AWGS-2014 and 2019 definitions. Abbreviation: AWGS, Asia Working Group for Sarcopenia.

3 | RESULTS

One hundred and fifty-six PLWH who were followed up in the clinic were invited to participate in this study, six refused to consent, and 150 participants were recruited. The mean age was 60±10 years, 88.0% were male, 98.7% were Chinese and the median (IQR) duration of HIV diagnosis was 13 [8–18] years. All participants were receiving antiretroviral therapy, with a current CD4 count of 574 (362–762) cells/mm^3, and 94% having undetectable HIV RNA (<20 copies/ml). Multimorbidity and polypharmacy were present in 45% and 43% of participants, respectively. The baseline demographic and clinical characteristics are shown in Table 1.

Among all participants, 26 (17.3%) and 41 (27.3%) had sarcopenia as defined by AWGS-2014 and AWGS-2019 criteria, respectively, while 27 (18.0%) had severe sarcopenia according to AWGS-2019 criteria (Figure 1). Among the 41 participants diagnosed to have sarcopenia by AWGS-2019 definition, all had low muscle mass, 31 (75.6%) had low muscle strength, with an additional number of 10 (24.4%) participants having low physical performance alone. Agreement between AWGS-2014 and 2019 definitions of sarcopenia was good (kappa 0.716), and so was agreement between AWGS-2014 definition of sarcopenia and severe sarcopenia defined by AWGS-2019 definition (kappa 0.794).

Both definitions of sarcopenia and severe sarcopenia were associated with older age, lower level of education, lack of employment, lower CD4 count, higher Charlson's comorbidity index, multimorbidity and polypharmacy. On multivariable analyses, sarcopenia defined by AWGS-2014 was independently associated with age, education and polypharmacy, while sarcopenia defined by AWGS-2019 was independently associated with age (Table 1 and Tables S1–S3).

Table 1. Baseline characteristics of all participants and participants with sarcopenia

Variables	All participants *N* = 150	AWGS-2014			AWGS-2019					
		Sarcopenia *n* = 26	No sarcopenia *n* = 124	*p*[a]	Sarcopenia *n* = 41	No sarcopenia *n* = 109	*p*[b]	Severe sarcopenia *n* = 27	No severe sarcopenia *n* = 123	*p*[c]
Age (years)[d]	60.3 ± 9.6	69.4 ± 7.6	58.4 ± 8.8	<0.001*	66.6 ± 8.9	57.9 ± 8.7	<0.001*	69.6 ± 7.8	58.3 ± 8.7	<0.001*
Male[e]	132 (88.0%)	22 (84.6%)	110 (88.7%)	0.519	35 (85.4%)	97 (89.0%)	0.577	23 (85.2%)	109 (88.6%)	0.743
Smoker[e]	22 (14.7%)	5 (19.2%)	17 (13.7%)	0.541	9 (22.0%)	13 (11.9%)	0.122	7 (25.9%)	15 (12.2%)	0.078
Alcohol intake ≥twice per month[e]	19 (12.7%)	3 (11.5%)	16 (12.9%)	1.000	4 (9.8%)	15 (13.8%)	0.511	3 (11.1%)	16 (13.0%)	1.000
Secondary education or above[e]	120 (80.0%)	12 (46.2%)	108 (87.1%)	<0.001*	26 (63.4%)	94 (86.2%)	0.002	14 (51.9%)	106 (86.2%)	<0.001
No employment[e]	71 (47.3%)	19 (73.1%)	52 (41.9%)	0.004	26 (63.4%)	45 (41.3%)	0.016	20 (74.1%)	51 (41.5%)	0.002
Duration of HIV diagnosis (years)[f]	12.7 (7.6–17.9)	13.4 (7.6–19.5)	12.7 (7.6–17.8)	0.827	15.8 (9.7–19.7)	12.3 (7.3–16.7)	0.044	14.4 (8.9–19.1)	12.7 (7.6–17.7)	0.430
History of AIDS-defining illness[e]	62 (41.3%)	13 (50.0%)	49 (39.5%)	0.324	18 (43.9%)	44 (40.4%)	0.695	14 (51.9%)	48 (39.0%)	0.220
Current CD4 count (cells/mm^3)[f]	574 (362–762)	362 (252–580)	601 (404–792)	0.001	413 (289–640)	597 (404–790)	0.022	353 (258–574)	601 (405–805)	<0.001*
Current CD4:CD8 ratio[f]	0.74 (0.50–1.08)	0.59 (0.38–0.95)	0.78 (0.58–1.12)	0.063	0.67 (0.42–0.94)	0.81 (0.56–1.13)	0.085	0.58 (0.39–0.76)	0.80 (0.57–1.13)	0.016
HIV RNA <50 copies/ml[e]	141 (94.0%)	25 (96.2%)	116 (93.5%)	1.000	40 (97.6%)	101 (92.7%)	0.445	26 (96.3%)	115 (93.5%)	1.000
Exposure to zidovudine[e]	44 (29.3%)	7 (26.9%)	37 (29.8%)	0.767	11 (26.8%)	33 (30.3%)	0.680	8 (29.6%)	36 (29.3%)	0.970
Exposure to stavudine[e]	41 (27.3%)	11 (42.3%)	30 (24.2%)	0.060	18 (43.9%)	23 (21.1%)	0.005	13 (48.1%)	28 (22.8%)	0.007
Hepatitis B infection[e]	14 (9.5%)	4 (15.4%)	10 (8.2%)	0.271	5 (12.2%)	9 (8.4%)	0.534	4 (14.8%)	10 (8.3%)	0.287
Hepatitis C infection[e]	9 (6.1%)	1 (3.8%)	8 (6.6%)	1.000	3 (7.3%)	6 (5.6%)	0.708	1 (3.7%)	8 (6.6%)	1.000

(*Continued*)

Table 1. (Continued)

Variables	All participants N = 150	AWGS-2014			AWGS-2019					
		Sarcopenia n = 26	No sarcopenia n = 124	p[a]	Sarcopenia n = 41	No sarcopenia n = 109	p[b]	Severe sarcopenia n = 27	No severe sarcopenia n = 123	p[c]
Charlson's comorbidity index[f]	2 (1–4)	4 (3–4)	2 (1–3)	<0.001	3 (2–4)	2 (1–3)	<0.001	4 (3–4)	2 (1–3)	<0.001
Multimorbidity[e,g]	67 (44.7%)	18 (69.2%)	49 (39.5%)	0.006	25 (61.0%)	42 (38.5%)	0.014	18 (66.7%)	49 (39.8%)	0.011
Polypharmacy[e,h]	64 (42.7%)	20 (76.9%)	44 (35.5%)	<0.001*	26 (63.4%)	38 (34.9%)	0.002	20 (74.1%)	44 (35.8%)	<0.001*
Moderate to severe depression[e,i]	16 (10.7%)	1 (3.8%)	15 (12.1%)	0.308	3 (7.3%)	13 (11.9%)	0.559	1 (3.7%)	15 (12.2%)	0.306
Appendicular skeletal muscle mass (kg/m^2)[d]	7.11 ± 1.23	5.98 ± 0.82	7.36 ± 1.17	<0.001	5.99 ± 0.78	7.55 ± 1.09	<0.001	5.97 ± 0.80	7.37 ± 1.17	<0.001
Handgrip strength (kg)[d]	29.3 ± 8.9	21.6 ± 6.3	30.9 ± 8.5	<0.001	23.5 ± 5.9	31.5 ± 8.9	<0.001	21.3 ± 4.9	31.1 ± 8.6	<0.001
6-metre walk gait speed (m/second)[d]	1.06 ± 0.22	0.83 ± 0.19	1.11 ± 0.20	<0.001	0.90 ± 0.20	1.12 ± 0.20	<0.001	0.86 ± 0.20	1.11 ± 0.20	<0.001
Five-time chair stand test (second)[d]	11.6 ± 4.0	14.9 ± 5.4	11.0 ± 3.4	<0.001	13.5 ± 4.8	10.9 ± 3.5	<0.001	14.6 ± 5.3	11.0 ± 3.4	<0.001
Short Physical Performance Battery[f]	11 (10–12)	9 (8–10)	12 (11–12)	<0.001	10 (8–11)	12 (11–12)	<0.001	10 (8–10.5)	12 (11–12)	<0.001

[a]Comparison between those with and without sarcopenia according to AWGS 2014 criteria.
[b]Comparison between those with and without sarcopenia according to AWGS 2019 criteria.
[c]Comparison between those with and without severe sarcopenia according to AWGS 2019 criteria.
[d]Data presented in mean ± standard deviation.
[e]Data presented in number (percentage).
[f]Data presented in median (25th percentile–75th percentile).
[g]Multimorbidity is defined as the presence of two or more chronic comorbidities.
[h]Polypharmacy is defined as taking five or more non-anti-retroviral drugs.
[i]Moderate to severe depression is defined as a PHQ-9 score of ≥10.
*$p = 0.05$ on multivariable binary logistic regression model (Details are presented in Tables S1–S3).
Abbreviation: AWGS, Asia Working Group for Sarcopenia.

The associations between different definitions of sarcopenia and various health outcomes are presented in Table 2. Sarcopenia defined by AWGS-2014 criteria and severe sarcopenia defined by AWGS-2019 criteria were associated with problems with mobility, physical functioning domain and PCS of SF-36. Both definitions of sarcopenia and severe sarcopenia were associated with problems with usual activities and impairment in IADL.

As for the individual components of the definitions of sarcopenia, muscle mass was not associated with any of the health outcomes, while handgrip strength, five-time chair stand test, gait speed and SPPB score were associated with one or more of the health outcomes, including EQ-5D-5L index, several EQ-5D-5L domains, physical functioning and PCS of SF-36, and impaired ADL and IADL (Table S4). Moreover, the different cut-offs for handgrip strength, gait speed and criteria for low physical performance in the AWGS-2014 and AWGS-2019 definitions had similar correlations with these health outcome measures (Tables S5a and 5b).

One or more of the definitions of sarcopenia were associated with a problem with mobility, a problem with usual activities, physical functioning, PCS and impairment in IADL, in the unadjusted and/or adjusted models. The other health outcomes did not show a significant correlation with any of the sarcopenia definitions. Table 3 shows the significant associations between various definitions of sarcopenia and health outcomes. Both sarcopenia defined by AWGS-2014 and severe sarcopenia retained an association with a problem with mobility and usual activities, impairment in IADL and PCS, after adjusting for age and sex. Both definitions of sarcopenia and severe sarcopenia were independently associated with impairment in IADL in the fully adjusted models. Sarcopenia defined by AWGS-2019 had a trend of association with the EQ-5D-5L index and PCS of SF-36.

4 | DISCUSSION

In this study, we aimed to determine the prevalence of sarcopenia using the two AWGS definitions and whether health outcomes were associated with these definitions of sarcopenia among Asian PLWH. The prevalence of sarcopenia defined by AWGS-2014 and AWGS-2019 and severe sarcopenia was 17.3%, 27.3% and 18.0%, respectively. Different definitions of sarcopenia were independently associated with age, education level, current CD4 count and/or polypharmacy. The AWGS-2014 definition of sarcopenia and severe sarcopenia defined by AWGS-2019 was associated with more health-related QOL outcome measures, while both definitions of sarcopenia and severe sarcopenia were associated with functional disability.

A recent meta-analysis revealed that PLWH had a 13% pooled prevalence of sarcopenia when using both muscle mass and muscle function to define sarcopenia [6]. Few studies have been performed in Asian populations to evaluate the prevalence of sarcopenia among PLWH [6]. Two studies performed in India defined sarcopenia using low muscle mass alone showing a prevalence of 40% in middle-aged men [21] and 18% in pre-menopausal women [22]. In one study performed in Malaysia, involving predominantly Chinese PLWH, the prevalence of sarcopenia (defined by AWGS-2014 criteria) was 8%, while the prevalence in a subgroup of PLWH older than 50 years was 17% [8].

Studies performed in the general Asian older adult populations with a large sample size revealed a consistent prevalence of sarcopenia ranging from 6% to 12% using the AWGS-2014 criteria [13, 23], while more recent studies using AWGS-2019 criteria demonstrated the prevalence of sarcopenia ranging from 11% to 18% [24, 25]. Our findings supported previous evidence showing a higher prevalence of sarcopenia among PLWH compared with matched HIV-uninfected populations [6, 8, 21, 22, 26].

We have identified older age, lower education level, lower current CD4 count and presence of polypharmacy as risk factors associated with sarcopenia. Older age, lower education level and lower CD4 count have previously been shown to correlate with sarcopenia or low muscle mass [6, 8, 27, 28]. On the other hand, the correlation between polypharmacy and sarcopenia was less well studied among PLWH. In a recent scoping review evaluating the relationship between sarcopenia and polypharmacy in the general population, polypharmacy and the number of medications were independently associated with sarcopenia in community-dwelling older adults in the majority of studies [29]. One longitudinal study in Japan demonstrated polypharmacy as an independent predictor of new-onset sarcopenia over a 5-year follow-up period [30]. Possible explanations include direct muscle toxicities via mitochondrial and metabolic pathways of multiple classes of medications and indirect mechanisms involving poor nutrition and reduced physical activity due to polypharmacy [31]. Moreover, the rate of polypharmacy is higher in those with comorbidity [32, 33]. Polypharmacy can be an indirect marker of increased comorbidity, which is also a risk factor for sarcopenia.

We observed a higher prevalence of sarcopenia when the AWGS-2019 definition was adopted, as compared with the AWGS-2014 definition. Similar observations were made in non-HIV-infected populations in Asia [24]. AWGS-2019 definition has more lenient cut-offs for defining weak handgrip strength and slow gait speed, and includes additional criteria of chair stand test and SPPB in defining physical performance. These changes resulted in more PLWH fulfilling the diagnosis of sarcopenia under the AWGS-2019 definition.

With the changes in the criteria defining sarcopenia, it would be important to determine which is the more appropriate definition to be adopted in PLWH [20]. To evaluate this issue, we determined the correlation between different definitions of sarcopenia and health outcomes, including disability and QOL.

EQ-5D-5L and SF-36 were both commonly used instruments for the assessment of QOL among individuals with sarcopenia in the general population. For example, in determining the construct validity of a sarcopenia-specific QOL measure, it was shown to have a positive correlation with both the EQ-5D-5L index as well as individual domain scores of these tools, including physical functioning of SF-36 and the domains of mobility and usual activities in EQ-5D-5L [34]. Therefore, these measures of both collective scores and individual domains will be useful in reflecting QOL among people with sarcopenia. In general populations of older adults, sarcopenia was associated with reduced health-related QOL, as

Table 2. Disability and quality of life measures of all participants and participants with sarcopenia

Variables	All participants $N = 150$	AWGS-2014			AWGS-2019					
		Sarcopenia $n = 26$	No sarcopenia $n = 124$	p^a	Sarcopenia $n = 41$	No sarcopenia $n = 109$	p^b	Severe sarcopenia $n = 27$	No severe sarcopenia $n = 123$	p^c
EQ-5D-5L index[d]	0.87 ± 0.17	0.83 ± 0.15	0.88 ± 0.17	0.208	0.83 ± 0.19	0.88 ± 0.16	0.092	0.83 ± 0.15	0.88 ± 0.17	0.196
EQ-VAS[d]	76.9 ± 14.24	75.7 ± 14.8	77.1 ± 14.2	0.649	75.9 ± 15.4	77.2 ± 13.8	0.627	74.7 ± 15.5	77.3 ± 14.0	0.388
EQ-5D-5L domains										
Problem with mobility[e]	20 (13.3%)	9 (34.6%)	11 (8.9%)	0.002	9 (22.0%)	11 (10.1%)	0.057	9 (33.3%)	11 (8.9%)	0.002
Problem with self-care[e]	7 (4.7%)	1 (3.8%)	6 (4.8%)	1.000	3 (7.3%)	4 (3.7%)	0.392	2 (7.4%)	5 (4.1%)	0.610
Problem with usual activities[e]	18 (12.0%)	8 (30.8%)	10 (8.1%)	0.004	10 (24.4%)	8 (7.3%)	0.009	8 (29.6%)	10 (8.1%)	0.005
Pain or discomfort[e]	81 (54.0%)	18 (69.2%)	63 (50.8%)	0.087	26 (63.4%)	55 (50.5%)	0.156	17 (63.0%)	64 (52.0%)	0.302
Anxiety or depression[e]	59 (39.3%)	9 (34.6%)	50 (40.3%)	0.588	17 (41.5%)	42 (38.5%)	0.743	11 (40.7%)	48 (39.0%)	0.869
SF-36 domain scores										
Physical functioning[d]	84.2 ± 17.2	77.3 ± 18.7	85.7 ± 16.6	0.024	80.5 ± 20.0	85.6 ± 15.9	0.105	77.0 ± 18.0	85.8 ± 16.7	0.016
Role limitations due to physical health[d]	74.8 ± 38.6	63.5 ± 44.3	77.2 ± 37.0	0.149	67.1 ± 42.7	77.8 ± 36.7	0.131	63.9 ± 45.1	77.2 ± 36.8	0.160
Role limitations due to emotional problems[d]	74.9 ± 39.4	67.9 ± 45.7	76.3 ± 38.0	0.388	71.5 ± 42.5	76.1 ± 38.2	0.525	74.1 ± 41.7	75.1 ± 39.0	0.906
Vitality[d]	64.8 ± 19.4	63.3 ± 20.8	65.1 ± 19.2	0.660	64.6 ± 21.0	64.9 ± 18.9	0.949	64.6 ± 20.6	64.8 ± 19.3	0.960
Emotional wellbeing[d]	71.8 ± 18.6	72.2 ± 19.5	71.7 ± 18.5	0.906	71.0 ± 20.0	72.0 ± 18.1	0.767	73.5 ± 18.9	71.4 ± 18.6	0.597
Social functioning[d]	83.8 ± 21.1	84.6 ± 20.4	83.7 ± 21.3	0.836	83.8 ± 22.9	71.0 ± 20.0	0.998	85.6 ± 20.1	83.4 ± 21.4	0.623
Bodily pain[d]	75.4 ± 23.2	69.5 ± 24.2	76.6 ± 22.9	0.159	70.1 ± 26.0	77.3 ± 21.8	0.087	71.8 ± 25.2	76.1 ± 22.8	0.376
General health[d]	53.7 ± 18.3	52.1 ± 17.9	54.0 ± 18.4	0.628	53.7 ± 17.4	53.7 ± 18.7	0.986	52.8 ± 17.8	53.9 ± 18.4	0.773
Physical component score[d]	45.2 ± 10.9	40.8 ± 12.0	46.1 ± 10.5	0.022	42.5 ± 12.4	46.2 ± 10.2	0.066	40.7 ± 11.9	46.1 ± 10.5	0.019
Mental component score[d]	51.0 ± 12.1	51.7 ± 11.5	50.9 ± 12.2	0.747	51.3 ± 11.8	50.9 ± 12.2	0.873	53.1 ± 10.7	50.6 ± 12.3	0.327
Disability										
Impaired ADL[e]	3 (2.0%)	1 (3.8%)	2 (1.6%)	0.437	1 (2.4%)	2 (1.8%)	1.000	1 (3.7%)	2 (1.6%)	0.451
Impaired IADL[e]	16 (10.7%)	7 (26.9%)	9 (7.3%)	0.008	9 (22.0%)	7 (6.4%)	0.014	6 (22.2%)	10 (8.1%)	0.043

[a]Comparison between those with and without sarcopenia according to AWGS 2014 criteria.
[b]Comparison between those with and without sarcopenia according to AWGS 2019 criteria.
[c]Comparison between those with and without severe sarcopenia according to AWGS 2019 criteria.
[d]Data presented in mean ± standard deviation.
[e]Data presented in number (percentage).
Abbreviation: AWGS, Asia Working Group for Sarcopenia.

Table 3. Association between sarcopenia by different criteria and selected health outcomes[a,b]

Health outcomes	AWGS 2014			AWGS 2019			Severe sarcopenia		
	Unadjusted odds ratio (95% confidence interval), *p*-value	**Model 1[c]**	**Model 2[d]**	**Unadjusted odds ratio (95% confidence interval), *p*-value**	**Model 1[c]**	**Model 2[d]**	**Unadjusted odds ratio (95% confidence interval), *p*-value**	**Model 1[c]**	**Model 2[d]**
Problem with mobility	**5.439 (1.965–15.050), $p = 0.001$**	**5.439 (1.965–15.050), $p = 0.001$**	2.948 (0.943–9.212), $p = 0.063$	2.506 (0.953–6.591), $p = 0.063$	1.618 (0.552–4.740), $p = 0.380$	1.618 (0.552–4.740), $p = 0.380$	**5.091 (1.851–14.003), $p = 0.002$**	**5.091 (1.851–14.003), $p = 0.002$**	**3.645 (1.256–10.576), $p = 0.017$**
Problem with usual activities	**5.067 (1.766–14.540), $p = 0.003$**	**5.067 (1.766–14.540), $p = 0.003$**	**3.178 (1.040–9.708), $p = 0.042$**	**4.073 (1.479–11.216), $p = 0.007$**	**4.073 (1.479–11.216), $p = 0.007$**	**4.073 (1.479–11.216), $p = 0.007$**	**4.758 (1.667–13.583), $p = 0.004$**	**4.758 (1.667–13.583), $p = 0.004$**	2.004 (0.630–6.369), $p = 0.239$
Impaired IADL	**4.708 (1.566–14.150), $p = 0.006$**	**5.237 (1.697–16.161), $p = 0.004$**	**5.237 (1.697–16.161), $p = 0.004$**	**4.098 (1.413–11.883), $p = 0.009$**	**4.451 (1.512–13.103), $p = 0.007$**	**4.451 (1.512–13.103), $p = 0.007$**	**3.229 (1.060–9.837), $p = 0.039$**	**3.494 (1.123–10.875), $p = 0.031$**	**3.494 (1.123–10.875), $p = 0.031$**
Health outcomes	Unadjusted unstandardized beta coefficient, *p*-value	Model 1[e]	Model 2[f]	Unadjusted unstandardized beta coefficient, *p*-value	Model 1[e]	Model 2[f]	Unadjusted unstandardized beta coefficient, *p*-value	Model 1[e]	Model 2[f]
EQ-5D-5L index	−0.046, $p = 0.208$	−0.046, $p = 0.208$	−0.023, $p = 0.586$	−0.052, $p = 0.092$	−0.052, $p = 0.092$	−0.052, $p = 0.092$	−0.046, $p = 0.196$	−0.046, $p = 0.196$	−0.032, $p = 0.428$
Physical functioning	**−8.337, $p = 0.024$**	−4.719, $p = 0.243$	0.673, $p = 0.869$	−5.109, $p = 0.105$	−1.856, $p = 0.583$	−1.856, $p = 0.583$	**−8.735, $p = 0.016$**	−5.181, $p = 0.197$	−2.040, $p = 0.613$
Physical component score	**−5.342, $p = 0.022$**	**−5.342, $p = 0.022$**	−1.305, $p = 0.618$	−3.661, $p = 0.066$	−3.661, $p = 0.066$	−3.661, $p = 0.066$	**−5.412, $p = 0.019$**	**−5.412, $p = 0.019$**	−2.287, $p = 0.346$

[a]Health outcomes with significant association with one or more definitions of sarcopenia on univariate analysis are presented in this table.
[b]Associations with *p*-value < 0.05 were presented in bold type.
[c]Model 1 shows the odds ratio, adjusted for age and sex.
[d]Model 2 shows the odds ratio adjusted for age, sex and all variables with significant independent association with sarcopenia.
[e]Model 1 shows the beta coefficient, adjusted for age and sex.
[f]Model 2 shows an unstandardized beta coefficient, adjusted for age, sex and all variables with significant independent association with sarcopenia.
Abbreviation: AWGS, Asia Working Group for Sarcopenia.

Luk FWL et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25988
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25988/full | https://doi.org/10.1002/jia2.25988

measured by EQ-5D-5L index [35–37] and domains of mobility, self-care, usual activity [35–37] and physical functioning [38–40]. The findings of our study population of PLWH were consistent with these observations.

The AWGS-2014 sarcopenia definition and severe sarcopenia in AWGS-2019 identified individuals with the most severe loss of muscle mass and function. Therefore, not unexpectedly, participants with sarcopenia in these two categories in our study had the most correlation with parameters associated with worse physical health-related QOL. In other words, these two definitions were able to identify individuals with the highest risk of poor health outcomes, and evidence-based interventions for sarcopenia to prevent future disability are urgently required for these individuals [41].

On the other hand, it is uncertain whether the less stringent AWGS-2019 definition of sarcopenia would include individuals who are in fact not at risk for poor health outcomes. We observed that the AWGS-2019 definition correlated with impairment in IADL and had a trend of correlation with poorer health-related QOL. The lower thresholds of handgrip strength, gait speed and physical performance in AWGS-2019 also had similar correlations with health outcome measures as the higher thresholds adopted in AWGS-2014 (Tables S5a and 5b). This suggested that these revised criteria for defining sarcopenia can potentially contribute to the early identification of PLWH at risk of functional disability, without over-diagnosing sarcopenia in low-risk individuals. These changes in AWGS sarcopenia definition can foster sarcopenia prevention and treatment programmes among PLWH. Implementing interventions at an early stage for the treatment of sarcopenia can potentially improve their QOL and avoid the development of disability in the future. We suggest that future research involving longitudinal study design and a larger sample size should be conducted to evaluate the correlation of incidence of poor health outcomes, including functional disability, hospitalization and mortality, with the revised definition of sarcopenia among Asian populations of PLWH.

The increase in the prevalence of sarcopenia with the changes in AWGS definitions was in contrast to a reduction in the prevalence of sarcopenia among PLWH with the change from EWGSOP1 to EWGSOP2 [20]. This reduction was partly due to more conservative cut-offs for the determination of low muscle strength and low muscle mass in EWGSOP2. Moreover, in EWGSOP2, physical performance was only adopted to define severe sarcopenia but not sarcopenia, while AWGS-2019 expanded the measures for physical performance to define sarcopenia. There were concerns with these changes in the revised EWGSOP2 criteria, which would limit its use in identifying at-risk PLWH with sarcopenia and prevent the implementation of early interventions for the avoidance of progression to disability [20, 42]. Our findings supported both AWGS and EWGSOP guidelines in including both muscle mass and muscle strength in defining sarcopenia. While muscle mass was not associated with any of the health outcome measures, muscle strength, as represented by handgrip strength and/or five-time chair stand test, correlated with several measures of QOL and disability. On the other hand, measures of physical performance, including gait speed and SPPB, correlated with even more health outcome measures (Table S4). These parameters had also been shown to predict mortality among PLWH [43, 44]. Our findings, therefore, supported AWGS-2019 in including the presence of either muscle strength or physical performance in the definition of sarcopenia. Monitoring of these parameters in older PLWH is important in the clinical setting to identify individuals who would benefit from interventions to improve physical function.

There are some limitations to our study. Firstly, we included a relatively small sample size involving PLWH of Chinese ethnicity. The results may not be generalizable to other Asian populations of PLWH. Secondly, this was a cross-sectional study, thus we could not make conclusions around the causation of the risk factors associated with sarcopenia. Likewise, a longitudinal study in the future will be needed to determine whether an early diagnosis of sarcopenia with the AWGS-2019 definition can be adopted to predict incident disability and other health outcomes. Longitudinal studies would also allow the determination of the impact of different interventions in treating sarcopenia on a decline in physical function and development of disability. Thirdly, the thresholds used to define low muscle mass, weak handgrip strength, slow gait speed and low physical performance were derived from older HIV-uninfected adults for AWGS definition. It is likely that this may under-estimate the true prevalence of sarcopenia among our cohort of PLWH, who had a younger chronological age. Future studies involving age- and sex-matched HIV-uninfected controls to determine the prevalence of sarcopenia among PLWH would be important. Moreover, we did not include a gold standard for measuring muscle mass (e.g. computed tomography scan [45]), this limited our determination of sensitivity and specificity of each definition of sarcopenia against a reference standard.

5 | CONCLUSIONS

Among this sample of Chinese PLWH, the AWGS-2019 definition identified a higher prevalence of sarcopenia compared with the AWGS-2014 definition. While the AWGS-2014 definition and severe sarcopenia defined by the AWGS-2019 criteria correlated with the most parameters of poorer health-related QOL, the AWGS-2019 definition could potentially identify early-risk individuals who may benefit from early interventions to prevent future disability.

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COMPETING INTERESTS

GL has received research grants and consultancy fees from Gilead Sciences, MSD and ViiV.

AUTHORS' CONTRIBUTIONS

FWLL: data collection, data analysis, writing original draft, review and edit writing. TL, HYH and YYC: data collection and review writing. SKC and VW: data collection, data analysis and review writing. TCYK: conceptualization, methodology and review writing. GL: conceptualization, methodology, data collection, data analysis,

writing original draft, review and edit writing, supervision. All authors have read and approved the final manuscript.

ACKNOWLEDGEMENTS

We would like to acknowledge Janssen, a division of Johnson & Johnson (HK) Ltd, for supporting part of the DXA tests for participants of this study.

FUNDING

This study was supported by the Hong Kong AIDS Trust Fund (MSS 319R).

DATA AVAILABILITY STATEMENT

The data used or analysed during this study are available from the corresponding author on reasonable request.

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SUPPORTING INFORMATION

Additional information may be found under the Supporting Information tab for this article:

Table S1. Multivariate regression analyses of variables associated with AWGS 2014 definition of sarcopenia.

Table S2. Multivariate regression analyses of variables associated with AWGS 2019 definition of sarcopenia.

Table S3. Multivariate regression analyses of variables associated with severe sarcopenia (AWGS 2019).

Table S4. Correlations between muscle mass, muscle strength and physical performance parameters and health-related quality of life and disability.

Table S5a. Correlations between different cutoffs of muscle strength (handgrip strength) and gait speed and health-related quality of life and disability.

Table S5b. Correlations between different cutoffs of five chair stand test, short physical performance battery (SPPB) and physical performance parameters and health-related quality of life and disability.

