

# Fostering healthy cognitive ageing in people living with HIV



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Prevalence and incidence of HIV among people aged 50 years and older continue to rise worldwide, generating increasing awareness among care providers, scientists, and the HIV community about the importance of brain health in older adults with HIV. Many age-related factors that adversely affect brain health can occur earlier and more often among people with HIV, including epigenetic ageing, chronic medical conditions (eg, cardiovascular disease), and age-related syndromes (eg, frailty). Extensive dialogue between HIV community leaders, health-care providers, and scientists has led to the development of a multidimensional response strategy to protect and enhance brain health in people ageing with HIV that spans across public health, clinical spaces, and research spaces. This response strategy was informed by integrated ageing care frameworks and is centred on prevention, early detection, and management of brain health issues associated with HIV (eg, neurocognitive disorders), with specific considerations for low-resource or middle-resource countries. A collaborative, international, and data-informed update of the diagnostic criteria for HIV-associated neurocognitive disorders is a cornerstone of the proposed response strategy. The proposed response strategy includes a dynamic, international, online knowledge hub that will provide a crucial community resource for emerging evidence on the brain health of people ageing with HIV.

## Introduction

The population of people aged 50 years and older living with HIV now represents the majority of people living with HIV worldwide.<sup>1</sup> An increasing number of older people living with HIV are experiencing premature, accentuated, and sometimes accelerated cognitive or brain ageing.<sup>2</sup> Emerging evidence suggests that older people living with HIV might be at up to 58% greater risk<sup>3,4</sup> of all-type dementia (or major neurocognitive disorder)<sup>5</sup> than people without HIV, although the risk is probably multifactorial depending on the degree of HIV control and the presence of various comorbidities.<sup>6</sup> Within the next 30 years, many people living with HIV will reach their 70s, an age at which prevalence and incidence of dementia strongly increases.<sup>7</sup>

Although antiretroviral therapy (ART) has greatly improved longevity among people living with HIV, there has been a relative neglect of issues that affect people ageing with HIV. Reviewing probable reasons for this neglect will assist in identifying and rectifying ongoing barriers to care and healthy ageing. Reasons for such neglect are likely to be multifactorial and include various forms of ageism among the general population,<sup>8</sup> among health-care providers and researchers, and even within the HIV community.<sup>9</sup> Moreover, most HIV specialists have not been trained to assess multidimensional aspects of ageing<sup>10</sup> and are unaware of the prevention framework for geriatric syndromes such as mild cognitive impairment and early dementia (more information on mild cognitive impairment is provided in the appendix [p 1]).<sup>11</sup> A more balanced counternarrative regarding proactively managing a chronic condition is now necessary as many people ageing with HIV do not have social support and are becoming increasingly isolated.<sup>12</sup>

This Position Paper was developed by the NeuroHIV and Aging Advocacy Group, which was formed through

a long-term dialogue between community leaders (most of whom are people living with HIV and some of whom are people living with HIV-associated neurocognitive disorders [HAND]), researchers, and health-care providers with the aim of finding immediate solutions for optimising cognitive, mental, and brain health for people ageing with HIV (appendix p 1). The group is informed by the 2022 calls to action (known as the Glasgow Manifesto)<sup>13</sup> by the International Coalition of Older People with HIV. The manifesto emphasises issues of quality of life in people living and ageing with HIV and the need for additional research and associated funding. The group is also informed by the 2022 update of the International Antiviral Society–USA treatment guidelines<sup>14</sup> and related consensus statements,<sup>15,16</sup> the WHO prevention guidelines for dementia,<sup>17</sup> and the integrated care<sup>18</sup> and ageing and health<sup>8</sup> frameworks. On the basis of these frameworks and the most recent research findings in neuro-HIV and ageing research, this Position Paper proposes a global multidimensional response strategy centred on prevention, early diagnosis, and management. Overall, the NeuroHIV and Aging Advocacy Group believes both health-care and research responses require a major refocus on this growing population. Our group would like to emphasise that although super ageing (ie, having no comorbidity; not taking any medication; and being neurocognitively unimpaired, functionally independent, physically active, and able to learn new and challenging things)<sup>19</sup> is not the most common experience (appendix p 2), expectations of healthy ageing are nevertheless realistic goals.

