# The *Lancet HIV* Commission on ageing and HIV: a global perspective

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## Executive summary

Global access to antiretroviral therapy (ART) for people living with HIV is a miracle of the modern era. Continued access to ART has extended the lives of millions of people living with HIV. At the same time, a growing number of people newly diagnosed with HIV are aged 50 years or older, and their treatment is often delayed. Older people at risk for HIV or living with HIV face unique challenges, such as combined stigma from age and HIV status, yet are often assumed to be at low risk for HIV. Older people with HIV are likely to have multiple comorbid conditions (multimorbidity), which adds increasing complexity to their care, and the global health community is only beginning to understand how ART-suppressed HIV influences this process. Crucially, few health-care systems are equipped to meet the multifaceted needs of this growing population.

Building on momentum from a Lancet Series on Ageing with HIV and The Lancet Summit: HIV and Healthy Longevity, this Commission's aim was to provide an international agenda to support ageing well with HIV. Core commissioners identified key domains for development with the goal of generating actionable recommendations to improve people's quality and length of life and reduce treatment disparities. Identified domains included: (1) how did we get here and where are we going, (2) HIV prevention and screening among older people, (3) initiating HIV treatment with a view to healthy ageing, (4) managing HIV treatment with a view to healthy ageing, and (5) systems of care. To further develop each of these domains, commissioners recruited international clinical and scientific experts and community representatives to serve on designated writing groups. These groups met via a series of teleconferences and face-to-face meetings. Finally, we solicited feedback from international community groups to ensure that the perspectives of people with lived experience were included.

We arrived at the present age distribution of people living with HIV due to the following factors: (1) age at diagnosis, (2) temporal trends in treatment, and (3) increasing longevity among people receiving ART. As new HIV infections outpace deaths, the size of the population of people ageing with HIV will likely grow. As of 2025, an estimated 11·5 (11·2–11·7) million people with HIV are older than 50 years, representing 29% of the total population living with HIV. Assuming a continuation of current trends, the median age of adults with HIV is expected to increase to 50 years by 2040, with 20·2 million people with HIV being older than 50 years of age and accounting for 51% of all people living with HIV. Importantly, in 2040, 96% of people with HIV older than 50 years are forecast to reside in low-income and middle-income countries (LMICs).

Targeted and tailored HIV prevention and screening services for ageing individuals are pressing needs. In addition to universal barriers to accessing HIV prevention and diagnostic services, ageing individuals increasingly face barriers related to their advancing age, functional limitations, increased socioeconomic vulnerability, end of formal employment, onset of chronic diseases, polypharmacy, limited health literacy, and caregiving responsibilities. These factors influence HIV risk for older adults in complex and dynamic ways.

This Commission lays out fundamental considerations for optimising health and wellbeing among people ageing with HIV within three clinical phases. The first phase is focused on establishing a healthy trajectory at any age, beginning at ART initiation and ending once a well-tolerated regimen has been established (typically 6–12 months). The second and third phases overlap with a shifting degree of emphasis, with greater focus on the screening and treatment of comorbid diseases in the second phase, and a larger focus on maintaining function in the third phase. The balance between these concerns shifts when functional limitations or multimorbidity occur, or the person is unlikely to live more than 10 years. For people with a substantial burden of physiological injury, comorbid disease, or functional limitations at the time of HIV diagnosis, issues addressed in the second and third phase will require more immediate attention. Throughout this process, the health-care provider should monitor the person's physiological age, minimise polypharmacy and functional limitations, and support self-care, good mental health, and a healthy lifestyle that includes excellent ART adherence.