Mwangala PN et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25977
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25977/full | https://doi.org/10.1002/jia2.25977

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Prevalence and factors associated with mild depressive and anxiety symptoms in older adults living with HIV from the Kenyan coast

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Abstract

Introduction: Empirical research on the burden and determinants of common mental disorders (CMDs), especially depression and anxiety, among older adults living with HIV (OALWH) in sub-Saharan Africa is inadequate. To bridge the gap in Kenya we: (1) determined the prevalence of CMDs among OALWH on routine HIV care compared to HIV-negative peers; (2) investigated HIV status as an independent predictor of CMDs in older adults; and (3) investigated CMD determinants.

Methods: In a cross-sectional study conducted between 2020 and 2021, the prevalence of CMDs and associated determinants were investigated at the Kenyan coast among 440 adults aged ≥50 years (257 OALWH). The Patient Health Questionnaire and Generalized Anxiety Disorder scale were administered alongside measures capturing biopsychosocial information. Logistic regression was used to examine the correlates of CMDs.

Results: No significant differences were found in the prevalence of mild depressive symptoms, 23.8% versus 18.2% ($p = 0.16$) and mild anxiety symptoms, 11.7% versus 7.2% ($p = 0.12$) among OALWH compared to HIV-negative peers, respectively. HIV status was not independently predictive of CMDs. Among OALWH, higher perceived HIV-related stigma, ageism, increasing household HIV burden, loneliness, increasing functional disability, sleeping difficulties, chronic fatigue and advanced age (>70 years) were associated with elevated CMDs. Among HIV-negative older adults, loneliness, increased medication burden and sleeping difficulties were associated with elevated depressive symptoms. Easier access to HIV care was the only factor associated with lower CMDs among OALWH.

Conclusions: On the Kenyan coast, the burden of moderate and severe CMDs among older adults is low; however, both OALWH and their HIV-negative peers have a similar relatively high burden of mild depressive and anxiety symptoms. Our results also suggest that determinants of CMDs among OALWH in this setting are predominantly psychosocial factors. These results highlight the need for psychosocial interventions (at the family, community and clinical levels) to mitigate the risks of mild CMDs as they are known to be potentially debilitating.

Keywords: common mental disorders; HIV infection; older adults; prevalence; correlates; Kenya

Additional information may be found under the Supporting Information tab of this article.

Received 26 January 2022; **Accepted** 31 July 2022

1 | INTRODUCTION

Common mental disorders (CMDs), especially depression and anxiety, are among the leading causes of disability worldwide [1, 2] and cost the global economy about US$1.2 trillion a year [3]. Notably, the global burden of both disorders has not reduced since 1990, despite compelling evidence of cost-effective interventions [4]. Efforts to address this substantial burden of CMDs should be directed at the most vulnerable in society, including older adults living with HIV (OALWH) residing in sub-Saharan Africa (SSA). In Kenya, the increasing population of OALWH [5] is experiencing an elevated incidence of chronic age-related conditions [6], all potentially resulting in an increase of CMDs.

The prevalence of depression among OALWH in SSA ranges from 6% to 59% [7] compared to 26% among their HIV-negative peers [8]. Outside SSA, estimates of depression among OALWH range from 19% to 45% in Asia [9, 10], 39%

to 90% in the United States [11, 12], 16% to 35% in Latin America and the Caribbean [13], and 28% in Europe [14]. Anxiety, on the other hand, ranges from 3% to 21% among OALWH in SSA [7] and 35% to 56% in high-income countries (HICs) [14, 15].

Understanding the determinants of CMDs among older adults is critical in designing and implementing contextually relevant mental health interventions. A recent review indicated that frequently reported determinants of depression among OALWH were mainly socio-demographic in nature [7]. Among psychosocial factors, HIV-related stigma [16], HIV status disclosure [16] and increasing disability scores have been associated with higher odds of depressive symptoms, while social support [17], resilience [16] and spirituality [17] have been shown to be protective factors. Biomedical and lifestyle factors, including alcohol use [17], current/former tobacco smoking [18] and back pain [19], have been associated with elevated levels of depression among OALWH. Among HIV-negative older adults in SSA, rural residence [20, 21], poor social network [20], living alone [22], being female [8, 20] and a lifetime of unskilled occupation [21] have been associated with elevated odds of depression. No study in SSA has examined the determinants of anxiety among OALWH.

Several reasons call for investigating depression and anxiety among older adults. Firstly, known risk factors for CMD, such as poverty, are more prevalent in older ages [23, 24]. Secondly, CMDs in late life are severely under-researched and underdiagnosed in primary care [7, 25]. Besides, the prognosis of CMDs among old adults appears to be worse than for young people [26]. Late-life CMDs may also elevate the risk of developing dementia [27]. Among people living with HIV (PLWH), depression and anxiety have been associated with non-adherence to combination antiretroviral therapy (cART), risky sexual behaviours, reduced quality of life and higher suicide rates [28–30]. Given that CMDs are rarely detected but can have serious health impacts on older people, it is increasingly important to assess for mild, moderate and severe levels to determine the scale of the problem [31].

To bridge the gap in Kenya, our study seeks to: (1) determine the prevalence of depressive and anxiety symptoms among OALWH compared to their HIV-negative peers; (2) investigate HIV status as an independent predictor of depressive and anxiety symptoms in the older adults; and (3) investigate the determinants of CMDs among older adults at the coast of Kenya.

2 | METHODS

2.1 | Study design and setting

This cross-sectional study was conducted at the Kenyan coast in Kilifi and Mombasa Counties between February 2020 and October 2021. The majority of Kilifi residents are rural dwellers whose main form of livelihood is subsistence farming and small-scale trading [32]. Kilifi has an adult HIV prevalence of 4.5% [33]. Mombasa County borders Kilifi County to the north and is considered urban. The common sources of income in Mombasa county include tourism, wholesale and retail trade. The Mombasa adult HIV prevalence is 7.5% [33].

2.2 | Study participants and recruitment

2.2.1 | *Older adults living with HIV*

OALWH were recruited from two public HIV specialized clinics in Kilifi and Mombasa Counties. As inclusion criteria, participants had to be aged ≥50 years of age, with a confirmed HIV seropositivity status, and on cART.

In both facilities, we were assisted by community health volunteers or healthcare providers in reviewing existing records to identify all potential participants. We used systematic sampling to identify potential clients for the study.

2.2.2 | *Older adults without HIV*

All HIV-negative older adults were recruited in Kilifi County. The Kilifi Health and Demographic Surveillance System was used to identify families with eligible older adults. Potential participants aged ≥50 were randomly identified from the existing database and followed up at their homes using GPS coordinates. To be included in the study, individuals had to be ≥50 years, and residents of Kilifi county, and provide consent for participation, including willingness to be tested for HIV using a rapid HIV testing kit (OraQuick) for a confirmation of HIV-negative status. We chose HIV-negative adults aged ≥50 years as our comparison group to the OALWH based on previous research [34, 35].

2.3 | Sample size calculations

Our sample size was calculated using previous studies from Uganda [36] and South Africa [35]. An overall sample size of at least 372 individuals was needed to detect a difference in CMDs between OALWH and HIV-negative community controls at 80% power and a 5% level of statistical significance. A sample of 450 participants was considered sufficient, allowing for missing data.

2.4 | Measures

The research instruments were programmed on android tablets using the Research Electronic Data Capture (REDCap) platform [37] for face-to-face interviewer administration. All research assistants were trained for 2 weeks by the first author prior to data collection.

2.4.1 | *Socio-demographic and asset index form*

Socio-demographic information was captured in REDCap. We also collected information on individual and family ownership of disposable assets for asset index computation. Participants were also asked to provide information on their access to social support, food security in the past week, the number of PLWH within the household and whether they were caring for a sick family member.

2.4.2 | *General health form*

We captured the participant's anthropometric details. Other information included hours spent on sedentary activities in a day, sexual activity, household HIV burden, number of medications one used and common somatic complaints.

Among OALWH, HIV-specific information questions were asked relating to the disclosure of HIV status and access to HIV care. Information regarding their current cART regimen and overall duration on cART was extracted from medical records. Blood samples were also collected from OALWH for viral load testing.

2.4.3 | *Psychosocial measures*

The brief 12-item HIV stigma scale [38] was utilized to assess participants' perceived HIV-related stigma. Higher scores indicate a greater level of perceived stigma. In the current study, this scale yielded good internal consistency alpha, 0.78 (95% CI 0.73, 0.83).

The 12-item World Health Organization Disability Assessment Schedule 2 (WHODAS 2) [39] was used to assess for functional disability among participants. Higher scores indicate a greater level of disability. In this study, the tool demonstrated good internal consistency alpha, 0.77 (95% CI 0.70, 0.84).

The UCLA 8-item loneliness scale [40] was used to assess participants' perceived loneliness. Higher scores equate to a greater level of loneliness. In the present study, this scale had acceptable internal consistency alpha, 0.61 (95% CI 0.56, 0.64).

The 20-item Ageism survey [41] was used to assess participants' experiences of ageism. Higher scores indicate more frequent experiences of ageism. In the current study, the internal reliability (Cronbach's alpha) was 0.89 (95% CI 0.87, 0.92).

2.4.4 | *Measures of common mental disorders*

The 7-item Generalized Anxiety Disorder scale (GAD-7) [42] and the 9-item Patient Health Questionnaire (PHQ-9) [43] were utilized to measure anxiety and depressive symptoms in the previous 2-week period, respectively. The total scores range from 0 to 21 for GAD-7 and 0 to 27 for PHQ-9. For GAD-7, total scores of 5–9, 10–14 and 15–21 represent mild, moderate and severe anxiety symptoms, respectively [44]. Total scores of 5–9, 10–14 and 15–27 indicate mild, moderate and severe depressive symptoms [45], respectively. A cut-off score of ≥5 for both PHQ-9 and GAD-7 was used to define a positive screen for depressive and anxiety symptoms in the current study, similar to previous studies in Ethiopia [46] and Tanzania [47]. In the present study, the internal consistency alphas for PHQ-9 and GAD-7 were good, 0.75 (95% CI 0.70, 0.79) and 0.74 (95% CI 0.70, 0.79), respectively.

2.4.5 | *Translation of new study measures*

All study questionnaires not previously adapted to the local language of Swahili underwent the recommended adaptation procedure in line with international guidelines [48].

2.5 | Statistical analysis

All analyses were carried out in STATA version 15.0 (StataCorp LP, College Station, TX, USA). Independent Student's *t*-test and Chi-square test were used to compare differences in continuous and categorical independent variables, respectively. We used proportions as percentages to estimate the prevalence of CMDs among OALWH and their HIV-negative counterparts. The Chi-square test was utilized to compare group differences on binary outcome variables. To investigate HIV status as an independent predictor of CMDs, we utilized logistic regression analyses adjusting for exposure variables that accounted for differences in CMDs. To examine the correlates of CMDs, we used logistic regression models to explore univariate relationships between the binary outcome variables and the different exposure variables. Exposure variables with a p-value < 0.15 in the univariate analysis were subsequently entered into the multivariable models using forward selection (data for OALWH and HIV-negative older adults were analysed separately for this set of analyses). In all models, collinearity was checked and for all tests of the hypothesis, a two-tailed p-value < 0.05 was regarded as statistically significant. The overall fit of the final models was examined by Hosmer and Lemeshow (HL) goodness of fit test where a p-value of > 0.05 was considered a good fit. The HL test results were cross-checked using McFadden's pseudo-R squared statistic.

2.6 | Ethics approval and consent to participate

The study was approved by the Kenya Medical Research Institute Scientific and Ethics Review Unit (Ref: KEMRI/SERU/CGMR-C/152/3804). Permission to conduct the study was granted by the research office Kilifi (Ref: HP/KCHS/VOL.X/171) and Mombasa (Ref: COH/Msa/RSC/04). All respondents provided written informed consent for their participation.

3 | RESULTS

3.1 | Sample characteristics

A total of 440 participants were included in this study, with a mean age of 60.1 (SD = 6.9) years. The participant response rate was 90%. This included 72 (16%) OALHIV in Mombasa and 368 (84%) in Kilifi. Most participants had formal education (63.2%), were unemployed (65.5%), lived in multigenerational households (81.6%) and cared for a sick family member (66.4%). OALWH were likely to be younger, unmarried, more educated, have lower monthly household income, live alone, with a smaller number of dependents and more food insecure (Table 1).

3.2 | HIV-related characteristics of OALWH

The majority of the OALWH had disclosed their HIV status (95.3%) and were on first-line cART treatment (90%). The mean (SD) duration of HIV treatment was 11.4 (4.3) years. Nearly, all (98.1%) of the OALWH had a viral load of ≤1000 copies/ml (Table 2).

3.3 | Prevalence estimates for CMDs

The prevalence of mild depressive symptoms was 23.8% among OALWH compared to 18.2% in the comparison group (p = 0.16). The prevalence of mild anxiety symptoms was 11.7% among OALWH compared to 7.2% in the comparison group (p = 0.12). The prevalence of comorbid mild depressive

Table 1. Characteristics of the study population by HIV status, *N* = 440

Characteristic	Total sample *N* = 440	HIV status		*p*-value
		Older adults without HIV, *n* = 183	Older adults living with HIV, *n* = 257	
Socio-demographic				
Age (years)				
50–59	227 (51.6)	84 (45.9)	143 (55.6)	0.02
60–69	171 (38.9)	74 (40.4)	97 (37.7)	
≥70	42 (9.5)	25 (13.7)	17 (6.6)	
Sex				
Female	258 (58.6)	98 (53.6)	160 (62.3)	0.07
Male	182 (41.4)	85 (46.4)	97 (37.7)	
Marital status				
Never married	12 (2.8)	4 (2.2)	8 (3.1)	<0.001†
Separated/Divorced/Widowed	181 (41.1)	45 (24.6)	136 (52.9)	
Married/cohabiting	247 (56.1)	134 (73.2)	113 (44.0)	
Education level				
None	162 (36.8)	90 (49.2)	72 (28.0)	<0.001†
Primary	182 (41.4)	65 (35.5)	117 (45.5)	
Secondary	73 (16.6)	22 (12.0)	51 (19.9)	
Tertiary	23 (5.2)	6 (3.3)	17 (6.6)	
Employment				
Unemployed	288 (65.5)	126 (68.9)	162 (63.0)	0.1
Employed	116 (26.3)	39 (21.3)	77 (30.0)	
Retired	36 (8.2)	18 (9.8)	18 (7.0)	
Monthly household income (Ksh)				
≤10,000	279 (63.4)	69 (37.7)	210 (81.7)	<0.001
Above 10,000	161 (36.6)	114 (62.3)	47 (18.3)	
Living arrangements				
Multiple generational families	359 (81.6)	169 (92.3)	190 (73.9)	<0.001†
Single generational families	41 (9.3)	6 (3.3)	35 (13.6)	
Alone	40 (9.1)	8 (4.4)	32 (12.5)	
Number of dependents, mean (SD)	3.2 (2.6)	3.6 (2.5)	2.9 (2.7)	0.01
Caring for a sick family member, OM = 2				
Yes	291 (66.4)	104 (57.1)	187 (73.1)	0.001
No	147 (33.6)	78 (42.9)	69 (26.9)	
Access to instrumental/social support				
None	199 (45.2)	93 (50.8)	106 (41.2)	0.07
Sometimes	215 (48.9)	83 (45.4)	132 (51.4)	
Most of the time	26 (5.9)	7 (3.8)	19 (7.4)	
Food insecurity (lack of food in the past week), OM = 3				
Never	293 (67.1)	134 (73.6)	159 (62.4)	0.002†
Sometimes	119 (27.2)	45 (24.7)	74 (29.0)	
Most of the times/always	25 (5.7)	3 (1.7)	22 (8.6)	
Asset index score[a]—mean (SD)	2.3 (1.5)	1.9 (1.2)	2.5 (1.6)	<0.001
Body mass index—mean (SD), OM = 11	24.9 (6.0)	24.7 (6.1)	25.0 (5.9)	0.7
Loneliness score[b]—mean (SD), OM = 3	13.9 (3.7)	13.0 (3.4)	14.6 (3.7)	<0.001
Functional disability score[c]—mean (SD), OM = 2	2.5 (4.3)	1.5 (3.0)	3.1 (4.9)	<0.001
Ageism score[d]—mean (SD)	4.2 (5.9)	3.0 (4.4)	5.0 (6.6)	<0.001
Hours spent in sedentary activities in a day, mean (SD), OM = 12	4.5 (2.6)	4.3 (2.1)	4.6 (2.9)	0.3

(*Continued*)

Table 1. (Continued)

Characteristic	Total sample *N* = 440	HIV status		*p*-value
		Older adults without HIV, *n* = 183	Older adults living with HIV, *n* = 257	
Sexually active, OM = 4				
Yes	206 (47.3)	105 (57.4)	101 (39.9)	<0.001
No	230 (52.7)	78 (42.6)	152 (60.1)	
Sleeping difficulties in the past month, OM = 4				
None	276 (63.3)	125 (68.3)	151 (59.7)	0.01[†]
Sometimes	131 (30.1)	53 (29.0)	78 (30.8)	
Most of the times/always	29 (6.6)	5 (2.7)	24 (9.5)	
Chronic fatigue				
Yes	56 (12.7)	21 (11.5)	35 (13.6)	0.5
No	384 (87.3)	162 (88.5)	222 (86.4)	
Number of medications participants are currently using, mean (SD), OM = 8	1.6 (1.6)	0.4 (1.2)	2.4 (1.2)	<0.001

Note: All numbers are reported as frequencies with percentages unless otherwise stated. *p*-values are for the difference between OALWH and their HIV-negative peers by sample characteristic. *p*-values have been derived from Chi-square test (or Fisher's exact test) and independent Student's *t*-test for categorical and continuous independent variables, respectively.
Abbreviations: Ksh, Kenya shillings; OM, observation with missing value; SD, standard deviation.
[a]Score range = 0–8, higher scores indicate better socio-economic status.
[b]Score range = 8–27, higher scores indicate greater loneliness.
[c]Score range = 0–33, higher scores indicate increasing disability.
[d]Score range = 0–34, higher scores indicate increasing ageism.
[†]Based on Fisher's exact test.

and anxiety symptoms among OALWH was 10.1% compared to 4.4% in the comparison group ($p = 0.03$) (Table 3).

3.4 | Association between HIV status and CMDs

In univariate and multivariate logistic regression analyses, HIV seropositivity was not significantly associated with depressive or anxiety symptoms (Table 4). However, HIV seropositivity was significantly associated with higher odds of a positive screen for depressive and anxiety symptoms co-occurrence in univariate but not in the multivariate model.

3.5 | Determinants of CMDs in OALWH

Table 5 presents results from logistic regression analyses exploring the determinants of CMDs among OALWH.

3.5.1 | Depressive symptoms

In the multivariable logistic regression model, factors significantly associated with higher odds of depressive symptoms among OALWH were functional disability, ageism, sleeping difficulties, chronic fatigue, increasing household HIV burden and perceived HIV-related stigma. Easier access to HIV care was significantly associated with lower odds of depressive symptoms.

3.5.2 | Anxiety symptoms

In the multivariable analyses, age ≥70, perceived loneliness, functional disability, ageism and sleeping difficulties were significantly associated with higher odds of anxiety symptoms among OALWH.

3.5.3 | Comorbid depressive and anxiety symptoms

In the multivariable analyses, perceived functional disability and ageism were significantly associated with higher odds of comorbid depressive and anxiety symptoms. Easier access to HIV care was significantly associated with lower odds of comorbid depressive and anxiety symptoms.

3.6 | Determinants of CMDs in HIV-negative older adults

The current work largely focused on OALWH. As such, we only provide a summary of the factors associated with CMDs among the HIV-negative older adults using the available data, particularly focusing on mild depressive symptoms whose prevalence was relatively high in the current sample, that is >10%. In multivariable analyses (Table S1), sleeping difficulties, perceived loneliness and increasing medication burden were significantly associated with higher odds of a positive screen for depressive symptoms among HIV-negative older adults. Greater sedentary behaviour and higher monthly household income were significantly associated with lower odds of depressive symptoms.

Table 2. HIV-related clinical and psychosocial characteristics of OALWH, *n* = 257

Characteristic	Mean (SD) or frequency (%)
HIV status disclosure	
Yes	245 (95.3%)
No	12 (4.7%)
Household HIV burden, mean (SD); OM = 5	1.4 (1.6)
cART regimen	
First line	233 (90.7%)
Second line	23 (8.9%)
Third line	1 (0.4%)
cART regimen change/interruption since HIV diagnosis	
Yes	110 (42.8%)
No	147 (57.2%)
Duration on cART (years), mean (SD), OM = 10	11.4 (4.3)
Viral suppression, OM = 45	
Yes	208 (98.1%)
No	4 (1.9%)
Access to HIV care, OM = 4	
Easily accessible	169 (66.8%)
Not easily accessible	84 (33.2%)
Perceived HIV-stigma score, OM = 1	
Personalized stigma[a]—mean (SD)	5.0 (1.9)
Disclosure concerns[b]—mean (SD)	8.6 (2.0)
Concerns about public attitudes[c]—mean (SD)	7.6 (2.2)
Negative self-image[d]—mean (SD)	6.4 (2.1)
Overall stigma[e]—mean (SD)	27.5 (5.4)

Abbreviations: cART, combination antiretroviral therapy; OM, observation with missing value; OALWH, older adults living with HIV.
[a]Score range = 3–12, higher scores indicate greater stigma.
[b]Score range = 3–12, higher scores indicate greater stigma.
[c]Score range = 3–12, higher scores indicate greater stigma.
[d]Score range = 3–12, higher scores indicate greater stigma.
[e]Score range = 12–44, higher scores indicate greater stigma.

4 | DISCUSSION

To our knowledge, this is the first study in Kenya and among the first reports from SSA investigating CMDs among OALWH compared to their HIV-negative peers. Our study found a relatively high burden of mild depressive and anxiety symptoms; however, HIV status was not independently associated with these symptoms. The correlates of CMDs in our study were predominantly psychosocial factors, many of which are potentially modifiable, thus highlighting the need to address the psychosocial needs of these adults alongside their biomedical needs.

Our finding of no significant differences in the prevalence of CMDs between OALWH and their HIV-negative peers is dissimilar to other emerging reports in SSA. In rural Uganda, OALWH on cART had a significantly lower prevalence of probable depression than their HIV-negative peers [36], similar to what was reported in rural South Africa [35]. Our finding also offers an interesting contrast to the predominant findings in HICs showing that OALWH present with worse CMDs than their HIV-negative peers [24]. The observed variation could reflect contextual differences across settings, for example healthcare systems, informal support systems and mental health resources that are likely to alter the risk profile of these adults. HIV status was not found to be an independent predictor of CMDs in our study. This observation is consistent with previous findings from South Africa [49] and Uganda [19] but contrasts with common research findings in HICs [24]. Our study may be part of an emerging body of evidence in SSA showing that the psychological health of OALWH is not worse than among those without HIV.

HIV-related stigma was significantly associated with higher odds of depressive symptoms among OALWH in our study. These findings are consistent with previous findings in the literature [12, 16, 50] and provide additional evidence of the critical role of addressing intersecting stigma in improving the mental wellbeing of OALWH. Relatedly, ageism was also significantly associated with higher odds of depressive symptoms, anxiety symptoms and their co-occurrence among OALWH. This finding is consistent with previous research conducted outside SSA [51]. Ageism could have an adverse impact on the mental health of OALWH through psychological, behavioural and physiological pathways [52]. Interventions addressing both ageist and HIV-stigmatizing attitudes at the community level will potentially improve the mental health of OALWH.

Increasing household HIV burden was significantly associated with higher odds of depressive symptoms among OALWH in our study. This may be related to the high caregiving burden often experienced by OALWH caring for HIV-positive children. This observation concurs with previous findings in the study setting [53].

Loneliness is common among older adults in general [54]. In this study, higher perceived loneliness was significantly associated with elevated odds of anxiety symptoms among OALWH and depressive symptoms among HIV-negative older adults. Our finding is consistent with previous studies from HICs [12, 55]. Theoretical models suggest that loneliness has cognitive, biological and social consequences that could potentially heighten the risk of subsequent CMDs [56]. Higher perceived functional disability was also strongly associated with higher odds of depressive symptoms, anxiety symptoms and their co-occurrence among OALWH in the current study, consistent with previous findings [19, 57, 58]. Since functional disability occurs frequently among OALWH, there is a need for early identification to help preserve functional independence.

Sleep disturbance is a prominent symptom in people with CMDs, especially depression, and was formerly regarded as a main secondary indicator of depression [59]. Nonetheless, multiple prospective studies have identified insomnia as an independent risk indicator for emerging or recurrent depression, suggesting that sleep problems are not necessarily secondary effects of CMDs but a predictive prodromal symptom [60, 61]. In this study, persistent sleep problems were significantly associated with higher odds of depressive symptoms, anxiety symptoms and their co-occurrence among OALWH and higher odds of depressive symptoms among HIV-negative

Table 3. Prevalence of common mental disorders in OALWH versus their HIV-negative peers

	Older adults without HIV, *n* = 181		Older adults living with HIV, *n* = 256		
	Number	Prevalence (95% CI)	Number	Prevalence (95% CI)	*p*-value
Severity of depressive symptoms					
Mild	28	15.5 (10.5, 21.6)	49	19.1 (14.5, 24.5)	0.3†
Moderate	5	2.8 (0.9, 6.3)	8	3.1 (1.4, 6.1)	
Severe	–	–	4	1.6 (0.4, 4.0)	
Positive depressive symptoms screen (cut-off ≥5)					
Yes	33	18.2 (12.9, 24.6)	61	23.8 (18.7, 29.5)	0.2
Severity of anxiety symptoms					
Mild	13	7.2 (3.9, 12.0)	26	10.2 (6.7, 14.5)	0.1†
Moderate	–	–	4	1.6 (0.4, 4.0)	
Positive anxiety symptoms screen (cut-off ≥5)					
Yes	13	7.2 (3.9, 12.0)	30	11.7 (8.0, 16.3)	0.1
Positive screen for comorbid depressive and anxiety symptoms					
Yes	8	4.4 (1.9, 8.4)	26	10.1 (6.7, 14.5)	0.03

Abbreviation: 95% CI, 95% confidence interval; OALWH, older adults living with HIV.
†Based on Fisher's exact test.

older adults. This finding is consistent with previous findings [59, 62, 63]. A combination of pharmacological and non-pharmacological interventions for sleep disturbances may effectively reduce and possibly prevent CMDs [64].

Chronic fatigue was also significantly associated with increased odds of depressive symptoms among OALWH in our study, similar to what has been reported elsewhere [65, 66]. Fatigue is a vital indicator of ageing-related declines in health and functioning [67]. Fatigue management strategies, such as adequate rest and sleep, are likely to improve the mental health of OALWH. Among HIV-negative older adults, an increased medication burden was also significantly associated with higher odds of depressive symptoms, consistent with previous findings [68]. While the exact mechanism for this association is unknown, we know that the use of medication increases as the number of medical conditions rises. Multiple medications, which are easily detected by clinicians, can provide an important clue to healthcare providers to further investigate depression in their clients.

Among socio-demographic factors, old age (≥70 years) was significantly associated with higher odds of anxiety symptoms in OALWH, while higher monthly household income was significantly associated with lower depressive symptoms among HIV-negative older adults. Mixed findings have been reported on these factors previously [69].

Easier access to HIV care was the only protective indicator for CMDs in OALWH in the current study. Given that many OALWH in Kenya face unique challenges with seeking HIV care services [70], programmes aimed at strengthening HIV care access or financial support have the potential to improve OALWHs' mental wellbeing. Further decentralizing HIV care into the community possibly utilizing community health workers may also be beneficial.

Among HIV-negative older adults, an increasing number of hours on sedentary activities was significantly associated with lower odds of depressive symptoms. More studies are needed to better understand the mechanism involved. Emerging data suggest that passive sedentary behaviours, for example television watching, increase the risk of depression, while mentally active sedentary behaviours, for example reading, may be protective against depression [71].

Most of our data (about 84%) were collected after the onset of the COVID-19 pandemic. Some studies have reported elevated levels of loneliness, depression, anxiety and insomnia among older adults following the outbreak of COVID-19 [72–74], while others have reported no changes before and during the pandemic despite increased loneliness during the pandemic [75]. Other studies have shown that younger populations have had higher rates of CMDs compared to older adults [76–79]. While it is possible that the emergence of the pandemic may have created an environment where the determinants of poor mental health could have been exacerbated, our study found low prevalences of CMDs, similar to previous research, suggesting higher resilience to the mental health effects of COVID-19 [80]. The long-term impacts of the pandemic remain unclear, especially in SSA where data on older adults' mental health are very scarce. More studies are needed to elucidate these findings.

The strengths of the current study include the focus on a neglected but rapidly growing population of OALWH, the use of a comparison group and sufficient sample size. Nonetheless, the cross-sectional nature of the study precludes any conclusion on causality. We recruited our OALWH from public HIV clinics, as such, our findings may not be readily generalizable to OALWH who may be out of care or attending private or urban HIV clinics or recruited from the community. We also utilized self-report screening measures which could be subject to reporting bias. Relatedly, the mental health screening measures do not give a clinical diagnosis of the studied CMDs, hence, we only report the symptomatology of these conditions.