## Risk factors for neurocognitive decline in people ageing with HIV

Over the past 20 years, our understanding of the underlying causes of declining cognitive health with

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older age in the general population has greatly changed. This knowledge evolution should inform issues of cognitive health in people ageing with HIV.<sup>20</sup> Poor cognitive health in older age is not, in most instances, a sudden disease, but rather associated with the accumulation of non-modifiable and modifiable risks and impacts across the lifespan (eg, trauma or environmental toxicities), with cardiovascular factors having a major influence from mid-life onwards<sup>21</sup> (figure 1). Because we now understand that changes in the brain occur years before the expression of more advanced symptoms, there is a window of opportunity to delay, lessen, and perhaps prevent and even reverse cognitive decline.<sup>21</sup> Additionally, in the international HIV context, some people living with HIV remain at risk of dementia as a result of opportunistic brain infections, because some people are not virally suppressed, develop virological failure despite HIV treatment, or present late for care with complications of advanced HIV. This primary risk factor for HIV disease progression and HIV-related cognitive decline in older people living with HIV should not be forgotten,<sup>20</sup> especially in the context of polypharmacy and multimorbidity.

### Prevention, early detection, and early management

Within our proposal, the neuro-HIV and HIV communities must understand that one of the key aspects of cognitive impairment or decline prevention is early detection of individuals who are at risk and early diagnosis.<sup>22,23</sup> Early prevention and treatment frameworks positively influence individual physical, cognitive, and mental health trajectories and associated morbidity and mortality;<sup>24</sup> they also contribute to health service and resource optimisation and the social and economic impact on others and society.<sup>25</sup> Having a clear framework to address the cognitive health needs of people ageing with HIV will particularly benefit low-resource and middle-resource countries, where expertise and infrastructure to manage cognitive symptoms, mental health, and multimorbidity are scarce, and resources need to be prioritised. This approach is supported by population data from evidence-based general health prevention policies and practices showing that, in high-resource countries with clear frameworks, the incidence of age-related cognitive decline is decreasing due to a reduction in cardiovascular risk and the adoption of healthier lifestyles<sup>22</sup> (eg, ones that include physical activity). These findings accord with multidomain interventions for modifiable risk factors that can reduce risk of cognitive impairment or decline.<sup>17</sup> In parallel, there is hope that novel pharmacological treatments that prevent neuronal injury or death or minimise these consequences might be available in the short-to-medium-term future.<sup>26</sup> Evaluations of memory clinics within models of integrated care show that these approaches are a feasible and effective way to provide evidence-based

cognitive care. Detection of patients who are at risk and early diagnosis supported by a multidisciplinary team and a dedicated funding structure yield substantial benefits to patients, their caregivers, and society.<sup>27</sup>

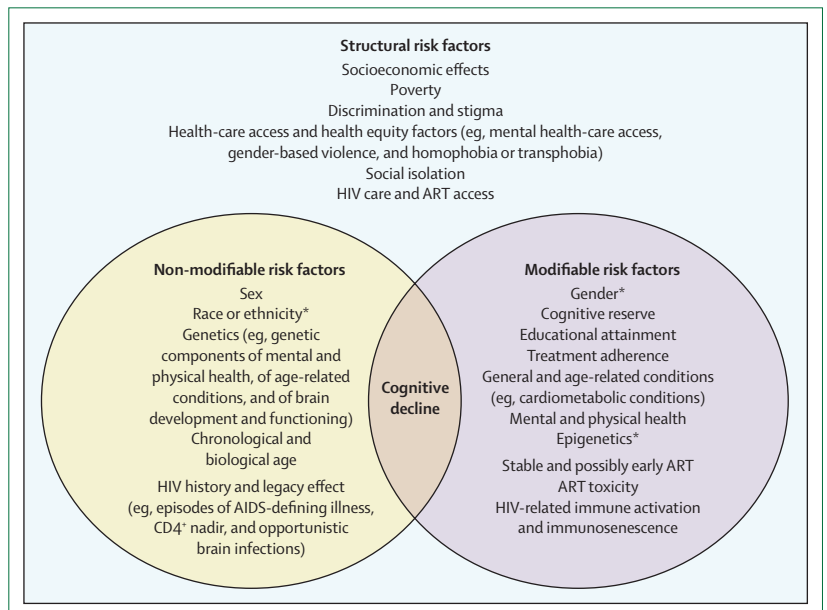
### Cognitive health literacy

The past 20 years have also seen major efforts to improve awareness and health literacy of the general population and clinicians regarding milder forms of cognitive impairment. This effort has led to novel guidelines supported by WHO on dementia and cognitive decline prevention.<sup>17</sup> In parallel, well curated websites have been developed by patient associations (eg, the Alzheimer's Association), providing information on diagnosis and prevention and information for caregivers (ie, traditional and non-traditional family members or friends). The HIV community, which has pioneered health literacy improvement efforts through community activism, can include cognitive health literacy in these efforts,<sup>28</sup> including in low-resource and middle-resource countries by adapting these existing resources across four recommended areas: the patient population (ie, people ageing with HIV); current and potential caregivers; health-care providers; and the general public.