Table 4. Association between HIV status and common mental disorders across the whole sample of older adults

	Positive screen for depressive symptoms		Positive screen for anxiety symptoms		Comorbid depressive and anxiety symptoms	
Covariate	**Crude analysis OR (95% CI)**	**Adjusted analysis aOR (95% CI)**	**Crude analysis OR (95% CI)**	**Adjusted analysis aOR (95% CI)**	**Crude analysis OR (95% CI)**	**Adjusted analysis aOR (95% CI)**
HIV status						
Seronegative	Ref	Ref	Ref	Ref	Ref	Ref
Seropositive	1.40 (0.87, 2.25)	0.54 (0.27, 1.07)	1.72 (0.87, 3.39)	0.46 (0.18, 1.19)	2.46* (1.09, 5.57)	0.74 (0.25, 2.22)
Sex						
Male		Ref		Ref		Ref
Female		1.68 (0.84, 3.38)		2.49 (0.95, 6.54)		1.93 (0.67, 5.56)
Age (years)						
50–59		Ref		Ref		Ref
60–69		0.89 (0.46, 1.70)		1.78 (0.71, 4.47)		1.72 (0.59, 4.98)
Above 70		0.56 (0.19, 1.69)		3.99* (1.08, 14.71)		3.94 (0.92, 16.94)
Marital status						
Never married		Ref		Ref		Ref
Separated/Divorced/ Widowed		0.14* (0.03, 0.69)		0.40 (0.06, 2.75)		0.83 (0.06, 11.27)
Married/cohabiting		0.12* (0.02, 0.62)		0.48 (0.07, 3.53)		1.26 (0.09, 18.17)
Asset Index score		0.77* (0.60, 0.98)		1.06 (0.77, 1.46)		0.91 (0.63, 1.32)
Sexually active						
No		Ref		Ref		Ref
Yes		2.61* (1.24, 5.47)		0.96 (0.38, 2.43)		0.81 (0.28, 2.29)
Functional disability score		1.18** (1.09, 1.28)		1.14* (1.05, 1.24)		1.14* (1.04, 1.24)
Loneliness score		1.12* (1.03, 1.22)		1.16* (1.04, 1.30)		1.12 (0.99, 1.27)
Ageism score		1.10** (1.04, 1.16)		1.16** (1.08, 1.24)		1.16** (1.08, 1.25)
Caring for a sick family member		2.08* (1.08, 4.02)		3.50* (1.32, 9.28)		3.07* (1.03, 9.20)
Chronic fatigue		3.14** (1.46, 6.72)		1.80 (0.69, 4.67)		1.86 (0.66, 5.24)
Sleeping difficulties for the past month						
None		Ref		Ref		Ref
Sometimes		4.62** (2.38, 8.98)		3.64* (1.47, 9.03)		4.69* (1.59, 13.88)
Most of the time/always		10.89** (3.57, 33.24)		4.89* (1.35, 17.63)		7.30* (1.76, 30.27)
Number of the final model		431		431		431
Hosmer–Lemeshow test		X^2 = 433.90; p = 0.25		X^2 = 307.20; p = 0.99		X^2 = 338.67; p = 0.99
Variance explained		35.0%		36.4%		38.8%

Abbreviations: aOR, adjusted odds ratio; CMD, common mental disorder; GAD, generalized anxiety disorder; OR, odds ratio; Ref, reference group.
*p-value < 0.05, **p-value < 0.001.

Despite the outlined limitations, this study has important implications for the care of older adults in our setting. We observed substantial levels of mild depressive and anxiety symptoms in both OALWH and their HIV-negative peers, highlighting the need for culturally appropriate mental health interventions in these older adults, regardless of their HIV status. Routine screening for CMDs should be strengthened to identify those at risk. Risk indicators for depressive symptoms, anxiety symptoms and their co-occurrence in this study were predominantly psychosocial factors. Unfortunately, there is a paucity of research on psychosocial interventions among OALWH [81] and those in the general population [82], especially in SSA. Our findings highlight the need to strengthen the evidence base for interventions for CMDs among older adults in low-resource settings like Kenya.

Table 5. Univariate and multivariable analysis of correlates of common mental disorders among OALWH

Covariate	Positive screen for depressive symptoms		Positive screen for anxiety symptoms		Comorbid depressive and anxiety symptoms	
	Univariate analysis OR (95% CI)	Multivariable analysis aOR (95% CI)	Univariate analysis OR (95% CI)	Multivariable analysis aOR (95% CI)	Univariate analysis OR (95% CI)	Multivariable analysis aOR (95% CI)
Age (years)						
50–59	Ref	Ref	Ref	Ref	Ref	Ref
60–69	0.77 (0.41, 1.44)	0.55 (0.23, 1.32)	1.18 (0.51, 2.72)	2.03 (0.66, 6.20)	1.12 (0.45, 2.76)	0.73 (0.19, 2.84)
≥70	1.35 (0.44, 4.15)	1.00 (0.19, 5.24)	4.19** (1.27, 13.80)	7.43** (1.25, 44.36)	4.55** (1.37, 15.09)	4.76 (0.70, 32.55)
Sex						
Male	Ref	Ref	Ref	Ref	Ref	Ref
Female	1.34 (0.73, 2.45)	1.36 (0.58, 3.19)	1.79 (0.76, 4.19)	2.17 (0.58, 8.08)	1.73 (0.70, 4.29)	2.59 (0.64, 10.45)
Marital status						
Never married	Ref	–	–	–	–	–
Separated/Divorced/ Widowed	0.19** (0.04, 0.82)	–	–	–	–	–
Married/cohabiting	0.16** (0.04, 0.73)	–	–	–	–	–
Education level						
None	Ref	–	Ref	–	Ref	–
Primary	0.80 (0.41, 1.57)	–	0.51* (0.22, 1.19)	–	0.52* (0.22, 1.25)	–
Secondary	0.78 (0.34, 1.80)	–	0.38* (0.11, 1.24)	–	0.20** (0.04, 0.96)	–
Tertiary	0.16* (0.02, 1.28)	–	0.28 (0.03, 2.30)	–	0.31 (0.04, 2.59)	–
Monthly household income (Ksh)						
≤10,000	Ref	–	Ref	–		
Above 10,000	0.33*** (0.12, 0.86)	–	0.13* (0.02, 1.02)	–	0.16* (0.02, 1.22)	–
Living arrangements						
Multiple generational families	–	–	–	–	Ref	–
Single generational families	–	–	–	–	2.11* (0.77, 5.78)	–
Alone	–	–	–	–	1.05 (0.29, 3.82)	–
Number of dependents, mean (SD)	–	–	0.87* (0.74, 1.04)	–	–	–
Caring for a sick family member						
No	Ref	–	–	–	–	–
Yes	0.63* (0.33, 1.16)	–	–	–	–	–
Food insecurity (lack of food in the past week)						
Never	Ref		Ref	–	Ref	–
Sometimes	2.92*** (1.55, 5.49)	–	4.21*** (1.75, 10.14)	–	5.95*** (2.18, 16.20)	–

(*Continued*)

Table 5. (Continued)

Covariate	Positive screen for depressive symptoms		Positive screen for anxiety symptoms		Comorbid depressive and anxiety symptoms	
	Univariate analysis OR (95% CI)	Multivariable analysis aOR (95% CI)	Univariate analysis OR (95% CI)	Multivariable analysis aOR (95% CI)	Univariate analysis OR (95% CI)	Multivariable analysis aOR (95% CI)
Most of the times/always	2.9** (1.11, 7.62)	–	6.21** (1.96, 19.70)	–	9.56*** (2.76, 33.15)	–
Loneliness score, mean (SD)	1.21*** (1.12, 1.32)		1.29*** (1.16, 1.43)	1.16** (1.01, 1.34)	1.28*** (1.15, 1.42)	
Functional disability score, mean (SD)	1.25*** (1.15, 1.35)	1.15** (1.04, 1.28)	1.19*** (1.10, 1.28)	1.10** (1.01, 1.20)	1.18*** (1.10, 1.27)	1.12** (1.03, 1.22)
Ageism score, mean (SD)	1.14*** (1.08, 1.19)	1.10** (1.04, 1.17)	1.17*** (1.10, 1.24)	1.14*** (1.06, 1.23)	1.17*** (1.11, 1.24)	1.23*** (1.13, 1.33)
Hours spent in sedentary behaviours in a day, mean (SD)	–	–	–	–	1.13* (1.00, 1.28)	–
Sexually active						
No	–	–	Ref	–	Ref	–
Yes	–	–	0.44* (0.18, 1.06)	–	0.44* (0.17, 1.15)	–
Sleeping difficulties in the past month						
None	Ref	Ref	Ref	Ref	Ref	–
Sometimes	6.59*** (3.18, 13.66)	3.51** (1.38, 8.89)	10.17*** (3.29, 31.47)	6.41** (1.73, 23.83)	11.75*** (3.28, 42.0)	–
Most of the times/always	25.60*** (9.00, 72.99)	8.82*** (2.33, 33.37)	18.25*** (4.94, 67.40)	6.18** (1.26, 30.22)	20.31*** (4.80, 85.96)	–
Chronic fatigue						
No	Ref	Ref	Ref	–	Ref	–
Yes	7.90*** (3.66, 17.02)	5.41** (1.78, 16.38)	2.68** (1.09, 6.62)	–	3.36** (1.33, 8.46)	–
Number of medications participants are currently using, mean (SD)	–	–	–	–	1.24* (0.94, 1.64)	–
HIV status disclosure						
Yes	Ref	–	–	–	–	–
No	2.40* (0.73, 7.85)	–	–	–	–	–
Household HIV burden, mean (SD)	1.30** (1.09, 1.55)	1.37** (1.08, 1.74)	1.20* (0.98, 1.47)	–	1.21* (0.98, 1.49)	–
cART regimen change/interruption since HIV diagnosis						
No	–	–	Ref	–	Ref	–
Yes	–	–	2.13* (0.97, 4.68)	–	1.88* (0.82, 4.34)	–
Access to HIV care						
Not easily accessible	Ref	Ref	Ref	–	Ref	Ref
Easily accessible	0.47** (0.26, 0.85)	0.35** (0.15, 0.83)	0.36** (0.16, 0.78)	–	0.29** (0.12, 0.68)	0.16** (0.04, 0.60)

(*Continued*)

Table 5. (Continued)

Covariate	Positive screen for depressive symptoms		Positive screen for anxiety symptoms		Comorbid depressive and anxiety symptoms	
	Univariate analysis OR (95% CI)	Multivariable analysis aOR (95% CI)	Univariate analysis OR (95% CI)	Multivariable analysis aOR (95% CI)	Univariate analysis OR (95% CI)	Multivariable analysis aOR (95% CI)
Perceived HIV-stigma score, mean (SD)						
Personalized stigma	1.21** (1.04, 1.41)	1.27** (1.02, 1.59)	1.16* (0.96, 1.42)	–	1.25** (1.02, 1.54)	–
Disclosure concerns	–	–	–	–	–	–
Concerns about public attitudes	1.23** (1.06, 1.42)	–	1.29** (1.06, 1.57)	–	1.23** (1.00, 1.51)	–
Negative self-image	1.22** (1.06, 1.40)	–	1.20** (1.00, 1.44)	–	1.36** (1.12, 1.66)	–
Overall stigma	1.11*** (1.05, 1.18)	–	1.10** (1.02, 1.20)	–	1.13** (1.04, 1.23)	–
n for the final model		251		252		245
Variance explained		41.7%		41.0%		42.0%
Hosmer–Lemeshow test		X^2 = 241.96; *p*-value = 0.35		X^2 = 210.85; *p*-value = 0.79		X^2 = 176.09; *p*-value = 0.99
cvMean AUC (95% CI)		0.91 (0.87, 0.96)		0.88 (0.82, 0.95)		0.92 (0.89, 0.96)

Note: Only a priori variables (age and sex), as well as those with *p*-value < 0.15 in the univariate analysis or multivariable $p < 0.05$, are presented here. Ten independent variables were fitted for the multivariable model on depressive symptoms, seven variables for both the anxiety symptoms and CMD comorbidity.
Abbreviations: aOR, adjusted odds ratio; cvMean AUC, cross-validated mean area under the curve for the final multivariable model; OR, odds ratio; Ref, reference group; OALWH, older adults living with HIV.
*p value < 0.15, **p value < 0.05, ***p value < 0.01.

5 | CONCLUSIONS

Ambulatory, out-patient OALWH and their HIV-negative peers from the community have similar levels of mild depressive and anxiety symptoms. Additionally, living with HIV is not predictive of CMDs in this setting. Our study provides an initial understanding of the determinants of CMDs from a low-resource setting. Modifiable risk factors, such as ageism, HIV-related stigma, loneliness, functional disability and sleeping difficulties, represent a target for preventive interventions through psychosocial interventions at the family, community and clinical levels.

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COMPETING INTERESTS

The authors have no competing interests to disclose.

AUTHORS' CONTRIBUTIONS

PNM, CRN and AA conceptualized the study. PNM, CRN, RGW and AA designed the study. PNM and CN programmed the study questions on tablets and managed project data for the entire study period. PNM analysed the data. PNM, CN, RGW, CRN and AA contributed to the interpretation of the data. PNM wrote the first draft of the manuscript and all the authors reviewed the subsequent versions and approved the final draft for submission.

ACKNOWLEDGEMENTS

We would like to thank all the participants who voluntarily took part in this study. We are grateful to the community health volunteers and healthcare providers at the HIV clinics for their overwhelming support during the study. We also acknowledge Sadaka Charo, Richard Karisa, Irene Kasichana, Maureen Nyadzua, Haprity Mwangata, Linda Moranga, Khamis Katana, Beatrice Kabunda, Katana Ngombo, Alfred Ngombo, Collins Kipkoech and Martha Kombe for their immense role in data collection. This work is published with the permission of the director of Kenya Medical Research Institute.

FUNDING

This work was funded by the Wellcome Trust International Master's Fellowship to PNM (grant number 208283/Z/17/Z). Further funding supporting this work was from (1) the Medical Research Council (grant number MR/M025454/1) to AA. This award is jointly funded by the UK Medical Research Council (MRC) and the UK Department for International Development (DFID) under MRC/DFID concordant agreement and is also part of the EDCTP2 programme supported by the European Union; (2) DELTAS Africa Initiative [DEL-15-003]. The DELTAS Africa Initiative is an independent funding scheme of the African Academy of Sciences (AAS) 's Alliance for Accelerating Excellence in Science in Africa (AESA) and supported by the New Partnership for Africa's Development Planning and

Coordinating Agency (NEPAD Agency) with funding from the Wellcome Trust [107769/Z/10/Z] and the UK government. The funders did not have a role in the design and conduct of the study or interpretation of study findings.

DISCLAIMER

DATA AVAILABILITY STATEMENT

Application for data access can be made through the Data Governance Committee of the KEMRI Wellcome Trust Research Programme who will review the application and advise as appropriate ensuring that uses are compatible with the consent obtained from participants for data collection. Requests can be sent to the coordinator of the Data Governance Committee using the following email dgc@kemri-wellcome.org.

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SUPPORTING INFORMATION

Additional information may be found under the Supporting Information tab for this article:

Table S1. Univariate and multivariable analysis of the correlates of depressive symptoms among HIV-negative older adults.

Farley SM et al. *Journal of the International AIDS Society* 2022, **25**(S4):e26005
http://onlinelibrary.wiley.com/doi/10.1002/jia2.26005/full | https://doi.org/10.1002/jia2.26005

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Progress towards the UNAIDS 90-90-90 targets among persons aged 50 and older living with HIV in 13 African countries

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Abstract

Introduction: Achieving optimal HIV outcomes, as measured by global 90-90-90 targets, that is awareness of HIV-positive status, receipt of antiretroviral (ARV) therapy among aware and viral load (VL) suppression among those on ARVs, respectively, is critical. However, few data from sub-Saharan Africa (SSA) are available on older people (50+) living with HIV (OPLWH). We examined 90-90-90 progress by age, 15–49 (as a comparison) and 50+ years, with further analyses among 50+ (55–59, 60–64, 65+ vs. 50–54), in 13 countries (Cameroon, Cote d'Ivoire, Eswatini, Ethiopia, Kenya, Lesotho, Malawi, Namibia, Rwanda, Tanzania, Uganda, Zambia and Zimbabwe).

Methods: Using data from nationally representative Population-based HIV Impact Assessments, conducted between 2015and 2019, participants from randomly selected households provided demographic and clinical information and whole blood specimens for HIV serology, VL and ARV testing. Survey weighted outcomes were estimated for 90-90-90 targets. Country-specific Poisson regression models examined 90-90-90 variation among OPLWH age strata.

Results: Analyses included 24,826 HIV-positive individuals (15–49 years: 20,170; 50+ years: 4656). The first, second and third 90 outcomes were achieved in 1, 10 and 5 countries, respectively, by those aged 15–49, while OPLWH achieved outcomes in 3, 13 and 12 countries, respectively. Among those aged 15–49, women were more likely to achieve 90-90-90 targets than men; however, among OPLWH, men were more likely to achieve first and third 90 targets than women, with second 90 achievement being equivalent. Country-specific 90-90-90 regression models among OPLWH demonstrated minimal variation by age stratum across 13 countries. Among OLPWH, no first 90 target differences were noted by age strata; three countries varied in the second 90 by older age strata but not in a consistent direction; one country showed higher achievement of the third 90 in an older age stratum.

Conclusions: While OPLWH in these 13 countries were slightly more likely than younger people to be aware of their HIV-positive status (first 90), this target was not achieved in most countries. However, OPLWH achieved treatment (second 90) and VL suppression (third 90) targets in more countries than PLWH <50. Findings support expanded HIV testing, prevention and treatment services to meet ongoing OPLWH health needs in SSA.

Keywords: ageing; HIV epidemiology; HIV testing; older PLHIV; PHIA; UNAIDS goals

Received 20 January 2022; **Accepted** 16 August 2022

1 | INTRODUCTION

Persons living with HIV (PLWH), including those in low- and middle-income countries, have experienced extended life expectancies due to the success of antiretroviral (ARV) therapies [1]. In 2014, the Joint United Nations Programme on HIV and AIDS (UNAIDS) launched the 90-90-90 global targets for 2020: 90% of PLWH will know their HIV status (first 90); 90% of those aware will receive sustained ARV therapy (ART) (second 90); and of these, 90% will achieve viral load suppression (VLS) (third 90) [2], as a stepping stone towards achieving the end of the AIDS epidemic as a public health threat by 2030 with 95-95-95 global targets for 2025 [3, 4]. In 2019, a modelling study examined data released by UNAIDS and found that 60 out of 170 countries were able to report on all three 90 targets; many of these countries, however, were not likely to achieve 90-90-90 targets by 2020 although three countries in sub-Saharan Africa (SSA) were among the six that achieved the model targets [5]. Studies of HIV prevalence among older adults, 50 years of age and older (50+), have shown increases in the number of older persons living with HIV (OPLWH), in general, and particularly in Eastern and Southern Africa [1, 6, 7].

With this growing and ageing population of OPLWH, it is important to focus on older adults and their risk for HIV as well as to understand how OPLWH have progressed towards the UNAIDS 90-90-90 targets in SSA [8]. A recent systematic review and meta-analysis using data published between 2014 and 2018 among PLWH aged 15 and older that examined progress towards 90-90-90 targets by a range of socio-demographics found a mixed picture in SSA [9]. Both males and females have made progress towards achieving the 90-90-90 targets by age group. Women within each age group demonstrated more progress along the cascade overall compared with men, and older adults achieved more progress towards the 90-90-90 targets than younger age groups [9].

To date, measuring progress towards 90-90-90 among the OPLWH has been challenging for several reasons. First, studies examining HIV in SSA have largely focused on younger adults, despite the growth in the number of OPLWH [1, 6, 10, 11]. Secondly, not all studies have reported on all three 90s, usually focusing on one or two of the 90s, with more recent attempts examining all 90-90-90 targets [5, 12–15]. Thirdly, most studies that assessed 90-90-90 progress have relied on programmatic data, which are restricted to the subset of the population living with HIV who have accessed services, rather than the entirety of people living with HIV [16].

We examined 90-90-90 target achievement by age and sex using nationally representative samples of adults in 13 SSA countries: Cameroon, Cote d'Ivoire, Eswatini, Ethiopia, Kenya, Lesotho, Malawi, Namibia, Rwanda, Tanzania, Uganda, Zambia and Zimbabwe. We further assessed the progress towards 90-90-90 targets among subsets of individuals by age strata among OPLWH. Finally, we assessed the associations between age and achievement of the 90-90-90 targets among OPLWH, by country, using Poisson regression models, to inform efforts to address gaps in services for this population.

2 | METHODS

2.1 | Data source

Data for the 13 countries (Cameroon 2017–2018, Cote d'Ivoire 2017–2018, Eswatini 2016, Ethiopia 2017–2018, Kenya 2018, Lesotho 2016–2017, Malawi 2015–2016, Namibia 2017, Rwanda 2018–2019, Tanzania 2016–2017, Uganda 2016–2017, Zambia 2016 and Zimbabwe 2015–2016) were collected as part of the Population-based HIV Impact Assessment (PHIA) surveys between 2015 and 2019. The PHIA surveys selected a nationally representative sample using a stratified two-stage cluster sampling design to provide a population-level assessment of the burden of HIV at national and sub-national levels [17, 18]. The surveys were funded by the United States President's Emergency Plan for AIDS Relief (PEPFAR) and conducted by ministries of health with support from ICAP at Columbia University, the University of California at San Francisco (Namibia PHIA) and the US Centers for Disease Control and Prevention (CDC). The PHIA survey design and implementation have been previously described [18, 19]. At the time the PHIAs were conceived, the HIV burden varied across these countries among 15–49 year old; seven countries had an HIV prevalence ranging from 1.5% to 7.3% (Ethiopia—1.5%, Rwanda—3.0%, Cote d'Ivoire—3.7%, Cameroon—4.3%, Tanzania—5.3%, Kenya—5.6% and Uganda—7.3%); four countries had an HIV prevalence ranging from 10.6% to 15.0% (Malawi—10.6%, Namibia—14.3%, Zambia—14.3% and Zimbabwe—15.0%); and two countries had an HIV prevalence above 20% (Lesotho—23% and Eswatini—26%). The ARV coverage varied among these countries at that time as well; six countries had ARV coverage below 50% (Cote d'Ivoire—24.4%, Cameroon—26.0%, Lesotho—35.0%, Tanzania—37.0%, Ethiopia—40.0% and Uganda—40.0%); and seven countries had ARV coverage well above 50% (Zambia—76.9%, Kenya—78.5%, Eswatini—82.0%, Malawi—83.0%, Namibia—90.0%, Zambia—90.0% and Rwanda—91.0%) [20–32].

2.2 | Eligibility criteria and survey domains

Eligibility criteria for this analysis were based on age ≥15 years old and whether the person slept in the household the night before the interview. Upper age limits for individual eligibility varied by country: 59 years of age for Lesotho and Zambia, 64 years of age for Cameroon, Cote d'Ivoire, Ethiopia, Kenya, Malawi, Namibia, Rwanda and Uganda, and no upper age limit in Eswatini, Tanzania and Zimbabwe. Household and individual interviews were conducted among consenting individuals (minors provided informed assent), capturing demographic, behavioural and clinical data, including self-reported HIV status, testing history and medication uptake.

2.3 | Laboratory procedures

Consenting participants provided blood specimens for HIV diagnostic testing, using the national HIV rapid testing algorithm and counselling was provided to all survey participants in their homes. Blood specimens for all HIV-positive participants were further tested for $CD4^+$ T-cell enumeration in

the household, viral load (VL) testing at central laboratories and qualitative testing for selected ARVs, at the University of Cape Town, South Africa. VL testing was performed on the Abbott *m*2000 (Abbott Molecular, Des Plaines, IL, USA), the bioMérieux NucliSens EasyMag/EasyQ (bioMérieux, Marcy-l'Étoile, France) or the Roche COBAS AmpliPrep/COBAS TaqMan (Roche Diagnostics, Pleasanton, CA, USA) platforms. VLS was defined as <1000 copies/ml [33].

2.4 | Ethics approval

The surveys were approved by the Institutional Review Boards at Columbia University Irving Medical Center, the University of California at San Francisco (Namibia only), the CDC and the local ethics board in each country.

2.5 | Measures

We examined 90-90-90 progress by sex and age (15–49, 50+) in the 13 PHIAs. The first 90 (HIV status awareness) outcome was defined as the proportion of participants who tested HIV positive during the PHIAs, who self-reported being HIV positive during the interview, prior to learning the result of household HIV testing, or if ARVs were detected in their blood. The second 90 (ART use among aware) was defined as the proportion of aware participants who self-reported taking ARVs or had ARVs detected in their blood, and the third 90 (VLS) was defined as the proportion of ART users who have HIV-1 RNA <1000 copies/ml.

Descriptive statistics and model variables included basic demographics, such as sex, age groups (50–54, 55–59, 60–64, 65 and older), residence and other measures of socioeconomic status as well as a variety of treatment outcome variables.

2.6 | Analysis

We calculated 90-90-90 estimates by age (15–49 and 50+) and sex for each of the 13 countries, and accounted for survey design with Jackknife variance estimation. These analyses were performed with SAS version 9.4. We calculated weighted percentages to describe demographic characteristics, partner's HIV status, time since HIV diagnosis and time on ART, among OPLWH from all 13 countries, using the Taylor Series method on variance estimation. We pooled the variance strata and Primary Sampling Units recorded on the country-level data files, re-numbered strata to make unique ones, then produced the variance estimates with the Taylor Series linearization method in the pooled dataset. We fit three multivariate Poisson regression models per country, one for each of the 90-90-90 targets, among OPLWH, to examine how 90-90-90 progress varied by age strata among OPLWH (50–54, 55–59, 60–64, 65 and older) [34, 35]. We adjusted the first 90 models for sex, residence, employed, wealth quintile, education, marital status and partner HIV status-self-reported. We adjusted the second 90 models for the same variables as the first 90 models as well as the number of years since diagnosis. We adjusted the third 90 models for the same variables as the first 90 and the number of years since initiating ART. We reported adjusted prevalence ratios (aPR) to measure the association between these factors and the 90-90-90 outcomes. We constructed models using Stata 15. All comparisons reported are significant at $p < 0.05$.

3 | RESULTS

3.1 | 90-90-90 targets

A total of 20,170 PLWH 15–49 years of age and 4656 OPLWH 50+ were included in the analyses. Figure 1 shows the progress towards 90-90-90 targets for each of the 13 countries. The target for awareness of HIV-positive status (first 90) was achieved among women aged 15–49 and among 50+ (women and men) in Eswatini, among 50+ (women and men) in Namibia, as well as among men 50+ in Lesotho. The target for ARV treatment (second 90) was achieved among those aged 15–49 (women and men) in six countries and among women aged 15–49 in four other countries, while the target was achieved in all 13 countries among 50+ (women and men). The VLS target (third 90) was achieved by those aged 15–49 (women and men) in one country and by women aged 15–49 in three countries and men aged 15–49 in one country, while the VLS target was achieved among 50+ (women and men) in eight countries and men 50+ in three countries and women 50+ in one country. Among those aged 15–49, women were more likely to have achieved the 90-90-90 targets than men; however among those 50+, men were more likely to have achieved the first (3 countries vs. 2 countries, respectively) and third (11 countries vs. 9 countries, respectively) 90 targets than women, with second 90 achievement being equivalent.

3.2 | OPLWH demographics

Among all 4656 OPLWH from the 13 countries, as noted in Table 1, there were more women than men (56.42% vs. 43.68%) identified, with the majority of OPLWH in the 50–59 age range (50–54 years: 46.27%; 55–59 years: 32.55%), the majority resided in rural areas (60.89%) and were not currently employed (57.23%). The OPLWH had a similar wealth status as the general population, with 61.65% in the upper 60% wealth quintile for their country. Most men (78.71%) were married or living with a partner compared with just 26.69% of women, while almost half of women (47.27%) were widowed compared with just 8.60% of men. The highest level of educational completion for most (58.37%) was a primary school. Most (79.44%) of the women reported no partner in the household compared with 31.75% of men, while 39.40% of the men reported having one or more HIV-positive partners compared to 8.20% of the women. Among OPLWH, 66.09% of the women reported having no sexual partners in the past 12 months compared with 20.04% of men, and 36.05% of the men reported that one or more of their partners think/told/tested HIV positive compared with 10.44% of the women.

3.3 | OPLWH treatment status

Among all OPLWH in Table 2, 21.25% were unaware of their HIV-positive status. Among OPLWH, 27.21% did not have ARVs detected in their blood and 26.50% were not virally

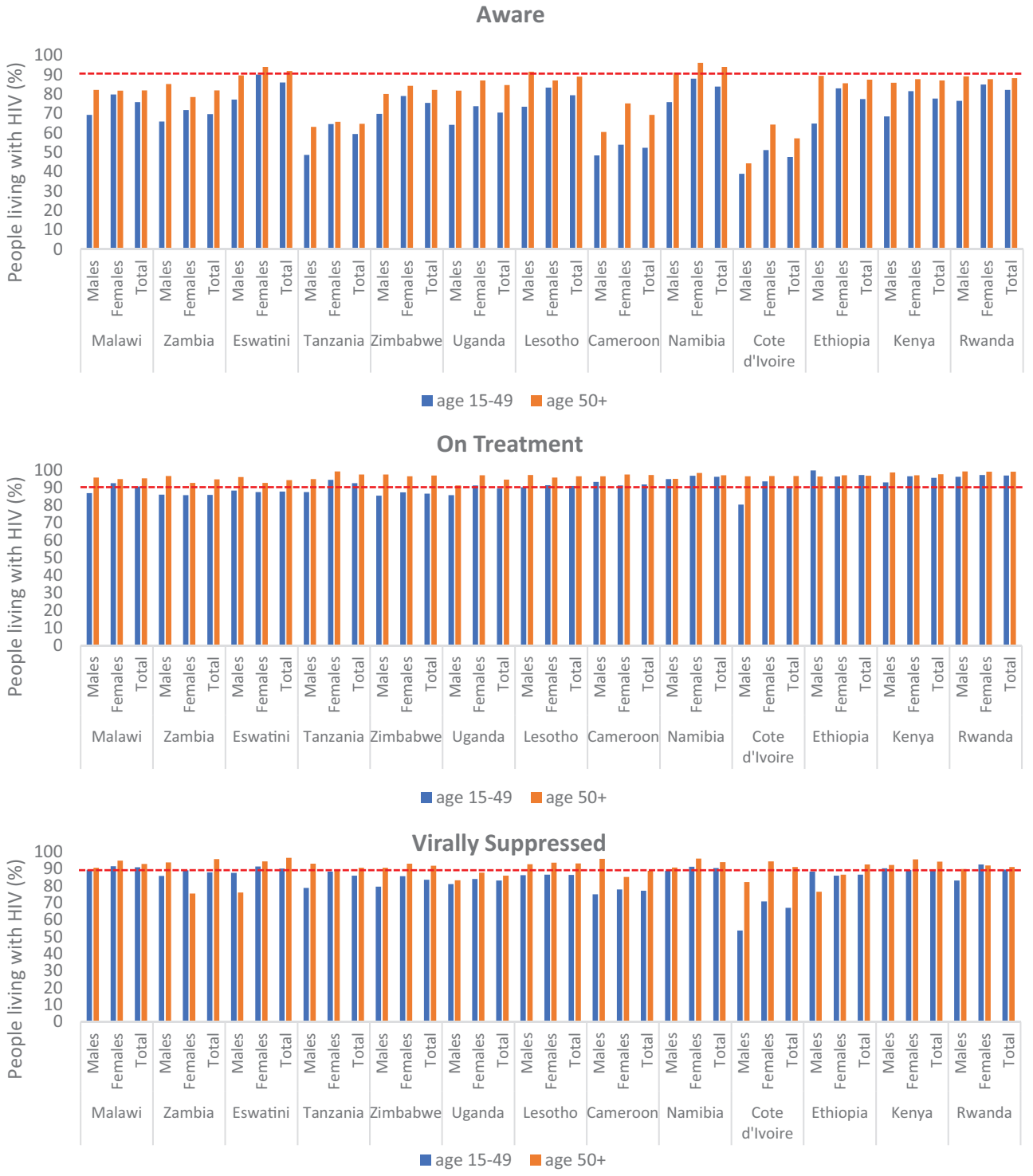

Figure 1. Antiretroviral-adjusted 90-90-90 estimates among 15–49 and 50+ years, 13 countries, Population-based HIV Impact Assessments, 2015–2019.

Notes: – – – – – – represents the 90-90-90 target; Survey dates: Cameroon 2017–2018, Cote d'Ivoire 2017–2018, Eswatini 2016, Ethiopia 2017–2018, Kenya 2018, Lesotho 2016–2017, Malawi 2015–2016, Namibia 2017, Rwanda 2018–2019, Tanzania 2016–2017, Uganda 2016–2017, Zambia 2016 and Zimbabwe 2015–2016.

Table 1. Pooled 13 country descriptive socio-demographic statistics among older persons living with HIV aged 50 and over

	Males		Females		Total	
	N	% (95% CIs)	*N*	% (95% CIs)	*N*	% (95% CIs)
Sex						
Male					1911	43.58 (42.15–45.02)
Female					2745	56.42 (54.98–57.85)
Age						
50–54	837	46.51 (44.01–49.01)	1275	46.08 (44.07–48.09)	2112	46.27 (44.73–47.81)
55–59	606	32.73 (30.52–34.94)	900	32.42 (30.64–34.19)	1506	32.55 (31.11–34.00)
60–64[a]	335	15.87 (14.45–17.3)	437	16.83 (15.38–18.27)	772	16.41 (15.41–17.42)
65+[b]	133	4.89 (4.08–5.69)	133	4.67 (3.67–5.67)	266	4.77 (4.08–5.45)
Residence						
Urban	640	38.21 (36.11–40.30)	939	39.81 (37.93–41.68)	1579	39.11 (37.72–40.50)
Rural	1271	61.79 (59.70–63.89)	1806	60.19 (58.32–62.07)	3077	60.89 (59.50–62.28)
Employed						
Yes	907	54.30 (52.06–56.54)	799	33.85 (31.99–35.72)	1706	42.77 (41.32–44.22)
No	1004	45.70 (43.46–47.94)	1943	66.15 (64.28–68.01)	2947	57.23 (55.78–58.68)
Wealth quintile						
Lower 40%	802	35.95 (33.87–38.02)	1288	40.20 (38.41–41.99)	2090	38.35 (37.00–39.69)
Upper 60%	1108	64.05 (61.98–66.13)	1455	59.80 (58.01–61.59)	2563	61.65 (60.31–63.00)
Marital status						
Never married	102	2.98 (2.35–3.61)	276	6.28 (5.27–7.30)	378	4.84 (4.24–5.45)
Married or living together	1449	78.71 (76.86–80.56)	764	26.69 (24.93–28.45)	2213	49.36 (47.65–51.07)
Divorced or separated	161	9.70 (8.26–11.14)	389	19.76 (17.96–21.56)	550	15.38 (14.05–16.71)
Widowed	196	8.60 (7.35–9.85)	1310	47.27 (45.33–49.21)	1506	30.42 (29.02–31.81)
Education						
None	246	10.45 (9.03–11.87)	551	26.02 (24.03–28.00)	797	19.22 (17.88–20.55)
Primary	1055	59.36 (57.20–61.52)	1589	57.61 (55.62–59.59)	2644	58.37 (56.79–59.96)
Post primary	605	30.18 (28.16–32.21)	592	16.38 (15.18–17.57)	1197	22.41 (21.28–23.53)
Partner HIV status-measured						
One or more partner HIV positive	749	39.40 (37.27–41.53)	265	8.20 (7.22–9.18)	1014	21.80 (20.41–23.19)
All partners HIV positive	393	23.96 (21.96–25.96)	128	5.37 (4.53–6.20)	521	13.47 (12.48–14.45)
Don't know or missing	82	4.89 (3.88–5.89)	191	6.99 (6.25–7.74)	273	6.08 (5.47–6.68)
No partner in household	687	31.75 (29.65–33.86)	2161	79.44 (77.97–80.90)	2848	58.65 (57.00–60.31)
Partner HIV status-self-reported						
One or more partner think/told/tested HIV positive	736	36.05 (33.84–38.26)	387	10.44 (9.52–11.35)	1123	21.52 (20.25–22.78)
All partners think/told/tested HIV negative	359	20.47 (18.75–22.19)	207	8.05 (6.99–9.10)	566	13.42 (12.43–14.41)
Don't know or missing	433	23.44 (21.45–25.42)	455	15.43 (13.93–16.92)	888	18.89 (17.58–20.21)
No partner in the past 12 months	370	20.04 (17.94–22.14)	1692	66.09 (64.09–68.09)	2062	46.17 (44.29–48.05)
Country						
Malawi	155	9.16 (8.11–10.21)	184	8.27 (7.44–9.10)	339	8.66 (8.15–9.17)
Zambia	148	8.79 (7.97–9.61)	184	6.74 (6.03–7.46)	332	7.64 (7.13–8.14)
Eswatini	243	2.16 (1.91–2.41)	337	1.69 (1.52–1.86)	580	1.90 (1.76–2.04)
Tanzania	149	17.76 (15.62–19.90)	225	20.51 (18.84–22.18)	374	19.31 (18.29–20.33)
Zimbabwe	348	16.00 (14.46–17.55)	428	11.95 (11.09–12.81)	776	13.72 (12.91–14.53)
Uganda	116	10.66 (9.73–11.59)	167	10.34 (9.25–11.44)	283	10.48 (9.76–11.20)
Lesotho	209	3.03 (2.65–3.41)	339	2.84 (2.60–3.09)	548	2.92 (2.72–3.12)
Cameroon	75	5.4 (4.67–6.13)	113	6.28 (5.56–7.00)	188	5.90 (5.35–6.45)

(*Continued*)

Table 1. (Continued)

	Males		Females		Total	
	N	% (95% CIs)	*N*	% (95% CIs)	*N*	% (95% CIs)
Namibia	183	2.12 (1.85–2.38)	311	2.34 (2.14–2.53)	494	2.24 (2.10–2.38)
Cote d'Ivoire	42	4.44 (3.68–5.19)	65	6.26 (5.12–7.39)	107	5.46 (4.79–6.13)
Ethiopia	33	3.72 (3.12–4.32)	52	3.22 (2.88–3.57)	85	3.44 (3.13–3.75)
Kenya	121	13.49 (12.10–14.88)	203	16.19 (14.96–17.42)	324	15.02 (14.23–15.80)
Rwanda	89	3.27 (2.90–3.65)	137	3.36 (3.04–3.68)	226	3.32 (3.14–3.51)

Note: Upper age limits varied by country.
[a]Excludes Lesotho and Zambia.
[b]Includes only Eswatini, Tanzania and Zimbabwe.
On residence, Lesotho had three categories: urban, rural and peri-urban, and peri-urban was collapsed into urban, while in Ethiopia, small urban was classified as rural and large urban was classified as urban.

suppressed. More than one-third (37.04%) of OPLWH had a CD4$^+$ cell count ≥500 per μl, 27.03% had a CD4$^+$ cell count of 350–499 per μl, 22.71% had a CD4$^+$ cell count of 200–349 per μl, 10.87% had a CD4$^+$ count of 100–199 per μl and 2.36% had a CD4$^+$ count of <100 per μl. Of all OPLWH, 12.68% indicated that they were never tested for HIV before the survey, and among those who were aware of their HIV-positive status, 6.82% had been diagnosed within the past year. Almost all OPLWH (96.99%) with detectable ARVs in their blood were taking first-line ART regimens (guidance at the time of the surveys) and more than half (54.84%) of those on ART indicated that they initiated treatment 5 or more years prior to the survey.

3.4 | OPLWH country-specific Poisson regression

Table 3 shows the first 90 awareness models for all 13 countries. There were no significant differences in awareness of HIV-positive status by age stratum among OPLWH ($p > 0.05$). In Table 4, the second 90 on treatment models for all 13 countries are presented. Three countries showed variation in the second 90 by older age strata but not in a consistent direction. With regard to the second 90, in Eswatini, those aged 60–64 who were aware of their HIV-positive status were more likely to be on treatment than those aged 50–54 years old (aPR: 1.06, 95% confidence intervals [CI]: 1.01–1.11, $p < 0.05$). In Cameroon, those aged 60–64 who were aware of their HIV-positive status were less likely to be on treatment than those 50–54 years old (aPR: 0.95, 95% CIs: 0.91–0.99, $p < 0.05$). In Rwanda, those aged 55–59 who were aware of their HIV-positive status were more likely to be on treatment than those 50–54 years old (aPR: 1.01, 95% CIs: 1.00–1.02, $p < 0.05$), while those 60–64 years of age were less likely to be on treatment than those 50–54 years old (aPR: 0.98, 95% CIs: 0.96–1.00, $p < 0.05$). Table 5 shows the third 90 VLS models for the 13 countries. One country showed higher achievement of the third 90 in an older age stratum. In Ethiopia, those aged 60–64 who were on treatment were more likely to have VLS compared to those 50–54 years old (aPR: 1.10, 95% CIs: 1.00–1.20, $p < 0.05$).

4 | DISCUSSION

Overall, OPLWH have made more progress towards achievement of 90-90-90 UNAIDS targets than PLWH aged 15–49. Progress by OPLWH towards 90-90-90 UNAIDS targets was noted in all 13 countries included in this analysis, which suggests they are well positioned to reach the 95-95-95 targets by 2025 as well. In two countries, Eswatini and Namibia, OPLWH have achieved all three 90-90-90 targets. In the other 11 countries, OPLWH have all achieved one or both of the second and third 90-90-90 targets. However, achievement of the first 90, that is awareness of HIV-positive status, continues to be a challenge [36, 37].

In the models we used, there was minimal variation demonstrated by age strata among OPLWH in the 13 countries. There was no variation in awareness by older age groups, three countries showed variation in treatment by older age groups—although not in a consistent direction, and one country showed higher VLS by an older age group. This lack of difference by age strata among OPLWH could indicate that those who have survived with HIV over the age of 50 are experienced with taking medications and older age does not diminish that fact.

Our findings are consistent with those from both a modelling study utilizing UNAIDS data and results from a systematic review and meta-analysis of 92 studies, which showed heterogeneity of 90-90-90 progress across countries, sex and age groups [5, 9]. Both studies, which did not specifically focus on OPLWH, noted more progress towards 90-90-90 targets among OPLWH compared with younger age groups, but neither examined progress among OPLWH in the various age strata within that group [5, 9]. Our findings among PLHIV aged 15–49 years were similar to other research as we also found that women were more likely to achieve the 90-90-90 targets than men; however, we noted different 90-90-90 progress among men and women among OPLWH in our study, with men making more progress to achieve the first and third 90 targets than women, while second 90 achievement was similar [5, 9].

A key finding highlighted by our study is the gap noted in the achievement of the first 90, that is awareness of HIV-positive status, among OPLWH [10, 37]. We found that

Table 2. Pooled 13 country descriptive clinical statistics among older persons living with HIV aged 50 and over

	Males		Females		Total	
	N	% (95% CIs)	*N*	% (95% CIs)	*N*	% (95% CIs)
Diagnosis and treatment status (ARV-adj)						
Unaware of HIV status	316	22.46 (20.16–24.76)	404	20.31 (18.72–21.89)	720	21.25 (19.94–22.56)
Aware of HIV status and not on ART	60	2.98 (2.36–3.60)	94	2.49 (1.98–3.00)	154	2.70 (2.30–3.11)
Aware of HIV status and on ART	1535	74.56 (72.20–76.91)	2247	77.20 (75.56–78.84)	3782	76.05 (74.71–77.39)
ARVs detected						
Yes	1467	70.39 (67.99–72.79)	2165	74.65 (72.92–76.38)	3632	72.79 (71.34–74.23)
No	437	29.61 (27.21–32.01)	566	25.35 (23.62–27.08)	1003	27.21 (25.77–28.66)
VLS						
Yes	1460	70.90 (68.51–73.29)	2176	75.51 (73.74–77.27)	3636	73.50 (72.02–74.97)
No	450	29.10 (26.71–31.49)	566	24.49 (22.73–26.26)	1016	26.50 (25.03–27.98)
CD4 cell count per μl						
<100	50	3.19 (2.58–3.81)	37	1.69 (1.13–2.24)	87	2.36 (1.95–2.76)
100–199	221	14.57 (12.89–16.25)	161	7.89 (6.48–9.31)	382	10.87 (9.77–11.97)
200–349	473	29.09 (26.69–31.49)	414	17.58 (15.79–19.37)	887	22.71 (21.11–24.30)
350–499	453	27.11 (24.88–29.34)	566	26.97 (24.90–29.04)	1019	27.03 (25.32–28.75)
≥500	500	26.04 (23.80–28.27)	1215	45.88 (43.58–48.17)	1715	37.04 (35.32–38.75)
Testing history						
Never tested	155	11.39 (9.49–13.29)	243	13.69 (12.15–15.22)	398	12.68 (11.67–13.70)
Tested in the past year	547	27.83 (25.98–29.68)	719	26.44 (24.75–28.13)	1266	27.04 (25.74–28.34)
Tested more than 1 year ago	1113	56.61 (54.22–59.01)	1663	56.27 (54.39–58.14)	2776	56.42 (54.98–57.86)
Don't know or missing	96	4.17 (3.42–4.93)	120	3.61 (2.85–4.37)	216	3.85 (3.33–4.38)
Number of years since diagnosis						
Less than 12 months	97	6.96 (5.98–8.02)	135	6.71 (5.78–7.64)	232	6.82 (6.11–7.53)
1 to less than 5 years	453	32.32 (29.97–34.66)	634	31.78 (29.84–33.71)	1087	32.01 (30.44–33.58)
5 years or more	868	60.73 (58.30–63.15)	1334	61.51 (59.59–63.43)	2202	61.17 (59.6–62.75)
Antiretroviral regimen (among ARV detected)						
First line (EVP, NVP and INSTI)	1435	96.89 (96.38–97.40)	2120	97.06 (96.30–97.83)	3555	96.99 (96.49–97.49)
Second line (PI, LPV and ATV)	29	3.07 (2.57–3.58)	42	2.71 (1.95–3.47)	71	2.86 (2.36–3.36)
Both	2	0.04 (0.00–0.09)	3	0.23 (0.22–0.23)	5	0.15 (0.13–0.17)
Number of years since initiating ART						
Less than 12 months	125	8.78 (7.77–9.79)	196	10.69 (9.25–12.12)	321	9.87 (8.96–10.78)
1 to less than 5 years	466	35.43 (33.07–37.79)	647	35.18 (33.15–37.22)	1113	35.29 (33.66–36.91)
5 years or more	758	55.79 (53.45–58.13)	1131	54.13 (52.11–56.16)	1889	54.84 (53.28–56.41)

Note: CD4 cell count does not include Kenya or Rwanda as CD4 testing was not conducted.
Abbreviations: ART, antiretroviral therapy; ARV, antiretroviral; VLS, viral load suppression; EVP, Emtricitabine/rilpivirine/tenofovir; NVP, Nevirapine; INSTI, Integrase strand transfer inhibitors; PI, protease inhibitor; LPV, Lopinavir; ATV, Atazanavir.
Definitions: Diagnosis and treatment status: Percent distribution of HIV-positive persons by HIV diagnosis and treatment status; ARVs detected: Percent distribution of HIV-positive persons by the presence of detectable ARVs; VLS: Among HIV-positive persons, percentage with viral load suppression (< 1000 copies/ml); CD4 cell count per μl: Among HIV-positive persons, percentage with CD4 count within each range; Testing history: Percentage of persons who ever received HIV testing and received their test results; Number of years since diagnosis: Percent distribution of HIV-positive persons by time since diagnosis; Antiretroviral regimen (among ARV detected): Among those with detected ARVs, percent distribution on first line, second line or both regimens; Number of years since initiating ART: Among those self-reporting taking ARVs, percent distribution of time since initiating ART.

21.3% of all OPLWH were unaware of their HIV-positive status before the surveys, and more than half (54%) of these unaware OPLWH had never previously been tested. Existing research suggests that older adults have less knowledge and understanding of HIV infection than younger age groups and are, therefore, less likely to seek testing [37]. Providers often do not consider older adults to be at risk for HIV so there is hesitation to discuss risk behaviours associated with HIV acquisition, such as inquiring into sexual activity and other risk behaviours, though older adults may have similar risks of HIV infection as younger adults [8, 10, 11, 38–40]. This provider bias combined with a lack of understanding of ongoing transmission risk for HIV infection in this population among both the providers and the older adults results in many missed

Table 3. Poisson regression models for awareness of HIV-positive status (first 90), Population-based HIV Impact Assessments, 13 countries, 2015–2019

Country	Aged 50–54			Aged 55–59			Aged 60–64			Aged 65+		
	n	% (95% CI)	aPR[a]	*n*	% (95% CI)	aPR[a]	*n*	% (95% CI)	aPR[a]	*n*	% (95% CI)	aPR[a]
Malawi	133	80.28 (73.57–86.99)	1.00	91	82.32 (74.81–89.83)	1.03 (0.87–1.22)	59	85.78.18–93.06)	1.04 (0.87–1.25)	NA		
Zambia	175	82.80 (79.39–86.22)	1.00	97	80.58 (76.53–84.62)	0.93 (0.84–1.03)	NA			NA		
Eswatini	203	92.05 (88.45–95.65)	1.00	140	92.77 (88.31–97.23)	1.01 (0.95–1.08)	111	91.68 (86.32–97.04)	0.98 (0.91–1.07)	84	90.61 (83.83–97.39)	0.99 (0.89–1.11)
Tanzania	107	69.95 (64.15–75.76)	1.00	77	69.43 (60.30–78.55)	0.96 (0.76–1.21)	43	54.99 (41.33–68.66)	0.83–(0.55–1.25)	30	47.61 (35.47–59.76)	0.73 (0.48–1.12)
Zimbabwe	242	85.33 (80.98–89.69)	1.00	195	81.74 (76.26–87.23)	0.95 (0.86–1.05)	121	82.32 (77.17–87.46)	0.96 (0.87–1.06)	92	75.91 (68.66–83.16)	0.89 (0.76–1.04)
Uganda	115	86.48 (82.72–90.24)	1.00	68	79.75 (73.49–86.00)	0.91 (0.74–1.13)	55	90.02 (85.58–94.46)	1.04 (0.88–1.23)	NA		
Lesotho	263	90.17 (87.22–93.11)	1.00	226	87.76 (84.38–91.13)	0.98 (0.92–1.04)	NA			NA		
Cameroon	55	70.03 (65.54–74.52)	1.00	33	68.39 (53.86–82.92)	0.96 (0.64–1.44)	38	69.30 (62.00–76.60)	0.98 (0.76–1.26)	NA		
Namibia	225	92.88 (89.51–96.24)	1.00	150	95.07 (92.27–97.87)	1.01 (0.95–1.07)	90	96.85 (92.88–100.00)	1.05 (0.97–1.13)	NA		
Cote d'Ivoire	27	70.02 (62.40–77.64)	1.00	22	55.27 (38.82–71.72)	0.86 (0.60–1.24)	11	42.48 (28.64–56.32)	0.61 (0.32–1.15)	NA		
Ethiopia	42	88.97 (84.62–93.32)	1.00	15	87.26 (82.22–92.30)	0.99 (0.78–1.26)	18	83.72 (70.56–96.88)	0.96 (0.70–1.33)	NA		
Kenya	134	87.64 (84.23–91.05)	1.00	87	80.75 (77.00–84.50)	0.91 (0.81–1.02)	62	96.06 (95.43–96.68)	1.07 (0.97–1.18)	NA		
Rwanda	88	85.10 (79.24–90.97)	1.00	68	88.94 (84.24–93.63)	1.06 (0.92–1.23)	44	95.21 (89.95–100.00)	1.12 (0.93–1.35)	NA		

Note: Upper age limits for individual eligibility varied by country: 59 years of age for Lesotho and Zambia, 64 years of age for Cameroon, Cote d'Ivoire, Ethiopia, Kenya, Malawi, Namibia, Rwanda and Uganda, and no upper age limit in Eswatini, Tanzania and Zimbabwe.

[a]Adjusted for sex, residence, employed, wealth quintile, education, marital status and partner HIV status-self-reported.

Table 4. Poisson regression models for antiretroviral therapy use among those aware of HIV-positive status (second 90), Population-based HIV Impact Assessments, 13 countries, 2015–2019

Country	Aged 50–54			Aged 55–59			Aged 60–64			Aged 65+		
	n	% (95% CI)	aPR[a]	*n*	% (95% CI)	aPR[a]	*N*	% (95% CI)	aPR[a]	*n*	% (95% CI)	aPR[a]
Malawi	126	96.29 (94.56–98.01)	1.00	85	94.47 (93.34–95.59)	1.01 (0.96–1.07)	57	94.5 (90.03–98.97)	0.99 (0.94–1.04)	NA		
Zambia	164	94.13 (91.05–97.21)	1.00	92	95.67 (93.06–98.28)	1.03 (0.95–1.11)	NA			NA		
Eswatini	189	91.85 (88.13–95.57)	1.00	131	93.31 (89.35–97.26)	1.01 (0.94–1.08)	109	98.79 (97.51–100.00)	1.06 (1.01–1.11)*	82	98.04 (95.31–100.00)	1.06 (1.00–1.11)
Tanzania	103	96.76 (95.83–97.69)	1.00	75	99.09 (97.58–100.00)	1.02 (0.98–1.05)	43	100.00 (100.00–100.00)	1.01 (0.96–1.05)	27	91.77 (77.97–100.00)	0.94 (0.66–1.32)
Zimbabwe	235	97.63 (95.90–99.35)	1.00	189	97.10 (95.42–98.77)	1.00 (0.96–1.03)	113	94.11 (90.28–97.95)	0.98 (0.93–1.03)	90	98.33 (95.99–100.00)	1.02 (0.97–1.07)
Uganda	105	93.62 (90.34–96.90)	1.00	66	96.35 (95.73–96.98)	1.03 (0.94–1.12)	52	94.04 (92.59–95.49)	1.01 (0.93–1.11)	NA		
Lesotho	253	95.43 (93.32–97.53)	1.00	222	97.94 (96.54–99.34)	1.01 (0.98–1.05)	NA			NA		
Cameroon	54	99.95 (99.83–100.00)	1.00	31	92.95 (91.73–94.17)	0.95 (0.89–1.02)	36	95.48 (94.55–96.41)	0.95 (0.91–0.99)*	NA		
Namibia	215	95.83 (92.99–98.67)	1.00	147	98.2 (96.43–99.96)	1.01 (0.97–1.05)	89	98.90 (96.71–100.00)	1.02 (0.97–1.06)	NA		
Cote d'Ivoire	24	95.39 (94.04–96.75)	1.00	20	96.45 (91.10–100.00)	1.01 (0.96–1.05)	11	100.00 (100.00–100.00)	1.11 (0.37–3.40)	NA		
Ethiopia	41	97.39 (96.76–98.03)	1.00	15	100.00 (100.00–100.00)	1.04 (0.94–1.16)	17	91.13 (88.96–93.3)	0.91 (0.74–1.12)	NA		
Kenya	129	96.67 (93.65–99.69)	1.00	85	97.83 (94.66–100.00)	1.02 (0.89–1.16)	62	100.00 (100.00–100.00)	1.04 (0.95–1.14)	NA		
Rwanda	87	99.21 (99.10–99.31)	1.00	68	100.00 (100.00–100.00)	1.01 (1.00–1.02)*	43	97.23 (96.81–97.65)	0.98 (0.96–1.00)*	NA		

[a]Adjusted for sex, residence, employed, wealth quintile, education, marital status, partner HIV status-self-reported and the number of years since diagnosis.
*$p < 0.05$.

Table 5. Poisson regression models for viral load suppression among those on antireotroviral therapy (third 90), Population-based HIV Impact Assessments, 13 countries, 2015–2019

Country	Aged 50–54			Aged 55–59			Aged 60–64			Aged 65+		
	n	% (95% CI)	aPR[a]	*n*	% (95% CI)	aPR[a]	*n*	% (95% CI)	aPR[a]	*n*	% (95% CI)	aPR[a]
Malawi	119	93.43 (90.02–96.84)	1.00	79	91.71 (86.25–97.18)	1.01 (0.89–1.15)	52	93.78 (90.32–97.25)	0.99 (0.88–1.12)	NA		
Zambia	154	93.49 (90.61–96.37)	1.00	91	99.39 (99.29–99.48)	1.07 (0.99–1.15)	NA			NA		
Eswatini	182	96.81 (94.61–99.02)	1.00	125	95.86 (92.55–99.18)	1.01 (0.95–1.07)	107	98.51 (96.43–100.00)	1.01 (0.98–1.05)	77	94.3 (89.04–99.55)	0.97 (0.89–1.05)
Tanzania	91	91.78 (89.08–94.49)	1.00	70	90.58 (81.37–99.78)	1.01 (0.90–1.15)	38	87.68 (81.39–93.98)	0.90 (0.72–1.11)	25	90.04 (84.80–95.28)	1.06 (0.97–1.16)
Zimbabwe	215	90.89 (87.67–94.11)	1.00	177	93.96 (90.87–97.05)	1.05 (0.98–1.12)	106	93.72 (88.1–99.35)	1.05 (0.96–1.14)	81	88.03 (81.05–95.01)	1.01 (0.89–1.14)
Uganda	93	88.63 (84.27–93.00)	1.00	58	86.75 (81.94–91.56)	1.06 (0.86–1.31)	39	77.02 (66.61–87.42)	0.94 (0.68–1.29)	NA		
Lesotho	233	91.97 (88.96–94.99)	1.00	211	95.03 (92.98–97.09)	1.01 (0.96–1.07)	NA			NA		
Cameroon	46	86.78 (78.44–95.11)	1.00	29	91.03 (89.34–92.71)	1.22 (0.69–2.18)	33	92.02 (84.51–99.54)	1.07 (0.82–1.39)	NA		
Namibia	197	93.29 (89.75–96.83)	1.00	137	93.92 (91.34–96.51)	0.99 (0.94–1.05)	85	96.73 (93.47–100.00)	1.03 (0.96–1.12)	NA		
Cote d'Ivoire	23	94.75 (92.55–96.94)	1.00	18	95.47 (95.12–95.81)	1.09 (0.49–2.45)	9	74.69 (55.14–94.24)	0.94 (0.72–1.23)	NA		
Ethiopia	38	92.56 (90.69–94.43)	1.00	14	98.07 (97.15–98.98)	1.01 (0.87–1.17)	15	86.20 (73.10–99.29)	1.10 (1.00–1.20)*	NA		
Kenya	120	93.01 (90.07–95.96)	1.00	80	94.61 (93.24–95.99)	1.02 (0.93–1.12)	60	97.00 (96.50–97.49)	1.03 (0.92–1.14)	NA		
Rwanda	81	92.52 (88.95–96.09)	1.00	63	91.37 (85.78–96.96)	1.01 (0.90–1.14)	38	87.36 (79.59–95.13)	0.98 (0.87–1.11)	NA		

[a]Adjusted for sex, residence, employed, wealth quintile, education, marital status, partner HIV status-self-reported and the number of years since initiating ART.
*$p < 0.05$.

opportunities for HIV testing, access to HIV prevention and initiation and retention in treatment services. Country HIV programmes could benefit from additional strategies to raise awareness among healthcare providers and increase health communication campaigns about testing and existing prevention interventions (such as knowledge of partner HIV status and the use of condoms, PrEP or treatment as prevention [U = U] for discordant couples) targeting older populations in SSA [41, 42].

Many OPLWH will wait to test for HIV until symptomatic which results in a delay in diagnosis of HIV and initiation of ART, resulting in poorer health outcomes [8, 38, 43]. In addition, age-disparate relationships are associated with higher HIV acquisition among adolescent girls and young women [44]. As such, more effective case-finding among older men may also have positive consequences on reducing onward transmission. Innovative testing strategies to reach older adults, such as establishing tailored testing initiatives for this age group, use of self-testing and delivery of testing through community-based services, have been shown to be useful to increase more frequent and earlier testing [5, 45]. In addition, OPLWH are managing other chronic health conditions and are at higher risk of developing age-associated non-communicable diseases, such as cardiovascular disease, neurocognitive disorders and frailty [46]. Older adults may be more likely to seek medical care for reasons other than HIV but provider-initiated counselling and testing may be overlooked for this population because they are thought not to be at risk [47]. These findings suggest the need for further sensitization and training for health providers to elicit sexual and history of risk behaviours among older patients and to offer them HIV testing as a comprehensive strategy to identify all HIV-positive individuals and combining with non-HIV care management, as part of routine provider-initiated counselling and testing [48, 49].