Cognitive health education for people ageing with HIV must encompass information on which the neuro-HIV clinical research community agrees (by true consensus), covering epidemiology, pathogenesis, diagnostic criteria (including degrees of severity of cognitive impairment), effects on daily life, treatment, and long-term prognosis. Most of the symptoms that people ageing with HIV experience constitute mild cognitive deficits, not dementia (appendix p 1). However, mild cognitive deficits can have repercussions on many aspects of everyday functioning with effects on self-confidence and quality of life<sup>29</sup> (appendix p 1). Regarding long-term cognitive functioning, emphasising that most people living with HIV who have well managed care have stable cognitive functioning over many years is important.<sup>30</sup> A cognitive health framework and programmes that encompass community input would greatly assist in modifying perspectives among people ageing with HIV on cognition and associated anxiety and depression and would encourage the use of evidence-based interventions and behavioural changes, particularly from middle age onwards (ie, from the age of 50 years), which are likely to maintain long-term cognitive health as people age. Steps on how to maintain healthy cognitive ageing and what to do when difficulties arise must be clearly outlined. Current recommendations, such as multidimensional screenings that include brain health, will make establishing whether someone is at risk for cognitive decline possible; and care pathways need to be clear for those patients who are at risk. Similar information should be provided to caregivers of people ageing with HIV, alongside ways to recognise early cognitive changes and support optimal responses to these changes to avoid

stigma and minimisation, which can delay or impede early detection and management. In our experience with older people at risk of cognitive decline, caregivers are often family members, spouses, partners, friends, and at-home nurses. In the context of the HIV community, caregivers could also include chosen families, peer navigators or educators, and certified peer counsellors. Further discussion with the HIV community in dedicated forums is needed to develop an understanding of models of caregiving, to identify existing knowledge in the community, and to identify knowledge gaps and needs. Health-care providers must be educated to avoid the dismissal of mild cognitive symptoms<sup>31,32</sup> and further stigmatisation of people living with HIV. Our experience in discussions with people living with HIV or HAND has been that many who were diagnosed with mild cognitive deficits were cycled through numerous doctors and experienced several dismissals about their concerns before seeing appropriate specialists and receiving adequate care. Crucial aspects have been identified as limitations for health-care providers in their capacity to recognise early cognitive deficits. These aspects include: poor education and training; difficulties in broaching the topic of cognitive issues; poor knowledge in the selection of cognitive screening instruments; the absence of an initial management plan; and poor infrastructure and an absence of institutional support to allow this work to be done.

The adaptation of existing resources for the general population to people with HIV should assist in improving cognitive health literacy in people living and ageing with HIV. There are websites (mostly in high-resource countries) that are available to the general ageing population that provide educational resources about cognitive health in older adults (eg, on the National Institute of Aging and Alzheimer's Association websites) that can be adapted to address cognitive health in people living with HIV in high-resource countries. There is also a major effort in translational research<sup>22</sup> attempting to address issues of inequity in access to neurological care.<sup>33</sup> These web resources provide links to ongoing therapeutic and intervention trials aimed at reducing cognitive decline risk. The Alzheimer's Association also includes guidelines on how best to address dementia stigma. However, a large gap exists in these resources and treatment approaches—none of these websites or translational efforts have been tailored to or have even begun to address the needs of people living with HIV, who are typically younger, have a higher rate of mental health needs, and include a wider range of people from other stigmatised groups and sexual minorities and people with lower educational and social opportunities. Furthermore, these websites do not include substantial input from a health disparity-informed framework. Crucially in the global HIV infection context, these resources are only from high-resource countries and require urgent adaptation to



**Figure 1: Risk factors for cognitive decline—evidence from neuroHIV research and general population studies applicable to people living with HIV**

Health equity factors to consider (although this list is not exhaustive): access to mental health care; childhood trauma; homophobia; transphobia; gender-based violence; socioeconomic status and race or ethnicity; and level and quality of education. Gender might be conceived as a modifiable risk factor (in addition to a non-modifiable risk factor) because of indirect effects of traditional differences in gender roles and associated socioeconomic opportunities (eg, education, work, and lifestyle opportunities). Many of these effects have an impact on dementia risk. In addition, access to hormone replacement therapy in menopausal women might influence dementia risk. ART=antiretroviral therapy. \*Need for additional evidence to specify the independent directions and magnitude of effects, especially in the HIV population.

low-resource and middle-resource countries, where HIV is most prevalent.