The finding that OPLWH were more likely to be aware of their HIV-positive status than younger PLWH may be due to survivor bias; those who remained unaware of their HIV-positive status longer were more likely to have died compared to those who became aware sooner, that is at a young age. Studies have shown that age is associated with adherence to ART and achievement of VLS [50]. One study that assessed mortality in SSA among HIV-positive individuals on ART found that sex differences in all-cause mortality and loss-to-follow-up noted in younger people were also present among those ages 50–59, with older women on ART at greater risk of death as they age compared with men [51]. Additionally, there is a potential cohort effect for mortality among the OPLWH who have survived to this point compared with younger PLHIV [38, 52]. There was a global mortality peak from AIDS-related deaths in 2005/2006, at a time when our OPLWH cohort was aged 35–50, and since 2010, there has been a 50% reduction in AIDS-related deaths in Eastern and Southern Africa [53]. Additionally, PHIA surveys in many countries were conducted before test and treat protocols and treatment with dolutegravir was fully rolled out, potentially contributing to some countries not achieving the third 90 yet [54–56].

The study has several strengths. One key feature is that the PHIA surveys provided nationally representative data for all 13 countries, including HIV-related biomarkers. Because the PHIA surveys are collected in the household, they capture information on those who may not be engaged in care and accessing health services, including older people who may be living with HIV and have yet to access treatment. The findings highlight the importance of expanding the age limits of all HIV surveys and surveillance efforts, to track progress among the growing population of OPLWH. The study also has some limitations. The surveys were all cross-sectional in nature and only represent one time point. However, repeat PHIA surveys have been done in several countries, which will permit the assessment of trends among OPLWH over time in the future. Additionally, the upper age ranges varied across PHIA surveys: two countries did not have data for ages above 59, and eight countries did not have data for ages 65 and older. We examined results of 90-90-90 achievement by upper age limit in each country and did not observe any differences in 90-90-90 achievement between countries based on upper age limit; successful achievement was distributed across all countries.

5 | CONCLUSIONS

In conclusion, finding gaps in the knowledge of HIV-positive status among OPLWH in several African countries highlights the importance of focused HIV awareness and the need to expand HIV testing efforts for older adults, as it impacts the care and treatment cascade and reduces longevity and quality of life. At the same time, HIV programmes and providers could use these findings to support improved HIV counselling, education and screening of older adults on risk behaviours and offer them HIV prevention, testing and treatment services.

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COMPETING INTERESTS

None to declare for any authors.

AUTHORS' CONTRIBUTIONS

All authors have read and approved the manuscript. SMF conceptualized, drafted and edited the manuscript. CW and RB conceptualized and conducted analyses and edited the manuscript. AL, SD, DH, ANK and TGH conceptualized and edited the manuscript. RN, NW, ML, MA, JMJ, NK, IP, NM, SSN, AOA, EWN, FMA, SL, JW, PC, OM, BKM, PN, DA, AK, SB, FN, GM, CBN, JDS, EKD, LED, RM-S, A-CB, YG, FE, TN, LT, RFK, WK, JM, SB, EK, GR, AA, CW, SB, KS, HKP, KB and ACV reviewed and edited the manuscript. WME and JJ conceptualized, reviewed and edited the manuscript.

ACKNOWLEDGEMENTS

We would like to acknowledge country leadership for their technical and administrative support in organizing and conducting the PHIA surveys. Our appreciation also extends to the data collectors for their dedication and all study participants for providing their information.

FUNDING

The PHIAs were funded by the President's Emergency Plan for AIDS Relief through the US Centers for Disease Control and Prevention (CDC) under the terms of cooperative agreements #1U2GGH000994 and 5NU2GGH001226.

DISCLAIMER

The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the official position of the funding agencies.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available upon request from the PHIA project website: https://phia-data.icap.columbia.edu/.

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Godfrey C et al. *Journal of the International AIDS Society* 2022, **25**(S4):e26002
http://onlinelibrary.wiley.com/doi/10.1002/jia2.26002/full | https://doi.org/10.1002/jia2.26002

COMMENTARY

Providing differentiated service delivery to the ageing population of people living with HIV

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Abstract

Introduction: Differentiated service delivery (DSD) models for HIV are a person-centred approach to providing services across the HIV care cascade; DSD has an increasing policy and implementation support in high-burden HIV countries. The life-course approach to DSD for HIV treatment has focused on earlier life phases, childhood and adolescence, families, and supporting sexual and reproductive health during childbearing years. Older adults, defined as those over the age of 50, represent a growing proportion of HIV treatment cohorts with approximately 20% of those supported by PEPFAR in this age band and have specific health needs that differ from younger populations. Despite this, DSD models have not been designed or implemented to address the health needs of older adults.

Discussion: Older adults living with HIV are more likely to have significant co-morbid medical conditions. In addition to the commonly discussed co-morbidities of hypertension and diabetes, they are at increased risk of cognitive impairment, frailty and mental health conditions. Age and HIV-related cognitive impairment may necessitate the development of adapted educational materials. Identifying the optimal package of differentiated services to this population, including the frequency of clinical visits, types and location of services is important as is capacitating the healthcare cadres to adapt to these challenges. Technological advances, which have made remote monitoring of adherence and other aspects of disease management easier for younger populations, may not be as readily available or as familiar to older adults. To date, adaptations to service delivery have not been scaled and are limited to nascent programmes working to integrate treatment of common co-morbidities.

Conclusions: Older individuals living with HIV may benefit from a DSD approach that adapts care to the specific challenges of ageing with HIV. Models could be developed and validated using outcome measures, such as viral suppression and treatment continuity. DSD models for older adults should consider their specific health needs, such as high rates of co-morbidities. This may require educational materials, health worker capacity building and outreach designed specifically to treat this age group.

Keywords: ageing; differentiated service delivery; person-centred care; co-morbidities integration; PEPFAR; HIV/AIDS

Received 3 February 2022; **Accepted** 1 August 2022

1 | INTRODUCTION

The President's Emergency Program for AIDS Relief (PEPFAR) is a U.S. Government programme launched in 2003 to address the growing HIV pandemic in areas of the world most affected by new infections and deaths from HIV [1]. The programme has grown rapidly in both scale and breadth of HIV treatment services offered over the last two decades, largely by prioritizing the identification of people living with HIV, linking them to HIV care and treatment, and ensuring treatment continuity to achieve and maintain viral suppression. By the end of the fiscal year 2021, the PEPFAR programme supported HIV treatment for nearly 19 million people with HIV across 50 countries, many of which are in Africa [2]. In 2021, among people accessing HIV services in PEPFAR-supported countries, 3.6 million or 21% were older adults—defined as 50 years or older. Of this cohort of older adults, 57% were female. This is a notable increase from only 5 years prior where the older adults made up 1.5 million (11%) people living with HIV on treatment (Figure 1). The growth in the relative and absolute population of older adults living with HIV reflects both new clients initiating treatment in this age group and clients who have been part of the PEPFAR programme in prior years ageing into this cohort, with the latter accounting for a larger portion of the increase [2]. Among countries supported by PEPFAR, there is considerable variation in the proportion of the cohort that is older adults, with ranges from 7% to 30% across cohorts in 2021 [3]. While this proportion is lower than in many North American and western European cohorts, where older adults comprise nearly 50% of the treatment population, the absolute number of older adults living with HIV in PEPFAR-supported countries is three

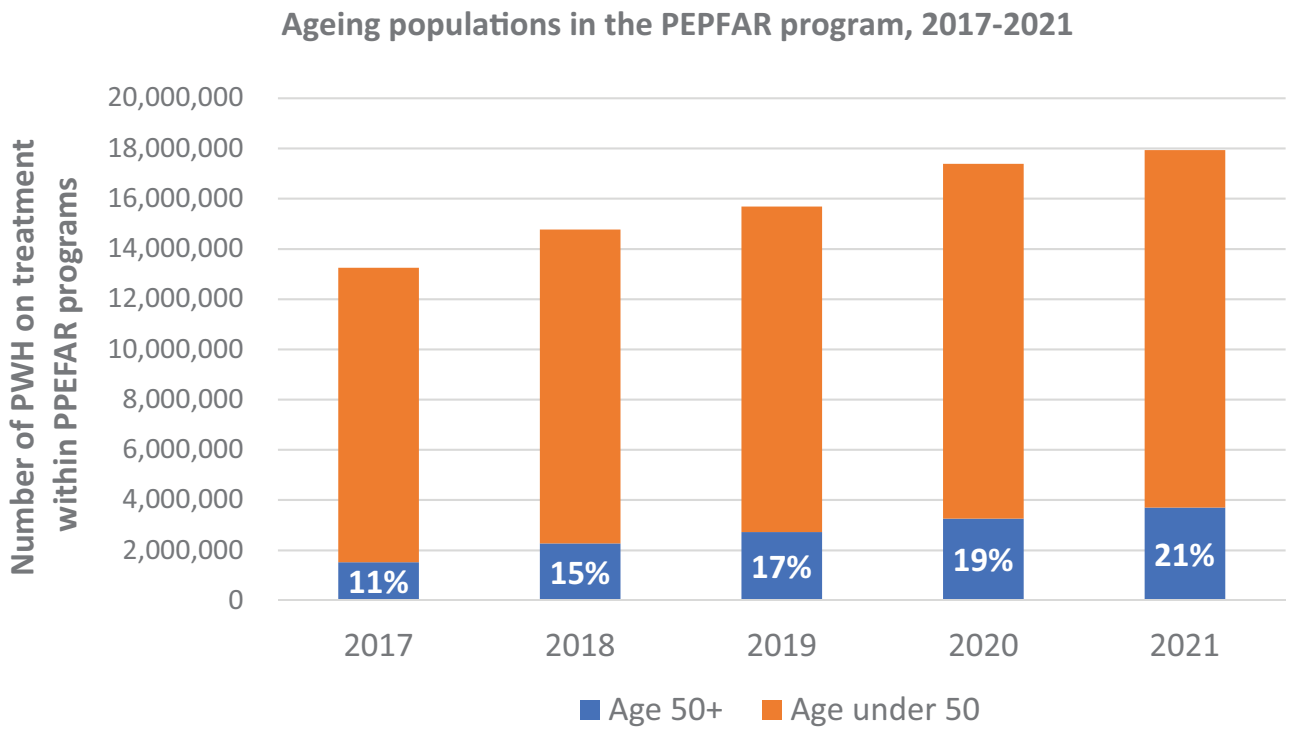

Figure 1. The number of people on HIV treatment in PEPFAR-supported countries, 2017–2021, among older adults and those under 50 years of age. Between 2017 and 2021, the proportion of the HIV treatment cohort 50 years of age and above has increased from 11% to 21%. Abbreviation: PWH, people living with HIV.

times higher [4] than those in North America and western Europe.

Since 2015, the World Health Organization has recommended differentiated service delivery (DSD) models for HIV treatment to support "treat all" and in recognition of the diversity of needs of people living with HIV [5–7]. DSD for HIV has been defined as a person-centred approach that adapts HIV services to meet the needs and expectations of people living with and at risk of acquiring HIV while acknowledging the constraints of the heathcare system. Adaptations for specific populations have addressed specific challenges, including stigma and discrimination, psychosocial support needs and provision of care outside of traditional clinical venues [8–11]. Endorsed by PEPFAR and the Global Fund [12], DSD has been included in national HIV guidelines and implementation has been scaled up, particularly in high-burden HIV countries. There has also been a concurrent focus on a life-course approach in HIV programmes. This life-course approach to DSD for HIV treatment has focused on earlier life phases—childhood and adolescence, families, and supporting sexual and reproductive health during childbearing years. Further, DSD for key populations—including men who have sex with men, people who inject drugs, sex workers and transgender people—has been designed to support improving HIV outcomes in these populations. Currently, there are no DSD models specifically designed for older adults, a rapidly growing cohort of individuals living with HIV.

In this commentary, we argue that with an ageing population of people living with HIV on treatment, health service providers and organizations acknowledge their unique challenges and consider developing DSD for HIV treatment models for older adults. We present common challenges faced by older adults living with HIV and suggest adaptations that might be considered and areas of research to ensure person-centred care for the ageing cohort of people living with HIV.

2 | DISCUSSION

2.1 | HIV and ageing in the PEPFAR programme

Older adults have better treatment outcomes as measured by treatment continuity and viral suppression compared with younger people in the PEPFAR programme. Older adults living with HIV have the lowest proportion of loss to follow up with less than 2% experiencing an interruption in treatment when established on ART in a given quarter globally [13]. Older adults living with HIV also have the highest viral suppression rates with over 99% of clients [13] in the age group with viral load results available being suppressed (defined as VL<1000 c/ml). Thus, as effective therapies have improved the lifespan of people living with HIV, programmes can strive to enhance the quality of life as individuals age by tailoring services unique to this age group [14].

2.2 | An ageing treatment cohort with specific health needs

Although older adults living with HIV may not need intensive, specific, support for HIV treatment compared with the specific counselling needs of younger people, they may have

social and mental health needs that warrant consideration in DSD models. Three specific health challenges should be considered for older adults living with HIV:

1. High prevalence of co-morbidities and associated treatments

Older adults bear a significant burden of non-communicable diseases, and some studies document a greater prevalence of co-morbidities in people living with HIV compared to those without HIV, including in African cohorts [15–17]. Many individuals with HIV have multiple co-morbidities with some of the most common being diabetes, hypertension, obesity and renal insufficiency [18]. Additionally, older adults living with HIV are at increased risk of severe outcomes from both the long-term complications of HIV treatment itself and other infectious diseases, including COVID-19 and tuberculosis; the morbidity risk for these conditions may be additive. Being on multiple drugs related to co-morbidities can create additional challenges for individuals living with HIV, including drug–drug interactions, adherence requirements for multiple medications and differing management requirements for chronic diseases [19]. Drug dispensation schedules for medicines other than antiretroviral therapy (ART) may differ significantly and the differences in frequency of required clinical and laboratory monitoring needed for other conditions can make management of these conditions more complicated, requiring multiple visits to healthcare facilities. There is a robust discussion in the international HIV treatment community about how best to build capacity within the healthcare system to provide holistic care for chronic diseases and provide integrated services for those with multiple co-morbidities, including HIV. As countries determine their best response, policymakers and healthcare providers may be able to leverage various PEPFAR-supported platforms—such as remote training modules for healthcare workers providing DSD, electronic medical records and drug dispensation tools—to achieve integrated service delivery to older adults.

2. High prevalence of geriatric syndromes

Older individuals have an age-associated decline of physiological reserve and function and intrinsic capacity, which include sensory (vision and hearing), nutrition, mobility, depressive symptoms and cognitive decline, resulting in increasing vulnerability to a variety of stressors, including co-morbidities. This has been called frailty in the medical literature and an increasing body of work identifies frailty as an independent risk factor for mortality and morbidity in both high resource and resource-limited contexts [20–22]. Frailty is prevalent in the few studies that have evaluated it in Africa being more common in women, with a similar prevalence in people living with HIV and in those without but may appear earlier in individuals with HIV [23–26].

Cognitive impairment is common among people living with HIV affecting up to 50% of individuals, including those who are on effective ART [27–30]. In older adults, cognitive impairment may complicate treatment especially when there are multiple co-morbidities [31]. Older adults commonly experience mental health challenges, both related and unrelated to their HIV status, including depression, isolation and loneliness [32]. Depression is a common neuropsychiatric comorbidity and is associated with "unhealthy ageing" characterized by accelerated neurocognitive decline [33]. The changes to daily life related to COVID-19 restrictions are also likely to have further exacerbated many of these factors. Loss of spouse, income and other life-changing events may further impact the mental health and wellbeing of these individuals.

Screening for frailty and other geriatric syndromes is recommended by many authorities but there is no consensus on the timing of screening and screening tools. Tools must be validated for the particular setting in which they are used [21, 22] and there are few studies evaluating evidence-based interventions to address these geriatric syndromes to scale in order to improve outcomes in this vulnerable group. DSD for older adults could be designed to account for culture-specific interventions and ageing-related geriatric syndromes most relevant to their populations.

2.3 | Where to from here

The provision of HIV treatment globally has been hailed as an unprecedented public health victory and the first chronic disease model scaled up in resource-limited settings. Cornerstones of HIV treatment programmes have been simple therapies, task-shifting and decentralization. Service delivery adaptations to the "building blocks" of services delivery—the frequency of services, the location of services and the package of services provided should be designed to address the specific challenges related to ageing. For example, where DSD for HIV treatment has reduced clinical consultations for many people by separating clinical consultations from drug refills, an older adult with co-morbidities may require different types of evaluations and monitoring to address their health needs.

1. Apply the key enablers from DSD for HIV treatment to expand integration

As outlined by Bygrave et al., DSD for HIV has been enabled by "simplified algorithms, optimized formulations, secure drug supply and strengthened monitoring and evaluation systems" [34]. In addition, the removal of user fees has supported improved uptake and access to HIV treatment and linkage to HIV care already has promoted linkage to overall healthcare use and access [35]. Management of comorbid conditions and linkage to community-based services for social support will likely be an important component of care provision. Even if all aspects of the health of an older individual cannot be addressed with the public health approach, certain conditions that are highly prevalent and amenable to an algorithmic approach to management and could be executed by providers with fewer years of formal medical training can result in substantial gains in further decreasing morbidity and mortality. Such conditions may include well-controlled hypertension [36] and diabetes. Mechanisms used to procure drugs for HIV can be extended to diagnostics and treatments for these conditions as well.

2. Adapt or develop screening tools and treatment algorithms for common co-morbidities validated in settings with high HIV burdens

Screening for cognitive disorders and mental health issues may be important in this population, and screening tools

appropriate for the cultural and age context may need to be developed or adapted. These tools will need rigorous validation in the population in which they are deployed. The "trans diagnostic approach" in which it is recognized that mental health disorders often co-occur and may have a shared underlying pathology has been helpful for the diagnosis and treatment of mental illness in resource-limited settings and would need to be adapted to include identification and treatment of age-related cognitive disorders [37, 38].

3. Follow country-based innovations where HIV services are evolving and adapting to changing needs

There are emerging nascent examples from countries to provide more person-centred care, primarily to improve the integration of common non-communicable diseases. In South Africa, the Central Chronic Medicines Dispensing and Distribution (CCMDD) programme pre-packs medications for chronic diseases, including HIV, hypertension and diabetes, for distribution through health facilities and community pick-up points. More than two million clients are provided with medications pre-packed by CCMDD, including 12% who are receiving ART plus other non-communicable disease medications [39]. During COVID-19, emphasis was placed on expanding the proportion of people collecting refills from community pick-up points [10]. The investments made in healthcare worker training, capacity building, creating and modifying algorithms for care could all be applied to the wider health sector and bring a chronic disease care model to many countries that do not currently have one.

In Ethiopia, there is strong interest in the ministry of health to leverage the systems and the DSD capabilities developed in the PEPFAR platform to support the management of chronic co-morbidities among people on ART. The country was early to adopt 6-monthly ART refills in 2017 [40], subsequently offering additional DSD for HIV treatment models and accelerating access to extended ART refills to specific populations, including pregnant and breastfeeding women and newly initiated people of treatment in response to COVID-19 [10]. To support the management of chronic diseases, it is anticipated that the experience gained from these successes in HIV treatment, including establishing national guidelines, technical working groups, scaled training and mentorship models, task shifting among health workers, data monitoring and use, and continuous quality improvement practices for HIV treatment, will provide a solid foundation for next steps with chronic disease management for older adults with HIV.

4. Increase research, including implementation science and qualitative research, that focuses on service delivery for older adults living with HIV

As countries and implementers innovate and adapt HIV services to the challenges of older adults, implementation research will be critical to understanding what works. Outcome measures, such as viral suppression and treatment continuity, are already established, but there may be other outcomes that are important to measure, including outcomes of co-morbidities. Quality of life, "loss of frailty" and community connectedness may be useful to measure. As individuals live longer, it will be important to compare mortality and co-morbidities to the non-HIV populations. These efforts have the potential to improve the health and wellbeing of the general population.

Most older adults in treatment programmes are "successful" patients: they have been on effective therapy, often for decades, and have experienced changes in ART regimen and delivery systems. These individuals have successfully navigated HIV treatment and may be a valuable resource for programmes. These older individuals may be more treatment literate with respect to HIV than their younger counterparts, but their treatment literacy needs are poorly understood. Treatment literacy is associated with positive outcomes for HIV and several chronic conditions, including heart failure and diabetes [41–43], such as the need for age-appropriate vaccines and falls prevention. The experience of older adults in PEPFAR programmes is poorly documented, and qualitative research in this area can inform how to provide the best information and care. More data are needed on the experience of older adults in treatment in PEPFAR settings and an effort should be made to harness the experiences of these individuals to improve care for all.

3 | CONCLUSIONS

It is time for HIV programming to include specific DSD for HIV treatment models to address the needs of an ageing HIV cohort. With global decreases in new infections and continual increases in the number of people living with HIV on treatment, an ageing HIV cohort is an indicator of the huge progress and success of the HIV response. Building on experiences of adapting services, HIV services for specific populations, such as adolescents and key populations, acknowledging the realities of an ageing cohort and learning how to best provide person-centred HIV care that will improve the quality of life of an older person living with HIV will be important.

The HIV needs of older adults are not limited to those living with HIV who are established on treatment. Older adults also require access to HIV prevention with their sexual health needs addressed beyond their reproductive years. Further, as the number of people living with HIV who do not know their status continually declines, HIV testing will be important for those previously not diagnosed and in this older cohort.

The initiative to care for the whole older adult will need commitment from global funders and in close partnership with ministries of health to achieve the best outcomes. As programmes are being implemented, care needs to be taken to develop outcome measures of success, document outcomes and successful models in the field so that they can be rapidly disseminated around the world to keep up with the pace of the ageing HIV population. Importantly, this would also align with the agreed-upon UN sustainable development goal (SDG 3) of "ensuring health lives and promote well-being for all at all ages" [44].

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COMPETING INTERESTS

AG is a deputy editor of the *Journal of the International AIDS Society*.

AUTHORS' CONTRIBUTIONS

AG and CG conceptualized the article. CG wrote the first draft. SV reviewed PEPFAR global and national data on ageing. Insight from Ethiopia was provided by MPS and from South Africa was provided by AG. All authors edited and approved the final manuscript.

ACKNOWLEDGEMENTS

The authors wish to thank Dr. Zenebe Melaku, ICAP Ethiopia Country Director for his insights and strategic thinking.

FUNDING

AG is supported by the Bill and Melinda Gates Foundation (INV002610).

DISCLAIMER

CG, SV and MPS wrote this in their capacity as US government employees; the views expressed are their own and should not be construed to represent the positions of the Department of State, the Centers for Disease Control or the Department of Health and Human Services.

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Murzin K et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25978
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25978/full | https://doi.org/10.1002/jia2.25978

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

"We can hardly even do it nowadays. So, what's going to happen in 5 years from now, 10 years from now?" The health and community care and support needs and preferences of older people living with HIV in Ontario, Canada: a qualitative study

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Abstract

Introduction: The population of people living with HIV (PLWH) is ageing consequent to effective treatment and a steady stream of new diagnoses among older adults. PLWH experience a greater burden of age-related comorbidities and poorer social determinants of health compared to their HIV-negative peers, yet comprehensive requisites for care and support as PLWH age remain poorly understood. Preferences And Needs for Ageing Care among HIV-positive Elderly people in Ontario, Canada (PANACHE ON), explored the health and community care and social support needs and preferences of a diverse group of older PLWH (age 60+) and described life course experiences among older PLWH that shape these needs and preferences and whether they are met.

Methods: PANACHE ON was a qualitative community-based participatory research study. In-person focus groups using a semi-structured interview guide were co-facilitated by pairs of trained older PLWH from July to October 2019. Purposive sampling bolstered the inclusion of communities disproportionately affected by HIV in Ontario. Descriptive analysis was used to summarize demographic data; participatory data analysis was conducted by a subset of the research team, with transcripts double-coded and analysed using NVIVO 12 Plus.

Results: A total of 73 PLWH participated, 66% identified as men. The mean age was 64 years (range 55–77) and median time living with HIV was 23 years (range 2–37). The current and anticipated needs of older PLWH, many of which were only partially met, included necessities such as food and housing, mobility and sensory aids, in-home support, social and emotional support, transportation and information. Three experiences—trauma, stigma and uncertainty—intersected in the lives of many of our participants, shaping their needs for care and support, and impacting the ease with which these needs were met.

Conclusions: Unmet health and social needs and limited control over the availability and accessibility of ageing-related care and support due to resource constraints or reduced capacity for self-advocacy results in anxiety about the future among older PLWH, despite their well-developed coping strategies and experience navigating systems of care. These study findings will inform the development of the first national needs assessment of older PLWH in Canada.

Keywords: HIV care continuum; quality of life; social support; structural drivers; North America; community

Received 19 January 2022; **Accepted** 31 July 2022

1 | INTRODUCTION

The number of people living with HIV aged 50 or older (PLWH50+) worldwide was projected to reach 7.5 million in 2020 [1], and in sub-Saharan Africa alone, will surpass 9 million by 2040 [2]. By 2030, it is estimated that one in four PLWH in high-income settings will be at least 60 years old (PLWH60+) [3]. In 2015, the median age of PLWH in Ontario was 48 and an estimated 4300 PLWH were 55 years old or older [4]. Given the excess burden of age-related comorbidities on PLWH [5], relevant ageing-related care and supports are long overdue.

The 2006 ROAH study, the first to assess the comprehensive needs of ageing PLWH [6], found that multimorbidity was the norm, depression and stigma common, and PLWH50+ had more unmet practical and emotional support needs than HIV-negative older adults. Since then, research in several jurisdictions has increased understanding of the lived

experiences of older PLWH and their impact on ageing-related needs for care and support [7–13].

A comprehensive needs assessment of older PLWH to inform policy and practice change has never been conducted in Canada. Four qualitative studies have provided most of the information available on the multi-dimensional wellbeing of PLWH50+ in Ontario. Of these, only one garnered detailed narratives on service use and unmet needs, engaging 11 PLWH50+ in one city in 2009 [14]. Data from these participants were also used to explore their housing and mental health experiences [15, 16]. A second examined factors contributing to disability and uncertainty among PLWH50+ in Southern Ontario [17, 18]. The remaining two explored successful ageing among PLWH50+ residing in two urban settings producing a significant body of literature detailing resilience strategies, environmental barriers to ageing well and trajectories of episodic disability over time [19–31]. Cultural considerations [32] and specific psychosocial issues affecting older PLWH in Ontario (i.e. cognitive health [33, 34], peer support [35], stigma [36, 37] and housing and food security [38]) have been investigated in isolation.

A literature review reveals gaps in our understanding of the comprehensive care and support needs of older PLWH in Ontario. Prior studies engaged PLWH50+ so findings were shaped by the responses of predominantly middle-aged participants, most of whom resided in urban settings in Southern Ontario. Involvement by women and racialized people has been underreported or lacking; data from the single study focused on service use are outdated; and an explicit focus on "ageing successfully" may have the limited analysis of the impact of poor social determinants of health among older PLWH lacking personal resilience strategies.

To address these gaps and inform development of the first national-level comprehensive needs assessment survey of older PLWH in Canada, we conducted a qualitative pilot study. The purpose was to describe the health and community care and social support needs and preferences of a diverse group of PLWH60+ from across Ontario. Additionally, we aimed to describe the life course experiences which shape their needs and the extent to which they are being met.

2 | METHODS

Preferences And Needs for Ageing Care among HIV-positive Elderly people in Ontario, Canada (PANACHE ON) was a community-based participatory research (CBPR) study. Approximately half of our 32-member research team identified as older PLWH (n = 18), many with academic research training, extensive CBPR experience and/or front-line roles in community-based HIV organizations (CBHO). The team was rounded out by clinician–researchers (n = 2), CBHO staff (n = 8) and academic researchers (n = 4). Our work was guided by CBPR principles like equitable partnerships, community and researcher capacity-building, mutual respect for all forms of knowledge and a commitment to translating research into action [39]. Most study activities, including data collection and primary analysis, occurred between May 2019 and August 2021.

PLWH60+ were recruited through CBHOs using posters and social media channels. Nine focus groups were planned; five were open to all PLWH60+, and four were designated for "priority populations"—communities disproportionately affected by HIV in Ontario [40] including those who self-identified as: gay, bisexual and other men who have sex with men (gbMSM); women; racialized persons; and people with drug use experience. Focus groups enable participants to build on or challenge ideas raised by others and provide the added value of peer support, a need well-documented among PLWH and older adults [41–43].

A semi-structured interview guide was developed collaboratively with PANACHE's Research Tool Development working group; content was based on relevant themes emerging from HIV and ageing literature and a prior concept mapping exercise engaging the full PANACHE team [44]. Seven intersecting themes were explored: social supports and stigma; sexual health; physical health; mental health; housing; food security; and finances. Existing partnerships with CBHOs were leveraged to support recruitment and establish comfortable meeting spaces. Eight peer research associates (PRAs) were hired and trained in focus group facilitation and co-facilitated in pairs.

Nine focus groups (5–13 participants) were conducted between July and October 2019. Self-reported demographic data, including birth year, estimated years living with HIV, gender identity, sexual orientation, racial background, household composition, income source and housing type, were collected using an anonymous survey prior to each focus group.

Focus group data analysis was conducted by a subcommittee of the PANACHE research team, including PLWH, and guided by DEPICT [45], a six-step model that facilitates participation in qualitative data analysis by stakeholders with differing levels of research literacy and experience. The model prioritizes collaboration and transparency. Two members engaged in "dynamic reading" of the transcripts, an inductive process for identifying ideas emerging from the focus group discussions; ideas were organized under the seven themes outlined in the interview guide and defined and/or exemplified using transcript data. Through "engaged codebook development," 74 ideas were consolidated into 25 codes by the analysis team. In the "participatory coding" phase, each transcript was coded independently by two team members. New codes were added as ideas emerged that did not fit elsewhere. Coded data were consolidated in NVIVO 12 Plus. "Inclusive review and summarizing of categories" as well as "collaborative analyzing" were done through 13 virtual analysis team meetings, as necessitated by COVID-19-related restrictions.

This study received ethics approval from the University of Toronto HIV REB Protocol #: 00037889. Participants provided written informed consent. PRAs facilitated confidentiality discussions at the start of each session.