### Brain health screening

Multidimensional screening that includes brain health is possible and has already been implemented in some HIV and ageing clinics. Best practice for health-care providers is summarised in panel 1. Brain health screening has three components: cognition, function, and mental health.<sup>34</sup> A screen might assist in streamlining care<sup>35</sup> and flagging an at-risk category rather than providing a diagnosis. Everyday functioning should be systematically assessed and might be the sole focus in some instances (as discussed later in the context of low-resource and middle-resource countries). This assessment can be assisted with existing standard tools<sup>36</sup> to develop a more systematic process. One way to gain time during the clinic visit is to have the patient (and ideally an informant) complete the questionnaire at home or in the waiting room before the visit. However, a review of the responses with the patient is essential to avoid minimisation or over-reporting of difficulties and to ensure patients understand the questions. All three possibilities are potentially meaningful when interpreting a cognitive screen result.<sup>37</sup> Open questions are recommended, on, for example, the most demanding aspects of everyday life.<sup>38</sup> Mental health should also be

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See Online for appendix

For more on the Alzheimer's Association see <https://www.alz.org/>

For more on cognitive health and older adults on the National Institute of Aging website see <https://www.nia.nih.gov/health/cognitive-health-and-older-adults#>

**Panel 1: Best practice for health-care providers screening for brain health****Choosing a tool***Do*

- Look out for the best tool for your specific population
- Ask a specialist
- Consider issues of cost, feasibility, training, available normative standards, and timing
- Select a tool that has been recommended for people living with HIV
- Consider evidence regarding whether the tool is culturally and linguistically appropriate and fair

*Do not*

- Use a screen recommended by someone who works in a different context
- Use only tools that you are aware of
- Use expensive tools, assuming their quality and accuracy
- Use the Mini-Mental State Examination, which has low sensitivity to HIV-associated neurocognitive disorders
- Test people on knowledge they have never previously encountered

**Context of use***Do*

- Use screening as part of a multidimensional examination
- Develop a systematic process
- Assess or query everyday activity

*Do not*

- Use screening in isolation
- Use screening only in people who complain of cognitive difficulties
- Ignore activities that have been abandoned

**Administration***Do*

- Practise and ensure standardisation
- Acknowledge any errors of administration, remedy them, and assess the impact on interpretation
- Consider any sensory deficits in interpreting results

*Do not*

- Use unstandardised procedures (for administration and scoring)
- Ignore errors in administration
- Ignore individuals' sensory deficits

**Interpretation***Do*

- Use normative standards that are suitable for the age, education, sex, language, and cultural background of your patient
- Combine knowledge on medical history to interpret test results
- Ask for advice from specialists
- Take time to report results to patients and explain the next steps

*Do not*

- Use one cutoff only and hope that it will work for most people with HIV
- Interpret results in isolation
- Minimise input from specialists
- Disclose results to third parties and potentially enable use of results to discriminate in employment opportunities<sup>1</sup>

**Timing***Do*

- Develop a systematic process to conduct screens annually for patients who are at risk and biennially for other individuals
- Consider specialists' advice on practice effects

*Do not*

- Do the screening whenever convenient
- Fail to consider practice effects on repeated administrations

systematically examined when doing cognitive screening.<sup>39</sup> Standard tools that encompass symptoms of depression, anxiety, and stress are recommended. Careful history taking about mental health, life stressors, and health disparities, lifestyle factors, and socioeconomic status should also be conducted. Although screening for mental health is done in conjunction with cognitive function, separate care pathways for the management of mental health issues should also be established for individuals who screen positive.

### Communication of cognitive health risk and cognitive diagnoses

Research outside the HIV field shows that people with lived experience of mild cognitive impairment and

professional organisations advocate disclosures of risk and cognitive impairment.<sup>40</sup> However, organisations and research addressing this topic emphasise that disclosure is a complex process<sup>40</sup> that demands a preparatory phase and long-term follow-up support in a well provisioned care system (figure 2).<sup>41</sup> Existing research in neuro-HIV<sup>42</sup> (see also appendix p 1) found that participants who underwent a complete neuropsychological examination and then received feedback from a health-care provider along with a diagnosis of asymptomatic neurocognitive impairment or mild neurocognitive disorder<sup>39</sup> were relieved of their anxiety and concerns about having dementia. Urgent research is needed to facilitate appropriate disclosure with people living with HIV, requiring a baseline of minimum standards and best practices that align with an early diagnostic framework.