3 | RESULTS

The PANACHE ON focus groups included 73 participants whose demographics are displayed in Table 1. The mean age of participants was 64 years and the mean time since

Table 1. Summary data PANACHE ON participants, *N* = 73

Characteristic	*n* (%)
Age, year	
Mean	64
Range	55–77
Gender identity[a]	
Man	49 (66%)
Woman	21 (28%)
Transwoman	1 (1%)
Two spirit	2 (3%)
Not specified	1 (1%)
Sexual orientation	
Gay	34 (47%)
Straight (heterosexual)	25 (34%)
Bisexual	8 (11%)
Asexual	3 (4%)
Not specified	3 (4%)
Racial background	
White	39 (53%)
Black	14 (19%)
Indigenous	6 (8%)
East Asian	3 (4%)
Latin-American	3 (4%)
Southeast Asian	2 (3%)
Mixed race	2 (3%)
South Asian	1 (1%)
Not specified	3 (4%)
Length of time living with HIV, years	
<10	11 (15%)
10–19	16 (22%)
20–29	27 (37%)
30+	18 (25%)
Unknown	1 (1%)
Housing	
Rent	51 (70%)
Own	12 (16%)
Housing facility	3 (4%)
Room (in house)	2 (3%)
Not specified	5 (7%)
Household composition[a]	
Live alone	45 (59%)
Live with a spouse or partner	14 (18%)
Live with a child/children	8 (11%)
Live with extended family	3 (4%)
Live with unrelated people	5 (7%)
Not specified	1 (1%)
Employment	
Employed full time	2 (3%)
Employed part time	9 (12%)
Income source	
Employment only	2 (3%)
One benefit source[b]	32 (44%)
Part time employment + at least one benefit	9 (12%)
Multiple benefit sources	29 (40%)
Not specified	1 (1%)

[a]Values do not equal the total number of study participants (*n* = 73) as some participants selected more than one response.
[b]Benefit sources reported included: Ontario Works (OW); Ontario Disability Support Program (ODSP); Old Age Security (OAS); Guaranteed Income Supplement (GIS); Canada Pension Plan (CPP); Canada Pension Plan—Disability (CPP-D); Private Pension; and Private Disability Pension.

HIV diagnosis was 22 years. Two-thirds of participants self-identified as men and one-third as women including one trans woman. Half identified their race as White. Most rented their dwelling or lived in supportive housing; and living alone was the norm (*n* = 45, 59%). Most relied on one or more public or private benefit programmes for income.

3.1 | Current needs of older PLWH in Ontario

Our focus group participants described varying needs ranging from basic survival to community inclusion. Affordable, safe, secure housing and healthy, plentiful food were the most cited needs, often arising because they were partially unmet.

Physical and mental health needs included medication, medical supplies, mobility aids, dental work, eyeglasses, hearing aids, psychological therapy and crisis response services. A few described needing another person physically present in their living space, or close by, in case of illness or injury, specifically falls. The need for more information on ageing (e.g. care options, financial planning and service navigation) was explicitly raised and a lack of clear understanding of government benefits was observed.

Several social and emotional needs were mentioned, including companionship, emotional, spiritual and peer support, and inclusion in the HIV community. Several participants linked their need for community engagement with the practical need to be mobile (e.g. to see friends and to get to their local CBHO), which was becoming more difficult with age.

3.2 | Needs: met and unmet

Participants reported using health services, including pharmacy, primary care, specialist care, dentistry/denturism, vaccination, laboratory, occupational therapy, vision and hearing services, and cognitive assessment and support. Many described seeking or accessing mental healthcare, including crisis intervention, psychiatry and counselling. Massage was the most mentioned complementary therapy need.

Not all participants' health needs were being met by all these services and barriers to fulsome service access included social determinants of health (e.g. inability to afford uninsured services, including complementary therapy, vision and hearing

services, dental work and certain vaccinations), provider issues (e.g. concerns about confidentiality, lack of knowledge about HIV and ageing) and structural challenges (e.g. siloed care, subjective assessments of eligibility for services and lack of just-in-time services). Several people underlined the need for coordinated models of care and patient–provider relationships where they felt heard. One long-term survivor felt abandoned by his local CBHO due to an unmet need for crisis care:

> "when I've called, "oh well we can't today, maybe we can bring someone out to you tomorrow", or…"why should we provide you that service?" So, I lay there no food in the house, medically sick, and unless I call the ambulance, which I don't have the money to pay, I've got two bills right now… I'm locked down." (Group 1, Participant 7)

Workarounds were often used to partially address unmet health needs, for example accessing free rehabilitation and complementary health services through local CBHOs, although these services were available on a time-limited basis or too infrequently. One modest income pensioner used a monthly plan to pay a substantial hearing aids co-pay. Compensatory strategies, such as recording passwords and employing physical or electronic reminders for appointments and medication, were used by several to manage lapses in memory.

Subsidized housing was relied upon by a large proportion, and although these services alleviated the pressure of paying market rent and prevented homelessness, they were the source of significant challenges. One woman described waiting 16 years for a subsidized unit and then being told it might take another 3–5 years for seniors' housing placement. Several described community housing living environments as extremely stressful due to the consistent presence of law enforcement and emergency services, crime, infestations, disrepair and bully managers.

Food banks and community meals, often provided by CBHOs, were used by many to address basic nourishment needs. Even so, participants lamented the lack of food choices and the need to ration the limited quantity of food provided. CBHOs were also a significant source of needed social and peer support among most participants. Even so, ageism within the HIV community and gaps in relevant HIV services (e.g. person-to-person appointment reminders and groups for PLWH60+) were raised.

Participants' unmet needs differed with their community size. Those residing in a major urban centre referred to "city stress" and feeling more vulnerable to victimization with age. gbMSM in one small city grieved the loss of local gay bars limiting spaces for socializing. Many living outside cities loved their surroundings but access to community services was limited by transportation issues and capacity within small CBHOs.

3.3 | Anticipated future care and support needs and preferences

There was a strong preference for ageing in the community, but many questioned the suitability of their current housing in the future. Several participants spoke of the potential need to move with age—whether to liquidate assets for retirement, downsize in response to increasing financial pressures or find housing to accommodate declining functional status (e.g. to be closer to transit services if they can no longer drive; to eliminate property maintenance)—but questioned available housing options.

Many older PLWH were uncertain as to their ability to live alone due to expected changes in mobility or capacity to perform instrumental activities of daily living (iADLs) (e.g. home maintenance and cooking), especially those living rurally. One respondent pre-emptively moved into a building with iADL supports in anticipation of future needs. A few mentioned family supports may enable ageing in place more easily, while others lacked informal caregiver support. Concerns were raised around the need to hide their sexual orientation or HIV status if relocating to a seniors' complex, subsidized housing building or long-term care centre for fear of stigma from other residents and/or staff. Participants questioned the safety of residential care for seniors, regardless of HIV status, due to neglect, understaffing, victimization and lack of regulatory oversight.

Several also worried about increasing isolation and loneliness with age or feared dying alone. Impaired vision and hearing, mobility challenges and declining function were potential contributing factors. At least one participant reported missing local CBHO social events due to episodic illness, and another worried worsening mobility would increase their reliance on visits from others.

3.4 | Lived experiences shape ageing care and support needs and preferences

Three intersecting themes emerged in our analysis—trauma, stigma and uncertainty—and their cumulative burden affected participants' present-day and future care and support needs, and the likelihood these are, or will be, met. Traumatic experiences across the life course often resulted in the loss of financial security and social and caregiving support. Experiences of HIV stigma and ageism increased isolation and reliance on formal services, and amplified concerns about discrimination in care settings. Current and common anxiety about meeting basic needs led to concerns about future resources.

3.4.1 | Past trauma and loss have compromised the safety net

Our participants described life-long traumatic experiences, often related to HIV, including diagnosis with poor prognosis, abandonment by loved ones after disclosure and significant losses (i.e. people, aspirations, sense of security and capital) due to illness; these experiences had both an immediate and enduring impact. Loss of intimate relationships decreased social capital, and for some, prohibited the development of new connections. Many worried about inadequate social support for ageing at home in the absence of practical support from their family of origin. One gay man living long-term with HIV described the challenge of seeking

support from those with whom you lack an established history:

> "I have been HIV for a very extended period of time, and have lost a lot of my connections, people have died. Period, that is our reality. As an individual, you don't have that sort of formative relationship with new people. So the dynamics in terms of looking for support from them is a bit different, it almost is nonexistent." (Group 1, Participant 4)

Hopelessness, bad advice and/or episodic illness led to material losses (e.g. earning potential and assets) for some, compromising their financial security. Many described living in poverty having given up opportunities to earn and save, dispensing with assets and being forced into an inescapable reliance on disability benefit programmes. Uncertainty about meeting basic needs for food and shelter was a daily reality for many. A gay man who was "new to HIV" described the swift and significant financial impact of starting disability benefits:

> "But I had RRSPs and everything, I saved all that, but… and I had a legal practice. But I got really sick when it happened. It wiped everything out." (Group 7, Participant 4)

Past HIV-related trauma impacted mental health and permanently compromised the social and financial safety nets of participants in our study shaping their emotional and practical care and support needs in older adulthood. Community-based services, especially CBHOs, helped meet social, informational and emotional needs, especially for those with limited informal support. Community support programmes for seniors helped with loneliness even for those with supportive partners:

> "There's a woman that works… a very young lady, a 22-year-old, she's wonderful. And she now calls me every day … Monday to Friday, at 4:30 and chats with me. Do you know what a ray of sunshine that has made in my life." (Group 3, Participant 7, Gay Man)

Programmes designed to address basic needs directly (e.g. subsidized housing and food banks) were insufficient, forcing the individual to make ends meet. Personal strategies to partially meet survival needs with limited resources included: living rurally, rationing food, using public utilities (e.g. internet in libraries) and paying with credit cards and high-interest loans; but these trade-offs added to participants' burden.

3.4.2 | Experiences of stigma shape assumptions about ageing care and support

Discriminatory treatment from others was a common experience. HIV stigma was enacted in one-on-one relationships and communities.

Participants also described the impact of embodying multiple intersecting stigmatized identities based on race, class, HIV, age, sexual orientation and drug use, such that they were unable to determine which biases were responsible for impeding access to resources or support. A racialized gay man described multiple layers of stigma in his cultural community, saying:

> "I'm from Jamaica myself, and trust me, okay, it's homophobic, it's HIV-phobic, it's every phobia you can conceive…" (Group 8, Participant 3, Racialized Gay Man)

Few participants described experiencing or observing HIV stigma when accessing health services; however, several shared the belief that doctors were dismissive towards people ageing with HIV, with one woman saying:

> "You know, 60-some years old and you've got HIV, so we're not going to bother looking into that… but it seems to be happening at a younger age than [*sic*] people that are positive because they're going well you're on bonus time anyway and…" (Group 5, Participant 1)

Several participants, especially gbMSM, adamantly refused to internalize HIV stigma and ended relationships to protect against it. In contrast, internalized stigma was evident in the narratives of others who described feeling ashamed about living or dying with HIV/AIDS or were hard on themselves for not disclosing to loved ones. One woman living with HIV long-term described how learning that Undetectable = Untransmittable changed her whole view of herself:

> "I phoned my partner right away and I said "I'm clean." And he goes "what are you talking about?" I said "I can't give it to you. I'm clean now." And for 20-some years I felt dirty because that's how the public perceived me, that because I had AIDS at that one time, that I was dirty." (Group 3, Participant 2, Woman)

Ageist assumptions and behaviours transcended multiple interactions and environments from dating to healthcare and community services to society. Participants described instances where they were tokenized, rejected and ignored by individuals and institutions. One individual observed that ageism in the HIV community is not addressed with the same urgency as other forms of stigma:

> "… and it's really strikingly so around the issue of age too, in this age… in this era of identity politics, and ageing issues just are not there, they're not ever there and you usually get a blank look when you bring them up at the conferences and so on." (Group 4, Participant 5, Diagnosed < 10 years)

Internalized ageism and ableism were also observed. One participant depicted ageing as the process of "transitioning from a productive life… to one where…you become someone who requires care." Another did not discuss ageing or their chronic illness with family to avoid being a "hindrance." Increasing difficulty with activities of daily living was "embarrassing."

Both internalized stigma and past and present experiences of discrimination increased anticipated stigma. We observed widespread fear of neglect and mistreatment in

ageing care that may impact willingness to engage regardless of need.

3.4.3 | *Uncertainty makes planning for care and support more difficult*

Some participants described experiencing uncertainty in their daily lives. Constant worry about paying for food and medicine tested their coping ability. One individual reflected on the need to adapt to the onslaught of new age-related illnesses:

> "…it just keeps evolving and it takes time to accept each one of these conditions. And we seem to hold in that pattern of waiting to be able to accept it and then something else happens." (Group 1, Participant 7, Gay man living long-term with HIV)

Overall, participants did not see their circumstances improving with time. Ageing was seen as an anxiety-provoking process of becoming more vulnerable and having insufficient resources to compensate for decreasing personal capacity. Participants used the words dread, worry, concern and panic to describe anticipated ageing-related changes in financial security, health, safety, autonomy, independence, care and social support.

Uncertainty about the availability and accessibility of appropriate formal ageing care and supports was common. In the women's focus group (Group 6), the eligibility criteria for assistive devices subsidies were not perceived as transparent or equitable. Some participants were unaware of existing subsidized or low-cost formal home and community care services that support ageing in place. Many worried their current income or future pension would be insufficient to meet basic needs or permit access to reputable residential ageing care. Inability to exercise control over how their current or future needs were met contributed to uncertainty and anxiety. One woman described giving up meaningful occupations while staying with family after a series of falls:

> "I don't want to give up my independence. Like since moving in with my brother I've given up my artwork, it's sitting at home not being done, I've given up my writing, I don't have a computer to work on, you know, I'm sitting there… I'm isolated with him for my safety, but I'm not able to do any of the things that make my life worthwhile." (Group 2, Participant 4, Heterosexual Woman)

4 | DISCUSSION

This qualitative study aimed to identify the care and social support needs and preferences of a diverse group of PLWH60+ in Ontario, Canada; and to describe lived experiences shaping these needs and affecting whether they are met. Our findings add to the existing body of literature since we purposively engaged PLWH60+, rather than PLWHIV50+; as well as those residing outside urban centres and those identifying as women and/or racialized persons.

We found that the basic needs of older PLWH, including safe, affordable housing and high-quality sufficient food, are only partially met by the existing social service infrastructure; previous studies have reported similar findings [9–11, 14, 38]. Government subsidies for vision and hearing aids are inadequate resulting in older PLWH having to pay out-of-pocket or go without. Older PLWH also rely on improvised self-management strategies to deal with memory changes since services in this domain are largely non-existent, especially outside urban centres [33]. Social and practical needs are met informally by family and friends in some cases, and predominantly by CBHOs among those with no or small social networks, but there is a lack of tailored programming for older PLWH [17, 28, 29]. The needs of older PLWH documented over the last decade continue to go unmet and are now much more pressing due to the growing proportion of PLWH60+.

The needs and preferences of our older PLWH are shaped by past and present experiences of trauma, stigma and uncertainty, a life course triad also described by other researchers [14, 15, 17, 19, 20, 31]. As the majority were diagnosed with HIV in their prime working and relationship-building years and currently rely primarily on government income supports, the adequacy of financial and social capital to live in comfort and dignity is a significant source of uncertainty [17, 18, 31]. Despite a strong preference for ageing in place, there is much unknown about how this will be operationalized.

The care and support needs raised in this study reflect those identified by community-dwelling older people with other chronic conditions or multimorbidity [46, 47]. Both experience uncertainty about the future, sensory impairment, difficulties with iADLs, social isolation and loneliness, and challenges navigating uncoordinated services; in response, they employ self-management and coping strategies, turn to informal caregivers and peers for support, and seek technological aids for mobility, vision and personal safety [46].

Older PLWH require care and support that accounts for a different life course trajectory than the ageing general population consequent to the impact of trauma, intersecting forms of stigma and uncertainty on their mental health [15, 36, 48–50]. The practical realities resulting from this triad of lived experiences, including their potential to shape the needs of older PLWH and affect whether these needs are fully met, have received less attention. A significant source of uncertainty is how needs will be met if participants become unable to live independently, as previously documented [18]. Many reject long-term care or seniors' housing for fear of HIV stigma and/or homophobia [9, 51, 52]. Although we did not hear many examples, the literature documents experiences of discrimination in healthcare and other institutional settings as common among older PLWH [14, 53]. Furthermore, Koehn et al. describe that, without careful planning, communal living environments can trigger stress among PLWH with trauma histories [54]. Based on their past experiences, residential seniors' care is not viewed as being safe by older PLWH.

The alternative is to access support to age in place, at home, but this option is also fraught with barriers. As in previous studies involving PLWH and sexual minority older adults [18, 55, 56], some participants worried about having inadequate social capital to address practical support needs. Ploeg

and colleagues found that HIV-negative older people with multimorbidity were "heavily dependent on their family caregivers for many kinds of support, without which, they would be unable to continue living in the community" even though the majority of those interviewed had an income greater than $40,000/year [47]. Older PLWH in our study with multimorbidity lacked both practical support from social networks and the financial means to pay for non-insured formal care.

Our findings are consistent with needs assessments conducted with older PLWH in other jurisdictions. Income, housing and food insecurity were common in older PLWH in other high-income countries [9–12, 53, 57, 58]. Financial issues among older PLWH in low- and middle-income countries affected access to HIV care in Uganda and quality of life in Brazil [59, 60]. Many ROAH 2.0 respondents indicated some difficulty with activities such as housework, getting to places outside walking distance and shopping [9–11]. Many of the current and anticipated support needs we identified, including access to appropriate mental health services, practical support within the home and opportunities to socialize, were also highlighted [9, 11, 14, 15, 17, 29]. The need for publicly funded sensory and dental care services for pensioners in Canada was discussed frequently among participants; these services were also identified as important components of a comprehensive care programme for older PLWH in the United States [8].

Our research demonstrates that older PLWH draw on their internal resources—knowledge, skills, strategies and self-efficacy—developed over years of living with a chronic illness, to plan for and manage ageing-related changes. As in previous studies, our participants described an array of practical and emotional coping strategies [15, 19–22, 24, 28, 29]. Despite their tenacity, upstream approaches are needed to ensure that all older PLWH have their needs met and can age with the same respect, honour and minimum of stress as their non-HIV-positive peers.

In addition to our primary findings, we noted a few population-specific differences. First, many of the older gbMSM living with HIV were outspoken about their HIV status as a strategy to identify and dismiss people who might stigmatize them, a strategy previously coined as pruning social networks [20]. Similarly, Kia et al. found that older gbMSM living with HIV used purposeful disclosure of their sexual orientation and HIV status to push back against stigmatizing service provider behaviour [61]. These findings suggest a preference for models of care that centre the experience of living with HIV among older gbMSM. Second, older PLWH living outside urban centres faced different challenges; they relied on infrequent transit services to access support programming and had greater concerns regarding HIV stigma, barriers also cited by rural-dwelling older PLWH in the United States [62]. These and other differences between population groups of older PLWH warrant more study.

This qualitative project was an important precursor to a planned national needs assessment of PLWH60+ in Canada. Inherent limitations in this pilot, such as the use of anonymous surveys to collect participant demographic information, limited our ability to contextualize individual participants' responses, except in cases where the speaker's own narrative identified aspects of their identity.

Despite our targeted recruitment strategy, our findings are based on the narratives of a small sample and not generalizable to all PLWH60+ in Ontario, especially those who are transgender, rural dwelling, not connected to community organizations or newly diagnosed. Furthermore, as two-thirds of our participants were HIV long-term survivors, our findings likely confound care and support needs related to ageing with HIV with those of long-term survivorship [63]. Ageing with HIV may be significantly different for people diagnosed in the era of improved HIV treatment.

Our semi-structured interview guide did not prompt study participants to frame their needs for care and support in the context of formal health or social support services. Barriers to service access arose organically in the discussion, baring the question which explored participants' ability to pay for services, support and resources to help meet their self-identified needs. As physician- and hospital-based services are paid by Ontario's provincial health insurance programme, the focus was more on needs related to the social determinants of health.

We illustrated the multidimensional needs of older PLWH in Ontario and described how a combination of life experiences common to PLWH60+ contributes to discrepancies in access to care and support services that address these needs in older adulthood. These findings draw attention to some of the existing policy and practice gaps and barriers for older PLWH in Ontario. Income support programmes, both disability- and ageing-related, and government-funded health insurance, for example, do not provide adequate benefits coverage to meet the holistic health needs of low-income older people, including many PLWH. CBHOs are an important and safe source of emotional and peer support for many older PLWH with small social networks, but lack programming specifically designed for older PLWH. Our study findings will inform advocacy in these areas and justify our next step to quantify the prevalence of certain experiences and the frequency of unmet service needs.

5 | CONCLUSIONS

PLWH experience ageing with the addition of three major burdens: trauma, stigma and uncertainty, which impact their health and social care and support needs and may not intersect as commonly among their ageing HIV-negative peers. Despite the resilience demonstrated by PLWH60+ in this study, systemic and structural barriers continue to contribute to inequities in the potential to meet ageing-related needs enabling PLWH to age in comfort and dignity. Changes to health and social policy are required to address these gaps.

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COMPETING INTERESTS

The authors declare no competing interests.

AUTHORS' CONTRIBUTIONS

KM and SLW are Co-Principal Investigators of PANACHE and coordinate all activities of the research team. KM and ER trained PANACHE ON PRAs, implemented the study protocol, oversaw the participatory data analysis and interpretation process and prepared the draft manuscript. SLW provided research mentorship to KM and ER, participated in data analysis and interpretation, and edited the manuscript. ER managed study data in NVivo. DMB, TC, GDS, EF and JDL participated actively in data analysis and interpretation and provided feedback on the manuscript.

ACKNOWLEDGEMENTS

The PANACHE Ontario project would not have been possible without the meaningful involvement of older PLWH and community allies and partners. To the Research Team Members, Peer Researchers (GDS, BG, JG, JDL, BM, EM, TP and CT) and Research Participants, we offer our sincerest thanks for your time and willingness to share your experiences and expertise. We would also like to thank the CBHOs that acted as host sites for our focus groups: AIDS Committee of Durham Region, Regional HIV/AIDS Connection, PARN—Your Community AIDS Resource Network, Alliance for South Asian AIDS Prevention, Committee for Accessible AIDS Treatment, Réseau Access Network, AIDS Committee of Toronto, AIDS Committee of Ottawa and The AIDS Network. Thank you to Afia Amoako who supported study implementation; Dr. Francisco Ibanez-Carrasco, James Watson and Dr. Andrew Eaton who supported the training of study PRAs; and Dr. Patty Solomon for sharing her qualitative research expertise.

FUNDING

Ontario HIV Treatment Network—CBR-1106.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Reynolds Z et al. *Journal of the International AIDS Society* 2022, **25**(S4):e26000
http://onlinelibrary.wiley.com/doi/10.1002/jia2.26000/full | https://doi.org/10.1002/jia2.26000

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Priorities for health and wellbeing for older people with and without HIV in Uganda: a qualitative methods study

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Abstract

Introduction: With improved HIV treatment availability in sub-Saharan Africa, the population of older people with HIV (PWH) is growing. In this qualitative study, we intended to understand (1) the lived experiences of ageing people in rural Uganda, with and without HIV, (2) their fears and health priorities as they grow older.

Methods: We conducted 36 semi-structured interviews with individuals with and without HIV in Mbarara, Uganda from October 2019 to February 2020. Interview guide topics included priorities in older age, physical functioning in daily activities, social functioning, HIV-related stigma and the impact of multimorbidity on health and independence. Interviews were conducted in Runyankole, transcribed, translated and inductively coded thematically by two researchers with tests for inter-coder reliability.

Results: The respondents were purposively sampled to be evenly divided by sex and HIV serostatus. The median age of respondents was 57 (49–73). Two-thirds were married or cohabitating, 94% had biological children and 75% cited farming as their primary livelihood. Overall, PWH considered themselves as healthy or healthier than people without HIV (PWOH). PWH rarely considered their HIV status a barrier to a healthy life, but some reported a constant sense of anxiety as it relates to their long-term health. Irrespective of HIV status, nearly all respondents noted concerns about memory loss, physical pain, reductions in energy and the effect of these changes on their ability to complete physical tasks like small-scale farming, and activities of daily living important to the quality of life, such as participating in community groups. Increasing reliance on others for social, physical and financial support was also a common theme. The most prevalent health concern among participants involved the threat of non-communicable diseases and perceptions that physical functioning may diminish.

Conclusions: In rural Uganda, we found that PWH consider themselves to be healthy and do not anticipate a different ageing experience from PWOH. Common priorities shared by both groups included the desire for physical and financial independence, health maintenance and social support for daily functioning and social needs. Entities supporting geriatric care in Uganda would benefit from attention to concerns about functional limitations and reported needs as people age with and without HIV.

Keywords: HIV; ageing; non-communicable disease; qualitative; sub-Saharan Africa; quality of life

Additional information may be found under the Supporting Information tab of this article.

Received 20 January 2022; **Accepted** 1 August 2022

1 | INTRODUCTION

Sub-Saharan Africa (SSA) as a region is experiencing significant demographic shifts [1]. Compared to other regions of the world, SSA has a smaller proportion of older aged persons as a share of the total population [2]. However, SSA is experiencing greater increases in life expectancies than other regions, resulting in a substantial projected increase in people over 50 years old. For example, as of 2020, Uganda has approximately 3.3 million people over the age of 50 with that number projected to grow to 12.4 million by 2050 (an increase from 7% to 14% of the population [3]). This growing demographic necessitates a comprehensive understanding of the lived experiences and priorities of older people.

Nonetheless, there is a relative paucity in the literature about ageing in SSA, despite repeated calls for a better understanding of this population group [2, 4–8]. Data collection and research is a core element of the *WHO's Global Strategy and Action Plan for Ageing and Health* [9]. There has been notable progress in quantitative data collection to describe ageing in SSA, such as the World Health Organization Study of Global Ageing and Adult Health (SAGE) [10], Ibadan Study of Ageing in Nigeria [11] and Health and Ageing in Africa: A longitudinal study of an INDEPTH community in South Africa (HAALSI) [12]. Yet, there continues to be a need for more varied research and national and sub-national studies. Specifically, qualitative research [13–16] can provide important insights into the lived experiences of older people as they are affected by their intrinsic capacity (cognition, mobility, psychological health, vitality and sensory) and external environment as defined by the *WHO Model of Healthy Ageing* [17].

A contributing factor to the health and wellbeing of older-age people in Uganda, and older-age people in Africa more broadly, is the increasing availability of treatment for HIV. As HIV disease is increasingly well-managed through antiretroviral therapy (ART), people with HIV (PWH) are living longer [4, 18–20]. As of 2019, close to 18% of the adult population with HIV in Uganda was over 50 years of age (230,000 out of 1.3 million adults with HIV) [21]. Not only are more Ugandans living longer, but many of them face the biomedical, social and emotional consequences of lifelong HIV infection.

In the global north, data on ageing PWH suggest they face an increased risk of physical comorbidities, such as cardiovascular disease [22], liver, kidney and bone disease [23], as well as premature geriatric syndromes [24, 25] compared to people without HIV. Moreover, they also must confront the impact of persistent stigma, discrimination, access to healthcare and changes in social support that may be unique to their status [26–28]. However, if and how these influences affect PWH in SSA is less well explored. Preliminary data from the region seem to suggest that PWH might have improved access to and engagement with the healthcare system [16, 29, 30] but that persistent stigma remains a major threat [31–36]. In this qualitative study, we intended to understand the lived experiences of ageing people in rural Uganda living with and without HIV, to better understand their fears and health priorities as they grow older, and advise on the design of future research and interventions to address the needs of this population.

2 | METHODS

The Quality of Life and Ageing with HIV in Rural Uganda study (NIH R01AG059504) is a mixed methods research study designed to identify intervention targets to improve functioning and quality of life for older aged PWH in the region. This paper describes the qualitative component of the study to understand determinants of quality of life among older aged PWH in Uganda. The results of these interviews informed the design and selection of measures for quantitative data collection for a prospective cohort study which has since begun enrolment and is ongoing. The study received approval from both the ethics committee at Mbarara University of Science and Technology, the Uganda Council for Science and Technology, as well as Mass General Brigham. Written informed consent was obtained for all participants.

Participants were consecutively sampled from an existing cohort of older individuals (48 years and older) with and without HIV [37] using two methods. First, PWH were eligible for enrolment if they had been taking ART for a minimum of 3 years and were in active care at the HIV clinic at Mbarara Regional Referral Hospital. Age and sex-similar people without HIV (PWOH) were identified using a study-based census of villages in the clinic catchment area and recruited from their homes [38]. We used the population study to identify comparators without HIV to minimize bias by co-morbidity or health-seeking behaviour that might arise from recruitment. HIV status was ascertained through annual HIV testing in the parent study and verbal confirmation of testing results included in prior study data, reflecting their lived experience. Of those approached for participation in the study, 100% agreed to participate.

In-depth interviews were conducted by a trained interviewer using a structured interview guide. Interview guide topics were identified and selected through a literature review process in collaboration with Ugandan colleagues. Topics included (1) definitions of and priorities for quality of life in older age; (2) physical functioning, including barriers and facilitators to completing daily activities; (3) social functioning, including familial responsibilities and position in the household; (4) HIV-related stigma; and (5) impact of multimorbidity on health and independence (see Table S1). Questions specific to the experience of living with HIV were only asked of participants with HIV. The interview guide was reassessed after it was piloted and reformatted to ensure more open-ended questioning. Interviews took place between October 2019 and February 2020. Interviews continued until saturation was achieved. A total of 36 interviews were completed.

Interviews were conducted in Runyankole, the dominant local language, by a man in his 30s, audio-recorded and translated to English during the transcription process. Inductive analysis was conducted using a thematic approach. A priori themes were used in the initial analysis, but additional themes and subthemes were identified as interviews were compared. Interviews were coded using Dedoose software [39]. A sample of interviews was coded by two researchers to ensure inter-coder reliability. There was generally good agreement between coders, with any differences resolved through discussion to reach a consensus. Following the initial coding, a matrix was developed to reorganize data into headings and sub-headings for further interpretation (see Table S2). The data were specifically analysed to examine for differences and similarities by HIV status.