## Models of care and implementation

A publication by Davis and colleagues,<sup>10</sup> focusing on North America and the UK, described three models of geriatric consultation: outpatient referral or consultation; multidisciplinary clinics offering HIV and geriatric care; and dually trained providers within one clinical setting. The authors found that “a patient-centered approach and the use of expertise across disciplines were universally identified as strengths”, whereas “logistical barriers and the reluctance of older people living with HIV to see a geriatric care provider were identified as barriers” to these approaches.<sup>10</sup> Therefore, the training of HIV specialists in the principles of geriatric medicine<sup>15,43,44</sup> and in early diagnosis or treatment, prevention frameworks that characterise modern neurology, and clinical trials streamlining<sup>45</sup> might improve management and outcomes of HIV and ageing. Although some HIV geriatric clinics and proposed HIV and ageing models of care exist and are inclusive of a screen of brain health (eg, the Orange Clinic in the UK and the Modena HIV Metabolic Clinic in Italy), we observed that, in most instances, the incorporation of neuropsychological, neurological, and neuropsychiatric expertise is often missing or inadequate (ie, not well targeted or not appropriate for the specific population). Consequently, cognitive impairment is not properly captured, and education resources on cognitive health in HIV are needed. Models of care optimally incorporating neurology, neuropsychology, and neuropsychiatry already exist in the general population in the form of memory clinics<sup>46</sup> and, more generally, in HIV neurology and psychiatry care in many high-resource countries, and less so in some low-resource and middle-resource countries. These models can be adapted to the care of ageing people living with HIV in the context of a multidimensional ageing clinic. This approach is supported by existing efforts showing successful implementation of frailty and cognitive screening. A UK-based model corroborates the fact that screening is welcomed by patients and is feasible if there is a contiguous management pathway in place.<sup>47</sup> In reviewing the literature, we found that there are very few studies making use of validated implementation science frameworks<sup>48</sup> to facilitate the developmental, validation, and sustainability phases of novel models of care by identifying enablers and barriers, guiding roll-out, and assessing effectiveness, particularly for health and economic outcomes (eg, in the Golden Compass Program<sup>49</sup>). Such translational studies should therefore be prioritised, and the model of care should be assessed as they are implemented to respond to the health-care urgency of people ageing with HIV.

## Specific considerations for low-resource and middle-resource countries

HIV is a global epidemic, and sub-Saharan Africa has the highest number of people living with HIV followed by

	Benefit of disclosing	Drawback of disclosing
Respect for people's autonomy	✓	
Health professionals' ethics: truth and transparency with patients What about caregivers, family, and partners?	✓	
Disclosure allows individuals to be involved in planning their own care and to understand or objectify what is happening	✓	
Disclosure enables caregivers (eg, family and partners) to anticipate care needs, prepare for changes, and understand what is happening to their loved ones	✓	
Qualifying for clinical trials and more recent trials for the prevention of cognitive decline	✓	
Receiving tailored and specialist care and feedback for treatment, planning, and preparation (where possible)	✓	
Lack of effective pharmacological treatments or cure However, medication adherence can be lower in people with mild cognitive decline		✓
Uncertainty of early diagnosis and prognosis Particularly true in people living with HIV who receive antiretroviral therapy		✓
Medicalisation, additional specialist care, and hospital visits These factors all add to health-care burden, especially in chronic conditions such as HIV infection		✓
Immediate or initial impact on mental health Not understanding one's own experiences can lead to depression and anxiety, yet receiving another complex diagnosis might add to the overall mental burden		✓
Stigma People living with HIV are worried about additional stigma on top of HIV and ageing, especially without dedicated health-care provision		✓
Guidelines, associated research with the perspective of people living with HIV, dedicated health structures, and pathways are crucially needed		

**Figure 2: Summary of the issues relevant to the disclosure of cognitive status in the non-HIV population and how this disclosure is relevant to people living with HIV**

Research in the general population has found that disclosure is needed to respect patients' autonomy and to correctly inform patients and caregivers about the nature of a patient's condition (to gain insight into a patient's functioning and behaviour). Disclosure is also best when providing a treatment plan for accessing therapeutic and behavioural intervention trials and should be inclusive of social support. Furthermore, research in high-income countries shows that a supportive health-care system with highly trained and informed health-care providers is needed for disclosure to encompass long-term follow-up and to ensure beneficial rather than harmful outcomes. This research has been primarily conducted in high-income countries, and with caregivers rather than with patients with lived experience, and does not include cross-cultural evidence and health disparity considerations relevant for people with HIV.

southeast Asia. Low-resource and middle-resource countries are faced with similar issues to high-resource countries,<sup>50</sup> but at a larger scale and with considerably fewer resources. Although most neuro-HIV publications come from high-resource countries, there is now strong evidence that standard neuropsychological testing is feasible in research settings in countries with high HIV prevalence.<sup>51,52</sup> However, integrated and multidimensional models of care as proposed in this Position Paper and adapted to low-resource and middle-resource countries (on the basis of building resources within their health-care frameworks) remain to be fully developed. Suggestions of differentiated service delivery models for ageing care in resource-limited settings already exist.<sup>53</sup> The response will have to accommodate local health authorities and non-governmental organisations working

For more on the **Orange Clinic** see <https://brightonsexualhealth.com/advice/the-orange-clinic/>

For more on the **Modena HIV Metabolic Clinic** see <https://www.clinicametabolica.it/home/>

**Panel 2: Challenges to consider in the application of early detection and diagnosis of cognitive impairment in low-income and middle-income countries**

**Culture and language**

Culturally appropriate and fair screening tools for cognition and function are needed,<sup>1</sup> including locally validated tools<sup>2</sup> and normative standards and the capacity to support research to address these gaps.

**Health-care resources**

Tools that can be used by non-specialists (due to low patient-to-doctor ratios) and access to clinics are needed.

**Health literacy**

Differing levels of health literacy—some settings do not have clear concepts or general knowledge about dementia and brain health. Concepts of cognitive functioning, dementia, and brain health might be unfamiliar, although strong variations exist.

**Health-care access**

Less access to health care in low-income and middle-income countries.

**Discrimination**

Greater or more complex exposure to bias, racism, or stigma in low-income and middle-income countries.

**Morbidity**

Greater exposure to multiple sources of morbidity and less access to treatment in low-income and middle-income countries.

**HIV disease**

Late HIV diagnosis or presentation and a higher prevalence of opportunistic and non-opportunistic CNS infections in low-income and middle-income countries.

**HIV treatment**

Delayed treatment with antiretroviral therapy (ART) at the onset of the HIV epidemic in low-income and middle-income countries; use of more toxic ART for a longer period; delayed access to the less toxic ART; and less access to a range of ART treatments due to their high cost.

**Demographics**

There are more women in low-income and middle-income countries. Women living with HIV in low-income and middle-income countries might have lived experience that includes greater health disparities, discrimination, and other issues such as gender-based violence and food insecurity. Histories of trauma are generally more common in low-income and middle-income countries.

**Socioeconomic disparities**

Poverty greatly affects health, including poor nutrition and exposure to environmental pollutants due to poor accommodation standards or occupational hazards; access to health care is restricted to emergency situations, if it exists at all.

**Government resources**

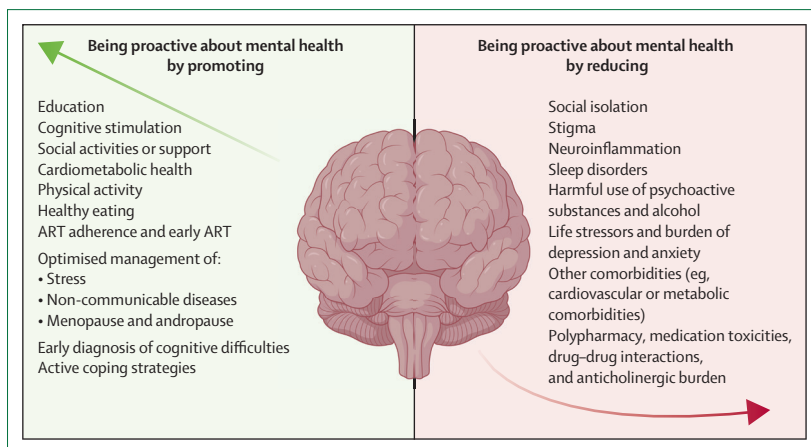
Fewer personal and government resources in low-income and middle-income countries.

**Technology**

Scarce or differential access to websites and electronic applications in low-income or middle-income countries.

**Ageing**

Biological drivers of ageing might differ in people living with HIV in low-income and middle-income countries.



**Figure 3: Summary of cognitive decline prevention strategies**  
ART=antiretroviral therapy.

with people living with HIV, complemented by integration with local capacities and resources. We

recommend the WHO guidelines on integrated care for older people (ICOPE)<sup>54,55</sup> for starting a response for people with lower education. ICOPE aligns with the WHO model for healthy ageing<sup>8</sup> and is a person-centred approach that concentrates on a person’s intrinsic capacity. ICOPE aims to optimise a person’s functional ability across the domains of sensation, mood, mobility, vitality, and cognition.<sup>56</sup> This framework is advantageous because it allows for the use of existing and validated tools by non-specialists and by community health-care providers. In people with higher education, adding a cognitive screening tool that can detect at least mild cognitive deficits is advisable as research has cumulatively shown low sensitivity for tools such as the HIV Dementia Scale (HDS) or the International HDS in low-resource and middle-resource countries. As for high-resource countries, research on screening test validation in the population of interest is required (ie, adaption, translation, and development of local normative standards). This research is currently conducted in

several low-resource and middle-resource countries, showing that health-care providers and researchers in this region see a need for their patients. In these studies, assessment of how cognitive screening fits within multidimensional care response and management is essential. As such, the assessment of mental health and functional status should always be considered in the development of a management plan and covering ART adherence.<sup>57</sup> In low-resource and middle-resource countries in which the ratio of mental health workers per 100 000 population is between 1·3 and 3·8, and far below the 62·2 in high-resource settings,<sup>58</sup> the incorporation of mental health screening as a minimum standard for cognitive health will require strategies to overcome these difficulties, such as the involvement of the local HIV

workforce who are experienced in dealing with the local patient population. Panel 2 summarises challenges relevant to low-resource and middle-resource countries in terms of the implementation of a prevention and early diagnosis management framework.