3 | RESULTS

3.1 | Sample characteristics

The 36 study participants were equally divided by HIV serostatus and sex (Table 1). The median age of the cohort was 57 (range, 49–73). A majority of study participants reported their highest level of education to be incomplete primary school (n = 22, 61%). All participants reported being

Table 1. Cohort characteristics

	Total cohort (*N* = 36)	People with HIV (*n* = 18)	People without HIV (*n* = 18)
Age, years, range, mean	57 [49–73]	57 [49–72,62]	57 [49–73,63]
Female sex, %, *n*	18 (50)	9 (50)	9 (50)
Education			
Did not complete primary school, %, *n*	22 (61)	11 (61)	11 (61)
Completed primary school, %, *n*	12 (33)	6 (33)	6 (33)
Completed secondary school, %, *n*	2 (6)	1 (6)	1 (6)
Employed	36 (100)	18 (100)	18 (100)
Farmer, %, *n*	27 (75)	10 (56)	17 (94)
No regular salary,[a] %, *n*	30 (88)	15 (83)	15 (94)
Marital status			
Single, %, *n*	1 (3)	1 (6)	0 (0)
Married/cohabitating, %, *n*	23 (64)	10 (56)	13 (72)
Divorced/separated, %, *n*	2 (6)	1 (6)	1 (6)
Widowed, %, *n*	10 (28)	6 (33)	4 (22)
Family structure			
Living alone, %, *n*	3 (8)	3 (17)	0 (0)
Has biological children,[b] %, *n*	34 (94)	17 (94)	17 (94)
Current primary caretaker for non-biological children,[c] %, *n*	20 (56)	10 (56)	10 (56)

[a]Two HIV-negative participants missing data, *n* = 34.
[b]Includes grown children who have moved out of the house.
[c]Includes nieces, nephews, and other relatives.

employed, with farming being the predominant source of livelihood among the cohort (*n* = 27, 75%). More PWOH identified as farmers compared to people with HIV (PWH) (94% vs. 56%). Additionally, the majority of the cohort reported not having a regular salary (*n* = 30, 88%), which was more common among those participants not living with HIV compared to PWH (83% vs. 94%).

Approximately two-thirds of the study participants were married or cohabitating (*n* = 23, 64%). Only three (8%) of participants lived alone (17% [*n* = 3] among PWH vs. none of PWOH). Most participants have living biological children (*n* = 34, 94%) and half are the current primary caretaker for additional non-biological children (*n* = 20, 56%).

3.2 | Self-perceived impact of HIV on health and quality of life

Generally, PWH did not consider their health or quality of life to be dramatically different from PWOH as they age. In fact, many PWH considered themselves healthy, their HIV status notwithstanding. "[HIV] does not affect me at any time and I might be better than HIV negative people," said a 57-year-old woman with HIV, a common sentiment. Another female respondent of 66 years noted her similarity to PWOH when she said, "Anyone can fall sick of anything whether they have HIV or not. There are people that are prone to any sicknesses regardless of having HIV or not."

Respondents did note there is a difference between those with well-controlled disease and those without the same level of adherence. One 72-year-old woman with HIV described it in the following way: "HIV is like flu or cough; if you are taking your medication as prescribed by the doctor, it does not affect your way of doing things in any way. [Sickness] happens to those who don't take their medication very well." One 70-year-old man illustrated a common sentiment among the participants about their expected longevity with ART:

> I am now confident that I will live for many years until the true medicine is discovered. I am also confident that when I continue taking my medication, I will still live and serve my family, the church, and the community as long as I am still taking my medication and not disorganized with old age.

Nonetheless, for a minority of participants, the knowledge of their HIV serostatus continues to affect the way they see themselves and their overall perception of their health. "Because of taking the drug daily, you feel no self-love, and if you happen to become sick by something small, you'll get worried that other sicknesses will come such as TB," said one 55-year-old woman with HIV.

3.3 | Changing perceptions about HIV in the ART era

Both PWH and PWOH noted historical shifts in the way HIV impacted families and individuals. PWH highlighted the burden of stigma and discrimination early in their disease progression prior to freely available treatment. "I'd […] ask them when they'd visit me, but they'd say they will make it. So, I'd know if it's due to the virus that they can't show up. Afterwards, all that ended, and they understood how HIV is

spread. They'd eat rice with me," said a 66-year-old woman with HIV.

Respondents frequently told of how life has improved for both themselves and their communities with better treatment and knowledge of the virus. As one 49-year-old man with HIV put it, "Honestly speaking, there is no HIV person that's treated unfairly! There is no trademark that points out an HIV positive person. Before they were affected by skin rash, and everyone knew the signs. Can you tell that I am HIV by merely looking at my skin?" While there was limited reporting of maltreatment of PWH, it was usually rationalized with some qualifier such as the person did not take ART routinely, was promiscuous or was self-stigmatizing. PWOH tended to agree with their PWH counterparts when they say, "now a person living with HIV is treated like any normal person […] He will remain healthy and will suffer other disease like any other people in the community" (57-year-old woman without HIV).

The most commonly cited reasons for this change in treatment and perceptions about PWH were the increasing availability of treatment for HIV and the pervasiveness of HIV infection in the community. As one 51-year-old woman without HIV stated, PWH are not stigmatized, "because one is worried that tomorrow or another day he will be HIV positive also." Most respondents noted this shift was most evident soon after ART became widely available for free.

3.4 | Shared experiences of physical and mental declines with ageing

PWH are not immune to the effects of ageing and felt that they are ageing similarly to their peers. A 49-year-old man with HIV sums it up when he says, I view myself as a normal person and I would not see any change of having HIV because I don't see any difference; I have developments just like an HIV-negative person only that I see that I don't have the energy that I had before like now.

While facing the expected declines of ageing, most HIV-positive respondents consider themselves to be healthy. By contrast, most PWOH generally considered themselves to have poor health due to ageing. One man without HIV of 52 years described his current health as the following: My hands pain, the whole body pains. That means that old age is affecting me. Because, back then I would work and then feel okay afterwards. But now, that is not the case. I feel all joints hardening and paining and I fail to work as I used to.

These health complaints are not unique to PWOH. When asked about health changes as they have aged, participants across all sub-groups reported reduced energy and strength, increased physical pains and aches, changes in sleep patterns and memory loss.

> My health has changed because nowadays I usually feel constant headache, sometimes I feel dizziness, my eyes are not seeing properly, and when I stand for a long time, I find myself in a fatigued state. When I work for a long time and I force myself to go an extra mile, I become very tired to the extent that when I sit somewhere I feel I do not want to move away until I have rested enough (52-year-old woman without HIV).

While some respondents attribute their declining functionality to a particular health condition (including HIV among PWH), most believe it is part of the normal ageing process. "When I go to the health facility and they don't diagnose any disease, then that makes me think that it is due to ageing," said a 59-year-old man without HIV.

Another concern for most respondents is changes in memory. Apart from some younger participants (under 60 years), respondents noted increased memory loss ranging from benign complaints, such as forgetting where they put their phone, to concerns of the impact on their daily activities. Respondents attributed these changes to multiple different causes: normal ageing, having "too many thoughts" (a synonym for worrying) and responsibilities, and, for PWH, a theory that it was due to a combination of ageing and HIV. One 62-year-old man with HIV alluded to such: "I really feel someone of 62 years wouldn't have started becoming forgetful." A number of respondents in both groups felt that with ageing comes more stressors and responsibility that affects memory and mental health. For example, a 55-year-old woman with HIV felt this way when she said:

> Those are people who will have had a lot of things to think about as they grow, for instance when a family is not independent as regards their needs, that's when you will find the head of the household thinking about a lot, thus in their old age they start to lose their memory.

While respondents did not believe memory loss could be treated, they believe it could be prevented or improved through reading, learning and maintaining relationships.

The stress that can cause memory loss was also reported to affect mood. Many respondents noted periods of depression, despondency and anxiety often brought about by situational stressors, such as fear of illness and death, financial constraints and lack of basic necessities for themselves and family. For example, one woman with HIV of 62 years said, "But for me being HIV positive I am always thinking I might die anytime." Notably, health concerns were less frequently cited as causes of depression or anxiety as compared to social stressors.

3.5 | Concerns about functional declines in daily activities with age

Most respondents highlighted shifts in their routine activities as they have aged. Some examples of limitations include reading less due to changing eyesight, walking and biking shorter distances or diminished socializing and participating in community groups. One woman without HIV of 57 years said she would "fail to maintain my position at the [Local Council] committee because I can no longer write and so I will not disturb anyone to keep writing for me." Loss of sexual desire was also mentioned by both groups. As one 64-year-old man with HIV said, "Back in the days, we young men would not bypass 'a dress', but these days I look at women like a dog would be looking at money notes." Even more disruptive is the decreasing ability to "dig" (farm and conduct small-scale food provision), including gardening, grazing of animals, selling of produce, and construction work—the means of income for many

respondents. "I used to remove the banana suckers myself but now I cannot. I would like to slash my compound, but I cannot manage it now, and now I have to use money to hire someone to do it. Now even raising a hoe is becoming a challenge and I may soon fail to dig," said a 54-year-old woman living with HIV.

Recognition that decreases in energy and increased chronic pain affect daily activities was nearly universal among respondents. Younger participants did not report major changes in their usual activities, but they anticipate changes as they continue to grow older. Among PWH, there is uncertainty if pain and loss of energy are associated with their HIV infection or ageing. Some seem quite certain that their physical changes are attributable to HIV infection or its treatment such as a 62-year-old male PWH who insists "Way back when I had not acquired HIV, I used to do all my work myself because I used to be energetic, unlike nowadays when I feel I am no longer so strong to accomplish all my activities." Other PWH respondents are more equivocal, such as a 55-year-old respondent who exclaimed, "I try to work sometimes and feel pain so I ask myself if its old age or it's HIV epidemic!" while others are insistent that HIV infection plays no role in their changing activities, such as a 66-year-old woman who reported, "I see old age in my life, because when I look back on my life and how I used to do a lot of chores with a child on back whilst fetching firewood; which I now walk the same distance but feel tired and notice that it's due to old age and not the HIV epidemic." Apart from HIV infection, respondents identify the cause of their challenges to usual activities to include reduction in energy and stamina, pain and physical weakness, other illnesses, increased sleep, and changes in memory and mental reasoning.

To accommodate changes in physical and mental ability, many respondents receive assistance with their usual activities. The primary activities which are assisted include working in the garden or plantation (weeding and harvesting), collecting and splitting firewood, cooking, cleaning, fetching water and grazing animals. Most often they described family members or younger people living with the respondents who serve this role, but occasionally it is friends, neighbours or hired help. One 73-year-old woman without HIV said, "I used to carry a full jerrycan of water but now I even struggle carrying a small jerrycan of water and that is why I stay with some children so that they can help me in one way or another." Both PWH and PWOH worry that some activities may go neglected or change as help diminishes, and they do not have the funds to hire casual workers.

3.6 | Health fears for the future

When participants were asked what conditions they are worried about developing in the future, many participants reported their primary concerns being developing uncurable, non-communicable diseases, such as cancer, diabetes and hypertension, with a particular emphasis on cancer. A 57-year-old woman without HIV sums it up when she says:

> Cancer […] claims lives of many people and you hear someone saying that instead of being killed by cancer I'd rather be killed by HIV. One says that with HIV, he or she can access any health facility and get tested and treatment accordingly and become fine. But with cancer, one has to die while in terrible pain.

Even among PWH, respondents fear non-communicable diseases. "[I] am worried about diabetes, blood pressure, and cancer. If those affect me then I won't fair well," said a 53-year-old man with HIV.

Respondents were also concerned about changes in physical abilities that would negatively impact social and physical functioning, such as deteriorating eyesight, hearing loss and loss of use of their hands or legs. A 49-year-old man with HIV said, "I ask God to help me not to ever break any of my limbs especially the arms because it'd be bad for me and my family, or what if I lost my eye, what would happen to me!" Respondents have very real fears of declining health and their ability to maintain their current lifestyle. For example, a 62-year-old man with HIV says, "I have a feeling of how my energy to do work keeps reducing. For example, yesterday I worked in my banana plantation, but that alone left me so weak through the whole night. This is a clear sign that my health is really deteriorating."

Lastly, respondents worry about acquiring infectious diseases, including tuberculosis and HIV (among the PWOH). "I fear getting infected with HIV because that virus deteriorates someone's health completely, and so there are some activities you will no longer do when you have HIV, which in turn reduces on the household income, as more money goes to treatment," said a 56-year-old woman without HIV. Apart from the fear of developing HIV, these responses were largely consistent across sex and HIV serostatus.

3.7 | Priorities for the future as they age

When asked about ideal ageing and priorities for themselves as they age, the responses aligned across gender, age and HIV status. According to a 60-year-old woman without HIV, ideal ageing looks like someone who:

> has what to eat and drink, has a good house to stay in, and she or he has prepared where to get some income like having livestock at home, and food security at home and he even has a motorcycle to take him to the hospital in case of sickness and does not depend on other people to survive or beg other people to give him or her money to do something.

The common themes coalesced around adequate nutrition, help with physical tasks, income-generating sources, such as land and livestock, a respectable home and transportation.

Financial security was seen by most as the key factor that allows for other goals and necessities to be met. It prevents dependency and ensures access to medical care. "The most poisonous situation is to become a needy person at an older age. For example, when one cannot even afford to buy himself a 'Headex' pill," said one HIV-positive 64-year-old man. Particularly, more passive income is most appealing as this group ages, whether that is through plantations with hired help, grazing livestock, rental properties or business that others work.

A repeated priority for ageing is having access to routine care and company around the house whether that is hired or family, with the preference being children or grandchildren.

> When I grow older than now, I would wish to be seated in one place, playing and having fun with my grandchildren as they make me smile, make fun of me, like how I used to play and make fun of my grandparents when I was still young, and I don't want to keep alone because I feel I will get bored if I keep alone […] I want my children to be near me so that I am able to tell them or ask them whatever I want and they give it to me in time. For instance if I tell them that I want like bread or rice, I need them to give it to me, because when they are far and I fail to get it, I may not feel happy (72-year-old HIV-positive woman).

Good health is something respondents aspire to maintain but recognize they may not be able to control. "Above all, good health is my priority because I want to have good health. Because if you have good health, others can follow," said a 59-year-old man without HIV. Part of good health is defined as being "peaceful" among respondents, which can be described as living without stress. A woman of 60 without HIV said, "I need to be with good health, free of diseases and also to be peaceful." Among some HIV-positive respondents, managing their HIV by adhering to their treatment regimen is a priority as they age, but it was not a commonly reported concern.

4 | DISCUSSION

This study investigated the experiences of older aged Ugandans, both with HIV and without, related to the quality of life, daily functioning and long-term health. Our findings suggest the differences between PWH and PWOH are subtle. In most cases, perceived quality of life and health was greater among PWH than among PWOH in our study. Intrinsic capacity (cognition, mobility, psychological health, vitality and sensory) [17] between the two groups seems similar, while both groups face changing physical functioning, activity levels, memory and disease burden as they continue to age.

A potentially unexpected finding from this work was the relative similarity in self-perceptions about health, quality of life, independence and longevity between people with and without HIV. By and large, this differs from work in the global north and elsewhere that has explored experiences of living with HIV [40–43] but corroborates findings from other research in Uganda [16]. The relative similarity we found between the groups could potentially be attributed to the study setting: namely, an environment where ART is largely available (particularly to those who we interviewed who, by design, were linked to HIV care) and where HIV stigma has decreased somewhat [31] despite its persistence in other domains [13, 32, 44]. There was recognition of the devastating impact of HIV in the past, but fewer expressed concerns about its impact on individuals and the community more broadly at present, even among PWH. While topics of self-perceived stigma among PWH were not specifically addressed in these interviews, our findings correlate with other research that has shown a greater perceived quality of life and resilience [45] with less internalized stigma among PWH [46]. This finding may also reflect a PWH population that is engaged in care and has a well-controlled disease [47, 48] rather than those facing a new HIV diagnosis or delaying treatment [32, 49, 50]. It may also suggest that self-perceived health can differ significantly from clinically defined health [51].

Our data suggest that health concerns, including among PWH, are principally related to non-communicable diseases and health conditions that could affect older-aged persons' ability to work and socialize. Notably, we found little evidence that older PWH are specifically concerned about the effects of HIV on their health or longevity. These health concerns follow worldwide trends in health threats evolving from infectious diseases to non-communicable diseases, including for PWH [52]. Pain, reduced energy and memory loss all have an impact on daily activities among older-aged Ugandans, with reports of pain and reductions in energy being nearly universal. These findings are similar to the existing evidence identifying the loss of independence in day-to-day functioning as a primary concern for older-aged persons [51, 53].

As people age, they have real concerns over financial stability, accessibility of medical care, food security, assistance with daily needs by caregivers and social contact. With a nascent geriatric care programme in Africa [54], there is the opportunity to design programmes to effectively meet the needs as well as the priorities of the ageing population. From a health perspective, there is a need for mental health support, pain management, routine evaluations for causes of fatigue, palliative care for chronic diseases and independent living skills programmes, all of which need to be affordable and accessible [9, 55]. From a financial and food security perspective, there is room for programmes, such as community savings groups (which are already in use), extension work to support farmers in their later years, business development programmes for older aged Africans and social security safety nets for the most disadvantaged. For social contact and assistance, social support groups and home care programmes can be implemented to support the social and cognitive functioning of the ageing population as well as the mental health and social isolation of family caregivers [56, 57]. The ageing population in SSA is quickly growing, and these programmes and policies are urgently needed.

Our findings should be interpreted in light of several limitations. There are some inherent differences between the PWH respondents and their PWOH peers. PWH on ART and in clinical care may reflect a population better engaged in healthcare and should not be taken to represent the experiences of those not on treatment. Additionally, the PWOH in this study were recruited from a slightly more rural area compared to the PWH respondents [58], but the two groups were approximately similar in as many ways as we could control. It is possible that HIV co-morbidities and illnesses apart from HIV that are not quantified may have influenced responses. The interviews were translated and transcribed before being analysed, and some nuance may have been lost in the process despite using native speakers for both interviewing and transcribing. The participants were drawn from a cohort with the non-standard age range of 48 and older, making comparisons to studies that utilize 50 years and older more difficult. Lastly,

while not a limitation per se, qualitative research is not meant to be representative of all PWH and the corresponding population without HIV. Findings are, therefore, not generalizable to the entire population.

5 | CONCLUSIONS

With changing demographic structures in the era of the widespread availability of HIV treatment, it will be critical to understand the priority and concerns of older-aged individuals as they represent an increasing proportion of this key population. In rural Uganda, we found that concerns of ageing are nearly universal, irrespective of HIV status, and include fears about acquiring non-communicable diseases, loss of independent physical functioning and diminished energy, as well as memory loss. Priorities for the future were financial and physical independence, access to care when needed, health maintenance and social connection. Medical care [9] and policy [55] should be designed to meet the needs of this growing population in SSA to ensure healthy ageing.

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COMPETING INTERESTS

ACT reports receiving a financial honorarium from Elsevier, Inc. for his work as Co-Editor in Chief of the Elsevier-owned journal *SSM-Mental Health*. All other authors declare no competing interests.

AUTHORS' CONTRIBUTIONS

ZR and RG conceptualized and drafted the manuscript as well as conducted the analysis. RS oversaw in-country data collection. MJS designed the research study. ACM, DS, SO, NN, MG, JS, ACT and SA were involved in drafting the manuscript and provided critical feedback on the full manuscript. All authors read and approved the final manuscript.

ACKNOWLEDGEMENTS

We sincerely thank the participants who offered their insights, the study staff who collected and managed the data, and the translator who provided this essential service.

FUNDING

The Quality of Life and Ageing with HIV in Rural Uganda is funded by the U.S. National Institute on Ageing (R01AG059504). Additional funding was provided by the U.S. National Institute of Mental Health (R01MH113494).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional information may be found under the Supporting Information tab for this article:
Table S1. Examples of interview questions by domain.
Table S2. Illustrative quotes by theme.

Marty L et al. *Journal of the International AIDS Society* 2022, **25**(S4):e25986
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25986/full | https://doi.org/10.1002/jia2.25986

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Projection of age of individuals living with HIV and time since ART initiation in 2030: estimates for France

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Abstract

Introduction: Thanks to antiretroviral treatment (ART), people living with HIV (PLHIV) are living longer and ageing. However, ageing involves increased risks of co-morbidities, which also depend on when PLHIV individuals started ART. To tackle the HIV age-related upcoming challenges, knowledge of the current and future age structure of the HIV population is needed. Here, we forecast the demographic profile of the adult population living with diagnosed HIV (aPLdHIV) in France until 2030, accounting for the impact of the ART initiation period on mortality.

Methods: We used national data from the French Hospital Database on HIV (ANRS CO4-FHDH) and a sample of the National Health Data System to, first, characterize the aPLdHIV in 2018 and estimate their mortality rates according to age, sex and ART initiation period. Second, we used national HIV surveillance data to define three scenarios for the numbers of newly diagnosed HIV cases over 2019–2030: 30% decrease in HIV cases (S1), status quo situation (S2) and epidemic elimination (S3). We then combined these data using a matrix model, to project the age structure of aPLdHIV and time since ART initiation.

Results: In 2018, there was an estimated 161,125 aPLdHIV (33% women), of which 55% were aged 50 or older (50+), 22% aged 60+ and 8% aged 70+. In 2030, the aPLdHIV would grow to 195,246 for S1, 207,972 for S2 and 167,221 for S3. Whatever the scenario, in 2030, the estimated median time since ART initiation would increase and age distribution would shift towards older ages: with 65–72% aPLdHIV aged 50+, 42–48% 60+ and 17–19% 70+. This corresponds to ~83,400 aPLdHIV (28% women) aged 60+, among which ~69% started ART more than 20 years ago (i.e. before 2010) and ~39% ≥30 years ago (i.e. before 2000), and to ~33,100 aPLdHIV (27% women) aged 70+, among which ~72% started ART ≥20 years ago and ~43% ≥30 years ago.

Conclusions: By 2030, in France, close to 20% of the aPLdHIV will be aged 70+, of which >40% would have started ART more than 30 years ago. These estimates are essential to adapt co-morbidities screening and anticipate resource provision in the aged care sector.

Keywords: ageing; demographic profile; time since treatment initiation; life expectancy; HIV epidemiology; modelling

Additional information may be found under the Supporting Information tab of this article.

Received 19 January 2022; **Accepted** 1 August 2022

1 | INTRODUCTION

Since the beginning of the HIV epidemic, great progress has been made to improve the health of people living with HIV (PLHIV). The introduction of combination antiretroviral therapy (cART) in 1996 has led to a rapid decrease in mortality [1]. With increased cART efficacy and tolerability over time, life expectancy (LE) within 3 years of cART initiation further increased and continued to increase even in the late cART era [2]. Currently, the LE of treated PLHIV approaches that of the general population [3, 4].

Consequently, HIV populations are ageing. According to UNAIDS estimates, in high-income countries, one-third of PLHIV were aged 50 or more in 2013 [5]. Ageing will involve new care challenges. First, age is associated with chronic conditions like non-AIDS defining cancers, cardiovascular, renal, liver, bone and neurological diseases, and HIV infection further increases the risk of these conditions [6]. Increased

burden of polypharmacy and risk of drug–drug interactions with cART could, therefore, represent an upcoming issue in HIV care [7, 8]. Second, ageing PLHIV will possibly need access to the assisted living facility for elderly people. Resource provision in the aged care sector will thus need to be addressed in the coming years, including specific HIV care training for medical staff.

To anticipate needs and resources, it is essential to foresee the number and age of PLHIV. Beyond age-related chronic morbidities, the period at which PLHIV started antiretroviral treatment (ART) is also key, as it reflects the type of ART regimen to which individuals had been exposed, the level of immune dysfunction reached before ART initiation, which varied according to ART guidelines, and indirectly the lifetime duration with HIV. At any age, comorbidity and mortality risks are higher for individuals ageing with a longer duration of HIV infection than for individuals who are seroconverted at an older age [9]. The period of ART initiation is thus likely to influence mortality risk, but also comorbidity risk and the potential occurrence of side effects of long-term treatment.

So far, none of the studies that projected the number and age structure of PLHIV accounted for the issue of the ART initiation period [10–16]. In this study, we propose to fill this gap and project the demographic profile of the adult population living with diagnosed HIV (aPLdHIV) in France until 2030. For this purpose, we estimated mortality rates according to the ART initiation period and considered several scenarios for the numbers of new HIV cases that will be diagnosed by 2030. We also used mortality rate estimates to provide updated estimates of LE for PLHIV currently on ART, by sex and ART initiation period and compared these estimates to those for the French general population.

2 | METHODS

2.1 | Data sources

Three data sources were used. First, the permanent beneficiary sample (Échantillon Généraliste des Bénéficiaires, EGB) is a representative cohort of the population covered by the main health insurance schemes, which monitors beneficiaries' healthcare consumption and long-term illness status. It is a sample of 1/97th of the insured individuals in France [17]. Second, the French Hospital Database on HIV (ANRS CO4-FHDH) is a nationwide open hospital cohort created, in 1989, to enrol adult PLHIV receiving medical care, in currently 182 hospitals located throughout France [18]. The FHDH is representative of PLHIV receiving care in France [18]. Data, including demographic characteristics, biological markers and ART regimen, are collected prospectively, at each outpatient visit or hospital admission, using standardized forms. By 2019, FHDH included data on ~210,000 individuals aged ≥18 years, including ~106,000 with at least one follow-up visit in 2019. Third, routine national surveillance on individuals newly diagnosed with HIV is managed by Santé Publique France [19].

2.2 | Projecting the demographic profile of aPLdHIV

To determine the demographic profile of aPLdHIV (i.e. age, sex and ART initiation period) by 2030, we first needed data, estimates or assumptions on three parameters: (1) the demographic profile of aPLdHIV in 2018, (2) the number and age distribution of newly diagnosed HIV cases over 2019–2030 and (3) the mortality rates of aPLdHIV in 2018 and of new cases diagnosed beyond 2018. Only adults (i.e. aged ≥18 years) were included in the analysis. Specifically, we considered 14 age groups: 18–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79 and ≥80.

2.2.1 | *Demographic profile of aPLdHIV in 2018*

To estimate the number and age distribution of aPLdHIV in 2018, we used data from EGB and an algorithm initially developed by the general health scheme fund to study chronic diseases (including HIV) in terms of numbers, prevalence rates, and so on [20]. For HIV, the algorithm relies on long-term illness status, dispensations of HIV-specific drugs and biological exams, as well as HIV diagnosis during hospital stays (see details in the Supplementary Material, Section A). We first used the algorithm to determine the numbers of beneficiaries, by sex and age group, who were receiving HIV care at least once over 2014–2018 and still alive in 2018. We then extrapolated these numbers to the whole population of France, by dividing them by the EGB representativeness (i.e. 1/97) and the proportion of the population covered by the health insurance schemes included in the EGB (i.e. 95.6% of the whole population). Then, we used data from EGB and FHDH to determine for each individual his/her date of ART initiation (Supplementary Material, Section B). We considered five ART initiation periods: 1985–1996, 1997–2005, 2006–2010, 2011–2016 and ≥2017; the choice of the periods was mainly based on the amount of available data and changes in ART eligibility criteria (Supplementary Material, Section C). Individuals who had not started ART by 2018 were assumed to initiate ART in 2019, as the median time between care entry and ART initiation was less than 1 month (FHDH data).

2.2.2 | *New HIV cases over 2019–2030*

To set the annual numbers of newly diagnosed HIV cases over 2019–2030, we projected the mean annual number of newly diagnosed cases over 2015–2018 according to three scenarios: a 30% decrease scenario (scenario 1, reference scenario), that is a linear decrease with 30% fewer cases in 2030 compared to 2015–2018, a status quo scenario (scenario 2, pessimistic scenario), with a steady annual number of cases over 2019–2030 and an epidemic elimination scenario (scenario 3, optimistic scenario), with a linear decrease in the number of cases until zero cases in 2030 (Supplementary Material, Section C, Figure S1). Scenario 1 was set as the reference as it is a broad extrapolation of the temporal trend in newly diagnosed HIV cases observed over 2012–2018. Age distribution of newly diagnosed cases over 2019–2030 was obtained by extrapolating that of cases newly diagnosed over 2010–2018 (Supplementary Material, Section C, Figure S2). We assumed that newly diagnosed individuals would initiate ART within their diagnosis year.

2.2.3 | *Mortality rates in 2018 and beyond*

To estimate mortality rates for aPLdHIV still alive in 2018, according to the ART initiation period, we used data on aPLdHIV enrolled in the FHDH who had at least one follow-up visit between 1 January 2017 and 31 December 2019 and a known date of ART initiation.

Person-years were calculated for each sex and ART initiation period separately. They were accumulated from 1 January 2017 or cohort enrolment, until death, loss to follow-up (LTFU, defined as no clinical visit for 18 months, in line with French HIV guidelines [21], Supplementary Material, Section D), or 31 December 2019, whichever came first. For LTFU patients, follow-up stopped 6 months after the last visit. Patients with a clinical visit within the 6-month period before 31 December 2019 were censored on 31 December 2019 (Supplementary Material, Section B).

As the number of deaths is underreported in the FHDH [22], it was adjusted using data from the health insurance schemes on beneficiaries living with HIV (Supplementary Material, Section E, Tables S1 and S2).

We then used a Poisson model, with age reached in 2018 by aPLdHIV and ART initiation period as covariates, to estimate mortality rates by sex and age group, stratified by ART initiation period.

It was not possible to estimate the mortality rate for individuals who started ART in 2017 due to a lack of follow-up data after ART initiation. Then, for these individuals and newly diagnosed cases over 2019–2030, mortality rates were assumed, conservatively, to be the same as those for individuals who started ART during 2011–2016. Likewise, due to data scarcity, the mortality rate for individuals aged 18–19 years was assumed to be the same as those for individuals aged 20–24 years.