### Non-pharmacological and pharmacological interventions

Promising results from lifestyle intervention trials continue to emerge<sup>59,60</sup> and the first significant therapeutic results in Alzheimer's disease have been reported.<sup>26</sup> Research in HIV also shows the benefits of selected non-pharmaceutical interventions on cognitive and mental health,<sup>61,62</sup> including in low-resource and middle-resource countries.<sup>63</sup> Physical and mental exercise can buffer

#### Panel 3: Call to action

##### Health care

- Develop a comprehensive health-care response with provision for low-income and middle-income countries that fits within a geriatric framework and encapsulates the unique needs, strengths, and intersectionality of people living and ageing with HIV
- Promote the establishment of HIV and healthy ageing clinics at which HIV and age care can be provided in a single place and stigma-free environment
- Adapt existing resources for the general population to meet the needs of people living and ageing with HIV
- Raise awareness about cognitive health issues among people ageing with HIV and their care providers to optimise the preparedness of appropriate health-care systems and remove fatalistic and denying perspectives that can further isolate or alienate people living and ageing with HIV
- Promote early diagnosis and intervention for patients who are at risk, focusing on modifiable risk factors such as cardiovascular health
- Empower people with lived experience to reduce stigma associated with cognitive changes in older age

##### Research

- Resolve issues with the HIV-associated neurocognitive disorder diagnostic criteria: carefully and constructively update the current diagnostic criteria for HIV-associated neurocognitive disorders to better reflect current research in neuro-HIV and integrate dementia (or major neurocognitive disorder) and gerontology research to improve the validity of diagnosis and prognosis of the updated criteria (appendix p 1)
- Advocate an increase in neuro-HIV research funding for the creation of large, international consortia (similar to those existing in the general population), which will help to establish the risk of cognitive decline in large and representative international cohorts with dedicated funding for low-income and middle-income countries and emphasising the participation of people older than 70 years

- Translate research by combining observational and translational studies with well recognised implementation research frameworks to develop and deliver prevention strategies and optimise existing treatments in real-world settings
- Assess cutting-edge tools to establish their safety and clinical usability (eg, artificial intelligence-based tools for self-monitoring)
- Develop best practice for cognitive or brain health risk disclosure in people living with HIV
- Establish or join therapeutic clinical trials for dementia prevention to assess safety and efficacy of promising dementia drugs in people living with HIV

##### Knowledge hub

- Compile and update evidence on cognitive and brain health needs and modern clinical recommendations for people living with HIV
- Provide dedicated content for all stakeholders: clients, community members, health-care providers, and the general public
- Reduce stigma through the knowledge hub by disseminating evidence-based, updated information, similar to websites for major neurocognitive disorder in the general population.
- Include voices and perspectives of people with lived experience (following the motto of nothing about us without us) to address issues such as cognitive decline, disclosure, and research translation
- Address social isolation by sharing strategies to address social isolation, improve connections, and enhance health literacy regarding cognitive health through peer support
- Advocate for the inclusion of people living with HIV in dementia and cognitive decline reduction trials (both pharmacological and non-pharmacological)—from which people living with HIV are mostly excluded

against cognitive deterioration (figure 3). Furthermore, education on dementia and training for the general public have gradually been disseminated,<sup>64</sup> assisting in reducing stigma related to dementia and promoting the need for support for dementia caregivers.<sup>65</sup> Implementation frameworks for health-care structures for cognitive decline prevention have been released. One of the most accomplished models comes from the European task force for brain health services.<sup>22</sup> This model includes organisation, structure, and challenges for implementation; risk factor profiling; risk discussion and communication of risk (although directed towards clinicians, this is a positive first step); multidomain behavioural cognitive health intervention; cognitive enhancement; and societal diversity, equity, and inclusion challenges.

### A call to action

The NeuroHIV and Aging Advocacy group's call to action is summarised in panel 3. Besides a health-care and research response, we propose the creation of an international online knowledge hub (as various sources of support are being sought). The online format will assist in addressing the size and complexity of the information required and the need to reach global communities. The hub will link existing resources (appendix p 3). This hub will also synthesise evidence for the cognitive health needs of people living and ageing with HIV with modern clinical recommendations (information that is crucially missing<sup>66</sup>), which will be updated as the field progresses and reaches a consensus towards a revised set of HAND diagnostic criteria. Our group will aim to continue to engage with all members of the neuro-HIV community and to engage more geriatricians and clinicians and researchers in dementia (including in low-resource and middle-resource countries) to develop a consensus that benefits people ageing with HIV, health-care providers, and researchers as soon as possible. Within this context and aiming to resolve issues with the current criteria (appendix p 1), our group favours a constructive and careful update<sup>67</sup> of the 2007 HAND diagnostic criteria<sup>39</sup> to enable historical comparisons, thus avoiding an immeasurable loss of data and knowledge. Our group would also welcome better integration of the past 15 years' advances in the neuro-HIV and HIV fields. Research has substantially advanced the assessment and operationalisation of functional change, which will help to improve the distinction between clinically relevant cognitive changes and some mild cognitive deficits without evidence of functional impact.<sup>37,68–70</sup> There is now a much better understanding of the effect of age-related vulnerabilities (eg, frailty), chronic immune activation, and inflammation (appendix p 1). Persisting low-level viral activity despite viral suppression within and outside the brain is recognised to have important effects (appendix p 1). Advanced neuroimaging has improved our understanding of the

nature of brain injury (ie, HIV vs other causes), which could also be integrated as proposed by Nightingale and colleagues in 2023.<sup>71</sup> Nightingale and colleagues<sup>71</sup> also propose a clearer presentation of all relevant clinical investigations, which would improve the criteria, making them more accessible and therefore more implementable. However, removing the standardisation of the neuropsychological assessment that was achieved with the 2007 HAND criteria<sup>39</sup> is not advisable. This change would put the neuro-HIV field at odds with other diagnostic criteria for other neurological conditions that have quantitative benchmarks for neurocognitive impairment closely aligned with the current HAND neuropsychological criteria. Updated criteria could benefit from a clinical algorithmic approach that describes the role of various clinicians and allied health-care providers in the diagnostic process, the integration of the community, and issues related to diagnosis disclosure. Operationalisation of criteria should be improved in such a manner that they can be used successfully in both high-resource countries and low-resource and middle-resource countries—both the 2007<sup>39</sup> and the 2023<sup>71</sup> proposed changes fail in this regard. Finally, any update must remain in harmony with recent advances in the diagnoses of other neurological disorders (eg, early motor neuron disease, mild cognitive impairment, and vascular cognitive impairment<sup>72</sup>), which promote early diagnosis<sup>73</sup>, and the dementia prevention framework.<sup>17</sup> Ideally, guidelines for management of HAND would follow this updated effort.

### Contributors

All authors contributed to the 3-year NeuroHIV and Aging Advocacy Group's meetings and discussions and the development of the group. All authors also contributed to revisions of the manuscript. All authors reviewed the first submitted version and the revised submitted versions of the manuscript. LAC led the writing of this Position Paper from conception to finalisation. SBR, CH, JL, JR, RJE, and ABM further contributed to the conceptualisation of the manuscript. CH, JL, JR, JB, ABM, EW, HG, KD, SPW, JV, RKH, KG, RJE, and SBR provided substantial input across the versions of the manuscript. RR, PLW, and KH provided specific contextual input for low-resource or middle-resource countries. MT designed the figures. SPW, HG, JB, JC, and KG provided English language editing.

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BJB reports royalties from Oxford University Press and Cambridge University Press; honoraria for presentations sponsored by the Neurological Association of South Africa, Jansen, and Biogen; patents (monoclonal antibody for quinolinic acid as part of test kit for monitoring multiple sclerosis severity and progression [PCT/IB2013/055902; patent office Australia], 2010; method and prognostic kit for monitoring multiple sclerosis [WO/2015/008111], 2013; and automatic fall and seizure detector [application number 2016904045 IP Australia Batch Reference SPBI-0001069085 by My Medic Watch]); a position as Chairperson of the data monitoring and ethics committee for the Lighthouse 2 phase 3 study of the antiretroviral Triumeq in Amyotrophic Lateral Sclerosis (King's College London, UK, and Tysabri Advisory Board Australia); and a role as a past President of the International Society for Neurovirology (2019–23). JV reports honoraria for presentations and research grants in trials sponsored by Merck, Janssen Cilag, ViiV Healthcare, and Gilead Sciences. KG reports support from the Advancing Clinical Therapeutics Globally for HIV/AIDS and Other Infections (ACGT) Network (funded by the US National Institutes of Health) as Protocol Director for ACTG trial



A5402, Cipla, and Dr Reddy's Laboratories. All other authors declare no competing interests.

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