2.2.4 | *Projection matrix model and projection of age and time since ART initiation*

We used a matrix population model to project the size of aPLdHIV until 2030, using estimates for aPLdHIV in 2018, scenarios on newly diagnosed cases over 2019–2030 and estimates of mortality rates (Supplementary Material, Section F). Distributions of time since ART initiation were also projected, together with age distributions, stratified by ART initiation period, using the same matrix model.

2.3 | Life expectancy

Using estimated mortality rates and the life table method [23], we estimated LE for PLHIV on ART, by sex, age and ART initiation period. LE at a given age is defined as the expected number of years of life remaining for those surviving to that age (Supplementary Material, Section H). LE for the general population at ages 20, 40 and 60 years in 2018 were obtained from the Human Mortality Database (https://www.mortality.org).

2.4 | Ethical statement

The ANRS CO4-FHDH project was approved by CNIL (French data protection authority) on 27 November 1991, Journal Officiel, 17 January 1992. To conform to new regulations, the ANRS CO4-FHDH was then approved by the CEREES (Expertise Committee for Research, Studies and Evaluations in the field of Health) on 20 July 2018 and as a hospital data warehouse by CNIL on 19 February 2021. The cohort received authorization to conduct research projects on the data warehouse by CNIL on 30 March 2021. All ANRS CO4-FHDH participants signed informed consent forms mentioning the use of data for research purposes. INSERM has regulatory permanent access to EGB data, according to Article R1431-13 of the French Public Health Code, as modified by Decree 2021–848 of 22 June 2021. All data were deidentified, thus informed consent was not necessary.

3 | RESULTS

Demographic characteristics (age, sex and country of birth) of participants in the three data sources are provided in Table 1.

3.1 | Mortality rates and life expectancies

We used data on 104,042 adults (35% women), enrolled in the FHDH, who initiated ART before 2017 and had at least one follow-up visit between 1 January 2017 and 31 December 2019 to estimate mortality rates (Supplementary Material, Figure S3), as well as LE, which are presented in Table 2 together with LE for the general population. For instance, LE for individuals aged 40 in 2018 who started ART over 2011–2016 was 39.2 years for men and 40.2 years for women. In comparison, it was, respectively, 40.9 and 46.3 years for the general population. In general, whatever the age group, LE was higher for individuals who initiated ART over 2011–2016, that is the most recent period, compared to those who initiated ART earlier. Whatever the period and age group, women had higher LE than men; however, this difference tended to decrease over time, from 7% to 10% for women who started ART over 1985–1996 to 3% to 4% for women who started ART over 2011–2016. In addition, for individuals who initiated ART over 2011–2016, that is those with the highest LE, the gap in LE compared to the general population was higher for women than for men, whatever the age group, ranging from 3.8 to 6.8 years for women and from 0.4 to 2.4 for men.

3.2 | Demographic profile of aPLdHIV in 2030

In 2018, an estimated 161,125 adults (33% women) were living with diagnosed HIV. Assuming a 30% decrease in the annual number of newly diagnosed cases over 2019–2030 (scenario 1) and using the population matrix model together with mortality rate estimates, we estimated that 195,246 adults (33% women) would be living with diagnosed HIV in 2030, that is an increase of 21% of the epidemic size. It was 207,972 assuming a steady number of newly diagnosed cases until 2030 (scenario 2) and 167,221 under the epidemic elimination scenario (scenario 3).

For all scenarios, we found that the age distribution of aPLdHIV would shift towards older ages in 2030 (Figure 1). For scenario 1, the proportion of individuals aged ≥50 increased between 2018 and 2030, from 61% to 68% for men and from 44% to 63% for women. The proportion of

Table 1. Sex, age and country of birth distributions of participants to the three data sources

	EGB—2014–2018		ANRS CO4-FHDH—2017–2019[a]		HIV surveillance—2015–2018	
	Men	Women	Men	Women	Men	Women
Total	108,871	52,253	67,721	36,321	17,141	7997
Age *N* (%)						
18–19	304 (0.3)	102 (0.2)	19 (0.0)	24 (0.1)	286 (1.7)	142 (1.8)
20–24	1522 (1.4)	1522 (2.9)	734 (1.1)	535 (1.5)	1741 (10.2)	633 (7.9)
25–29	3450 (3.2)	2638 (5.0)	2061 (3.0)	1246 (3.4)	2523 (14.7)	1231 (15.4)
30–34	5682 (5.2)	3145 (6.0)	3536 (5.2)	2587 (7.1)	2490 (14.5)	1445 (18.1)
35–39	9233 (8.5)	6189 (11.8)	4816 (7.1)	4536 (12.5)	2297 (13.4)	1384 (17.3)
40–44	9538 (8.8)	8726 (16.7)	6773 (10.0)	5832 (16.1)	2014 (11.7)	1021 (12.8)
45–49	13,190 (12.1)	7102 (13.6)	9994 (14.8)	6108 (16.8)	1936 (11.3)	681 (8.5)
50–54	21,003 (19.3)	7407 (14.2)	13,136 (19.4)	5959 (16.4)	1554 (9.1)	545 (6.8)
55–59	18,264 (16.8)	6392 (12.2)	11,504 (17.0)	4371 (12.0)	1021 (6.0)	384 (4.8)
60–64	10,451 (9.6)	3856 (7.4)	6711 (9.9)	2382 (6.6)	177 (3.6)	276 (3.4)
65–69	7102 (6.5)	1725 (3.3)	4326 (6.4)	1326 (3.7)	611 (2.3)	160 (2.0)
70–74	5682 (5.2)	1623 (3.1)	2453 (3.6)	820 (2.3)	387 (1.1)	64 (0.8)
75–79	1826 (1.7)	913 (1.7)	1060 (1.6)	363 (1.0)	65 (0.4)	21 (0.3)
80+	1623 (1.5)	913 (1.7)	598 (0.9)	232 (0.6)	31 (0.2)	10 (0.1)
Country of birth[b] (%)						
France			48,252 (71.3)	13,304 (36.6)	10,678 (61.4)	431 (21.9)
Sub-saharan Africa			9427 (13.9)	17,704 (48.7)	3566 (20.5)	5453 (63.9)
Europe			2969 (4.4)	933 (2.6)	870 (5.0)	247 (2.9)
America/Haïti			2778 (4.1)	2143 (5.9)	1232 (7.1)	639 (7.5)
Other (North Africa/Asia/Oceania)			4295 (6.3)	2237 (6.2)	1034 (6.01,865)	324 (3.8)

[a]Individuals enrolled in the FHDH, who initiated ART before 2017 and had at least one follow-up visit between 1 January 2017 and 31 December 2019.
[b]No data on country of birth are available in the EGB.
Abbreviations: EGB, permanent beneficiary sample (Échantillon Généraliste des Bénéficiaires); ANRS CO4-FHDH, French Hospital Database on HIV.

Table 2. Remaining life expectancy (in years) according to the age reached in 2018, for the general population[a] and for people living with HIV (PLHIV) who initiated ART, by period of ART initiation and sex

Period of ART initiation	Age reached in 2018					
	20 years		40 years		60 years	
	Men	Women	Men	Women	Men	Women
1985–1996	x	x	35.0 (33.7–36.3)	37.4 (35.8–39.0)	19.7 (19.1–20.3)	21.6 (20.4–22.8)
1997–2005	54.4 (52.1–56.7)	56.9 (54.9–58.9)	36.2 (35.5–36.9)	38.2 (37.3–39.1)	20.5 (20.0–21.0)	22.1 (21.2–23.0)
2006–2010	56.8 (53.9–59.7)	60.0 (57.7–62.3)	38.4 (37.4–39.4)	41.0 (39.6–42.4)	22.5 (21.5–23.5)	24.4 (23.1–25.7)
2011–2016	57.7 (56.5–58.9)	59.1 (57.3–60.9)	39.2 (38.1–40.3)	40.2 (38.6–41.8)	22.9 (21.8–24.0)	23.9 (22.3–25.5)
General population[a]	60.1	65.9	40.9	46.3	23.3	27.7

Note: Mean remaining life expectancy (and 95% confidence interval) for PLHIV were estimated from mortality events among PLHIV enrolled in the French Hospital Database on HIV (ANRS CO4-FHDH) who had at least one follow-up clinical visit between 1 January 2017 and 31 December 2019.
[a]Values for the general population were obtained from the Human Mortality Database (https://www.mortality.org).

individuals aged ≥60 doubled, from 24% to 47% for men and from 17% to 36% for women, like the proportion of individuals aged ≥70, from 8% to 18% for men and from 7% to 14% for women. These proportions were slightly lower for scenario 2 (Figure 1c,d) and slightly higher for scenario 3 (Figure 1e,f). Whatever the scenario, we estimated that, in 2030, there would be ~83,400 individuals (~28% women) aged ≥60 and ~33,100 individuals aged ≥70 (~27% women); in comparison, in 2018, it was, respectively, 35,715 (~25% women) and 12,582 (~27% women).

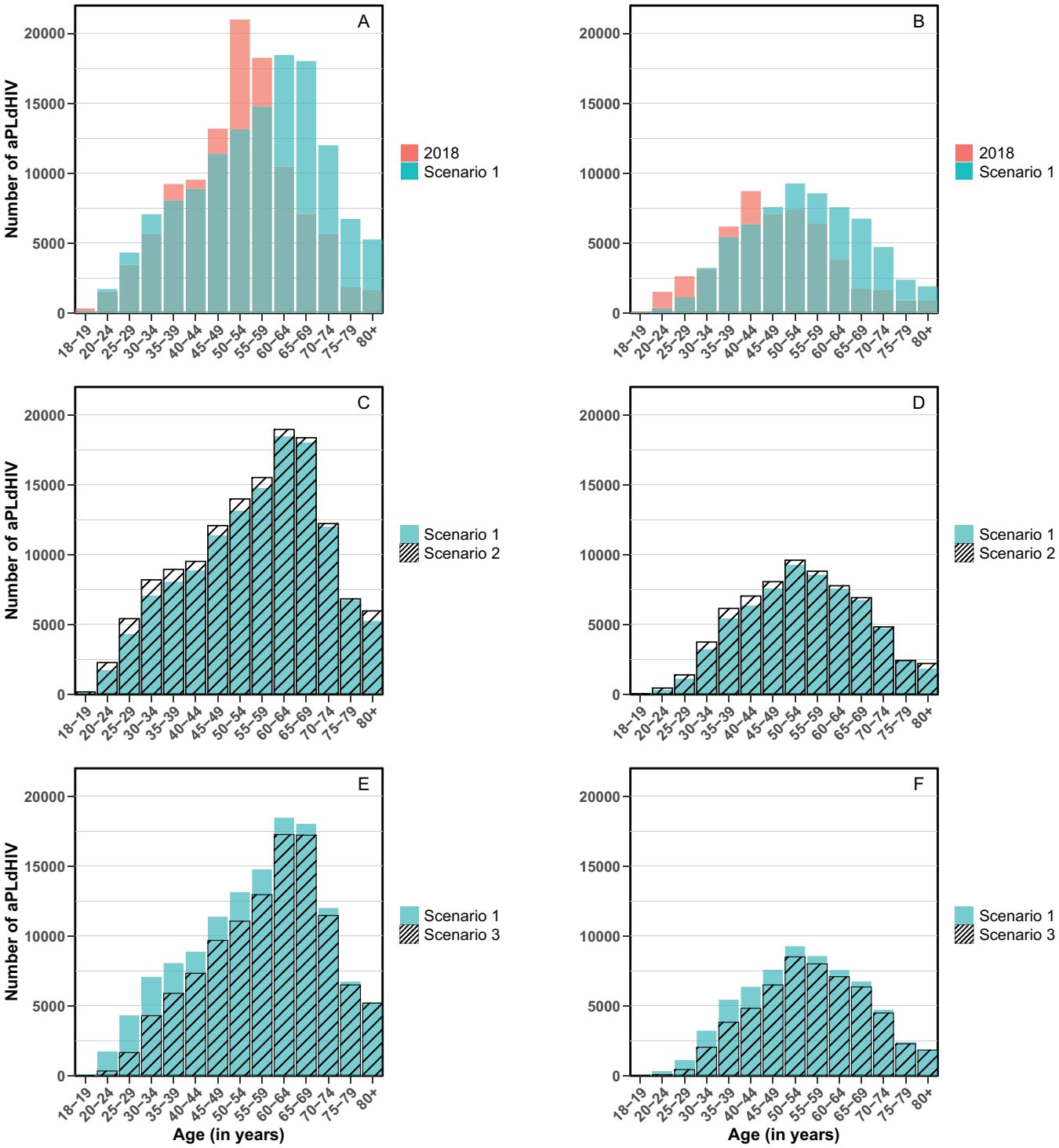

Figure 1. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, according to different scenarios. Numbers and age distributions for men (a) and for women (b), in 2018 (in red) and in 2030 (in turquoise) for scenario 1 (i.e. 30% decrease in newly diagnosed HIV cases between 2018 and 2030). Comparison of the numbers and age distributions of adults living with diagnosed HIV in 2030 for scenario 1 (in turquoise) and scenario 2 (i.e. status quo situation with a steady annual number of new HIV cases over 2019–2030, black diagonal stripes) for men (c) and for women (d), and for scenario 1 and scenario 3 (i.e. epidemic elimination with zero new HIV cases in 2030, black diagonal stripes) for men (e) and for women (f). Detailed assumptions made for the number and age of newly diagnosed HIV cases in 2019–2030 can be found in the Supplementary Material, Section C.

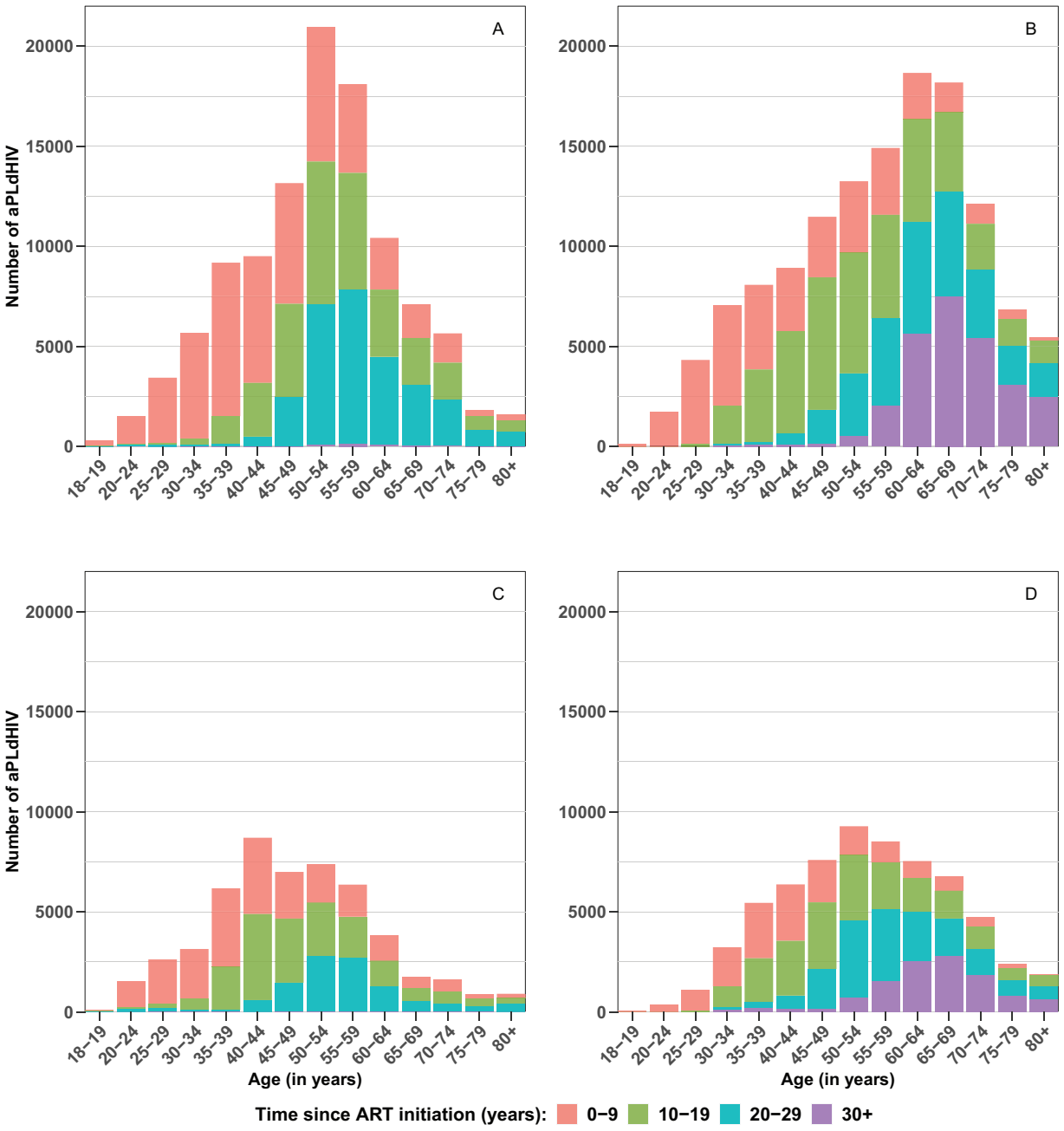

Figure 2. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (a and b) and women (c and d) in 2018 (a and c) and in 2030 (b and d) for scenario 1 (i.e. 30% decrease in newly diagnosed HIV cases between 2018 and 2030). Results for other scenarios can be found in the Supplementary Material, Section I and Figures S4 and S5.

3.3 | Projected time since ART initiation

Proportions of individuals who started ART more than 20 or 30 years ago will increase over 2018–2030 (Figure 2), especially for older age groups. For brevity, we only present results for scenario 1, results for other scenarios are described in the Supplementary Material, Section I. Proportions of individuals with ≥20 years of ART exposure will increase from 27% to 42% for men and from 21% to 44% for women. In particular, for individuals aged ≥60, these proportions will increase from 43% to 68% for men and from 33% to 67% for women. Proportions of individuals with ≥30 years of ART exposure will increase from <1% to 21% for men and from <1% to 18% for women. In particular, for individuals aged ≥60, these proportions will increase from 1% to 39% for men and from <1% to 37% for women. In consequence, the median time since ART initiation will increase, especially for older age groups. For individuals aged ≥60, it

will increase from 18.4 (IQR 10.4–22.4) to 25.9 years (17.6–33.4) for men and from 15.2 (7.9–21.4) to 25.8 years (16.8–33.1) for women, while for individuals aged <60, it will only increase from 9.8 (4.8–19.0) to 12.0 years (6.5–17.8) for men and from 11.0 (5.2–17.7) to 14.5 years (7.5–21.8) for women.

Of note, we estimated that, in 2030, 83,659 individuals (34% women) would have started ART ≥20 years ago and 38,492 individuals (30% women) would have started ART ≥30 years ago—versus, respectively, 40,667 and 573 in 2018 (Figure 2). Among men who started ART ≥20 years ago, 77% would be aged ≥60, 33% ≥70 and 8% ≥80. It was, respectively, 54%, 21% and 4% for women. Among men who started ART ≥30 years, 89% would be aged ≥60, 40% ≥70 and 8% ≥80. It was, respectively, 75%, 29% and 6% for women.

4 | DISCUSSION

We projected that by 2030, the HIV epidemic in France would be growing, most likely by more than 20%, and ageing, with a doubling of the proportion of individuals aged ≥60 and ≥70. More than two-thirds of aPLdHIV would be aged ≥50, ~50% aged ≥60 and ~20% aged ≥70. Interestingly, whatever the scenario considered for the epidemic dynamics over 2019–2030, we estimated that ~83,000 individuals will be aged ≥60 in 2030, including ~33,000 aged ≥70. Our results are in line with studies forecasting the age structure of the HIV population in other high-income countries [10, 11, 13, 14, 16]. It was estimated that the proportion of PLHIV on ART aged ≥50 would be 73% in 2030 in the Netherlands [13] and 54% in the United States [16], and ~75% in 2035 in the United States and Italy [14]. Bretaña et al. [10] performed projections for Australia, considering three scenarios for the future number of newly diagnosed cases over 2018–2027. They highlighted that, whatever the scenario, the age distribution of PLHIV would have its highest peak in the 55–59 age group in 2027, which aligns with our findings of highest peak in the 60–64 age group for men and 50–54 for women.

In addition, our study predicts that in 2030, in France, there will be more than 38,000 individuals who would have started ART more than 30 years ago (i.e. before 2000), with most of them being aged ≥60 (85%, ~33,000), 37% aged ≥70 (~14,000) and 8% aged ≥80 (~3000). These individuals were thus exposed to the first generation of nucleoside reverse transcriptase inhibitors (AZT and D4T) and protease inhibitors, which have been associated with body morphology changes and cardiovascular diseases [24, 25]. In addition, ART duration and time living with diagnosed HIV infection have been associated with increased risk of multimorbidity [7, 9], but also with psychological morbidity and lower quality of life [26, 27], which should be considered as part of integrated HIV care. To the best of our knowledge, our study is the first to project time spent since ART initiation for an HIV population. However, previous studies emphasized other important aspects of the projected demographic profile of HIV populations, which we were unable to take into account. First, a study investigating the capacity of current cART to offer long-term HIV control found that the median time until exhaustion of treatment options was 45.5 years (IQR 34.0–61.0 years) [28]. Furthermore, some studies showed important heterogeneity in the projections of PLHIV according to race/ethnicity, with an older projected population of white PLHIV compared to Black and Hispanic minorities [11, 29]. Other studies [13, 14] focused on the burden and prevalence of age-related co-morbidities: Smit et al. [13] predicted that in 2030, 84% of PLHIV in the Netherlands will have at least one age-related non-communicable disease, with 28% having three or more, mainly due to cardiovascular disease. This could generate complications due to drug–drug interactions for 40% of patients with the currently recommended first-line HIV regimen. Finally, a study for Australia [15] highlighted that the number of PLHIV in non-metropolitan areas, where the PLHIV median age is higher, is expected to increase at a greater rate than that in the major cities.

We also found that the LE of adults who started ART from 2011 onwards was either equal to or approaching that of the general population: for instance, at age 60, in 2018, it was ~23 and ~24 years for, respectively, men and women living with diagnosed HIV versus, respectively, ~23 and ~28 years in the general population. Individuals who started ART in 2005 or earlier, and are still alive in 2018, had lower LE, but the difference was only 2–4 years. This can have important implications for health-related insurance policies for PLHIV. Marcus et al. [30] reported an overall LE of 56.0 years at age 21 over 2014–2016, close to our estimates for individuals of age 20 in 2018, ranging from 51.4 to 57.4 years. Studies that estimated LE for earlier periods of follow-up found, expectedly, lower LE than ours [3, 31]. We also found that although women living with diagnosed HIV had higher LE than men, the gap in LE compared to the general population was higher for women than for men, which is in line with previous results [2, 3]. Potential explanations for this higher gap include later access to HIV care for women than for men. However, in France, the time between infection and care entry was estimated to be shorter for women than for men [32, 33]. Another explanation is that among women living with diagnosed HIV in France, a vast majority were born abroad (63%, of which 77% in sub-Saharan African countries, Table 1), while among men, a vast majority were born in France (71%). Hence, differences in socio-economic levels and access to healthcare system between born-abroad and born-in-France individuals, but also the stigma and marginalization, probably play an important role in the observed sex difference in the LE gap between PLHIV and the general population [34, 35].

The main novelty of our approach is that it accounts for the impact of the ART initiation period on mortality rates to project the demographic profile of the HIV population. In addition, our projections for the population size aged ≥60 are robust to assumptions regarding epidemic dynamics over 2019–2020. However, our study also has a number of limitations. First, the projection method and LE estimates rely on the assumption that age-specific mortality rates estimated over 2017–2019 will remain constant over 2019–2030. On one hand, lower mortality beyond 2019 would lead to higher LE estimates and a larger HIV population in 2030. On the other hand, higher mortality among older age groups, due to covid-19 during 2020–2021 for instance, could lead to a decrease in LE, total population size and proportions of older PLHIV in 2030. Second, several limitations affect HIV

care data. Data on deaths in FHDH were not comprehensive and were adjusted for under-reporting, with potential inaccurate adjustments (Supplementary Material, Section G for details). As health insurance schemes do not collect data on the HIV exposure group, this factor could not be accounted for. Third, we could not include individuals aged <18 years for population size estimates. According to health insurance and HIV surveillance data, this could represent ~5200 individuals in 2030, comprising ~4000 individuals aged <18 years living with diagnosed HIV in 2018, plus ~100 individuals who could be newly diagnosed each year over 2019–2030. Fourth, our global LE estimates do not capture the comorbidity-free LE. This was estimated to remain much lower for PLHIV than for the general population (9.5 years difference in a US cohort of insured adults [30]). Finally, with HIV becoming more prevalent among older adults, transmission risk in higher age groups might increase, if, for instance, older PLHIV are not adherent to their treatment. This may impact the age distribution of individuals becoming newly infected, with for instance more individuals seroconverting at an older age. As a consequence, interventions explicitly targeting older individuals may be needed, as older individuals were recently shown to be at increased risk of delayed presentation for HIV care [36].

5 | CONCLUSIONS

By 2030, in France, close to 20% of the adult population living with diagnosed HIV will be aged ≥70 (i.e. ~33,000 individuals), of which >40% would have started ART more than 30 years. Ageing of the HIV population has important implications for care, generating an increase in comorbidity prevalence and treatment complexity. Our findings can help to measure the burden of ageing and anticipate healthcare needs, resource provision and screening guidelines in HIV care, in France but also in other high-income countries. Indeed, our estimates probably provide a broad picture of what is likely to occur in terms of HIV population ageing in other settings, with similar historical access to ART and free access to care.

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COMPETING INTERESTS

VS reports lecture fees from ViiV (2019), Gilead (2019, 2020) and Janssen-Cilag (2020), outside the submitted work.

DC reports an HIV grant from Janssen (2019–2020) and personal fees from Gilead (2020) and Pfizer (2022) for lectures, outside the submitted work.

LM, AR, SG and YD declare no competing interests.

AUTHORS' CONTRIBUTIONS

LM and VS designed the research. LM performed the research. All authors analysed the data. LM and VS drafted the manuscript. All authors critically revised the manuscript for important intellectual content.

ACKNOWLEDGEMENTS

LM is grateful for the financial support of the ANRS, in the form of a postdoctoral research fellowship. All authors thank Adam Trickey for his help with the methodology of life expectancy estimation. We are grateful to all ANRS CO4-French Hospital Database on HIV (FHDH) participants and research assistants, without whom this work would not have been possible. Members of FHDH-ANRS CO4 are listed at https://anrs-co4.fhdh.fr/. For the purpose of Open Access, a CC-BY public copyright licence has been applied by the authors to the present document and will be applied to all subsequent versions up to the Author Accepted Manuscript arising from this submission.

FUNDING

FHDH is funded by the ANRS-MIE, the Institut National de la Santé et de la Recherche Médicale (INSERM) and the French Ministry of Health.

DATA AVAILABILITY STATEMENT

Anyone can submit a research project to the ANRS CO4-FHDH scientific committee and obtain access to the data after approval by the scientific committee. Applicants should use a standardized form available on the ANRS CO4-FHDH website (https://anrs-co4.fhdh.fr) to describe the context and objectives of the study. The scientific committee reviews the submitted projects twice a year. For successful applicants with adequate statistical expertise, the data can be transferred with French data protection agency CNIL approval; otherwise, the ANRS CO4 FHDH statistical centre analyses the data cooperatively with the applicant.

Our institution has permanent access to the EGB given by its governance (ministerial steering). Without permanent access, an access request to the EGB for a project requires authorization from the Health Data Hub (https://www.health-data-hub.fr/depot).

Anyone can submit a research project to Santé Publique France and obtain access to the routine HIV surveillance data after approval by the scientific committee, by writing to ANSP-DMI-VIC@santepubliquefrance.fr.

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SUPPORTING INFORMATION

Additional information may be found under the Supporting Information tab for this article:
Supplementary Material

Figure S1. Annual number of newly diagnosed HIV cases over 2019–2030 according to the three scenarios, for men (A) and for women (B). In green: linear decrease with 30% fewer cases in 2030 compared to 2015–2018 (scenario 1). In blue: status quo situation with a steady annual number of new HIV cases over 2019–2030 (scenario 2). In red: epidemic elimination with zero new HIV cases in 2030 (scenario 3).

Figure S2. Projected adult newly diagnosed HIV cases by age group at diagnosis over 2019–2030 for men (A) and for women (B).

Figure S3. Mortality rates of adults aged ≥20 years living with diagnosed HIV in 2018, according to age and ART initiation period, for men (A) and women (B).

Figure S4. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D) under scenario 2 (i.e. status quo situation with a steady annual number of new HIV cases over 2019–2030).

Figure S5. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D) under scenario 3 (i.e. epidemic elimination with zero new HIV cases in 2030).

Table S1. Data from the French National Health Data System and the FHDH for the years 2017, 2018 and 2019 on the number of individuals living with diagnosed HIV and deaths among them, stratified by age group.

Table S2. Data from the French National Health Data System for the years 2017, 2018 and 2019 on the number of beneficiaries living with diagnosed HIV (BLHIV) and deaths among them, stratified by age group.

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AUTHOR INDEX

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Website: www.jiasociety.org

eISSN: 1758-2652

Contact details

Editorial office:
Avenue de France, 23
CH-1202 Geneva
Switzerland

Email: editorial@jiasociety.org

Tel: +41 (0) 22 710 0800

Publisher

The *Journal of the International AIDS Society* is published by John Wiley & Sons Ltd on behalf of the IAS - International AIDS Society

John Wiley & Sons Ltd
9600 Garsington Road
Oxford, OX4 2DQ UK

Telephone: +44 1865 776868

Email: customer@wiley.com

Production Editor

Gowthamantony Raja (Email: gr@wiley.com)

Abstracting and Indexing Services

The *Journal of the International AIDS Society* is indexed in a variety of databases including PubMed, PubMed Central, MEDLINE, Science Citation Index Expanded and Google Scholar. The 2020 Journal Impact Factor is 5.396, Journal Citation Reports (Clarivate Analytics, 2021).

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