Health systems originally built around relatively vertical models or age-based geriatric thresholds need to evolve to meet the multifaceted needs of people ageing with HIV. Even integrated health networks often consist of multiple vertical services nominally connected through referral pathways, each with separate queues, forms, schedules,

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For the French translation of the executive summary see Online for appendix 1

For the Portuguese translation of the executive summary see Online for appendix 2

For the Spanish translation of the executive summary see Online for appendix 3

For the Swahili translation of the executive summary see Online for appendix 4

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### Key messages

- More people are ageing with HIV than ever before. Assuming the continuation of current trends, the number of people ageing with HIV is forecast to grow over the next 15 years to 20·2 million, accounting for 51% of all people living with HIV. Importantly, 96% of these people will reside in low-income and middle-income countries.
- With increasing prevalence, an increasing proportion of new diagnoses will occur among people older than 50 years, and they are more likely to be diagnosed late. HIV prevention and screening need to be better tailored to people older than 50 years.
- Once the person is on an effective ART regimen, health care should focus on maintaining viral suppression, facilitating healthy ageing, and supporting what matters most to the person.
- The excess burden of morbidity experienced by people ageing with HIV can be minimised through thoughtful screening and treatment for comorbid conditions, promotion of self-care, social integration, community engagement, and use of non-pharmacological treatments, when possible, to avoid adverse effects of polypharmacy.
- Chronological age is a poor proxy for physiological age. It is important to consider a person's likely remaining survival and their individual priorities when setting health-care goals. Guidelines for ageing-associated conditions should specify the expected survival time necessary to benefit. Once a person has less than 10 years of expected survival, guideline-directed care might be inappropriate.
- Vertical (disease-specific) health systems are insufficient for the complex needs of populations ageing with HIV. Diagonalisation can be achieved in two ways: either by broadening existing vertical HIV resources through the integration of services (dedicated care) or by strengthening referrals to and provision of HIV interventions in services shared for the general public (designated care).
- Health is not the sole purview of health care. People ageing with HIV, their caregivers, their communities, and the larger internet community have essential roles to play. Key barriers to be overcome include health care and internet access, health literacy, the digital divide, HIV and ageing stigma, and a health-care checklist mentality.
- The world is ageing with and without HIV, and training programmes for health-care providers have failed to adapt to the needs of an ageing population. Supporting healthy ageing with HIV from antiretroviral therapy initiation to end-of-life planning will require HIV providers to develop new foundational competencies in relevant core disciplines of geriatrics, family and internal medicine, palliative care, and psychiatry.
- The following research should be prioritised and tailored to what is feasible in a given setting (eg, available resources, clinical structures, and population requirements):
  - Detailed surveillance data on people older than 50 years
  - Approaches to tailoring HIV prevention strategies for people older than 50 years
  - Structural and behavioural approaches to establishing a healthy diet and exercise
  - Approaches to linking people with HIV specific and nonspecific community and digital resources that support healthy ageing
  - Approaches to medication reconciliation and deprescribing to minimise adverse drug effects
  - Effectiveness of basing screening and prevention interventions for comorbid disease on physiological (rather than chronological) age
  - Impact of shared decision-making on quality of life in the context of multi-morbidities
  - Implementation and evaluation of diagonalised care models at scale

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and, often, insufficient data-sharing agreements. Every referral can introduce additional travel, unreimbursed expenses, duplicated testing, and extended waiting periods. For older people living with HIV who might have decreased mobility, autonomy, or financial constraints, these obstacles can lead to disengagement from care.

Complexity-competent approaches could better integrate existing HIV programmes into broader chronic disease management or develop specialised HIV services that incorporate geriatric expertise and wellness programmes. Digital and data-driven innovations can help to extend care outside of clinical settings and empower people with self-monitoring tools, guide health-care workers with standardised protocols, and enhance community-based care. The key challenge lies in ensuring feasibility and sustainability. We explore practical strategies—ranging from reconfiguring referral pathways to implementing digital innovations—that can strengthen the continuum of care. By charting these realistic pathways, care can move beyond only survival outcomes towards comprehensive, long-term wellbeing for an ageing population.

We propose a paradigm shift in HIV treatment from a narrow focus on ART initiation and maintenance to one that encompasses healthy ageing across an extended lifespan. Treatment priorities should be informed by what matters most to the person and, as they age, this new paradigm implies an increasing focus on maintaining function and minimising the complexity of health-care systems. Health is not the sole purview of the health-care provider or their institutions. The person, their health-care providers, and local and digital communities have essential roles to play. Barriers to be overcome include health literacy, health-care silos, internet access, the digital divide, and both HIV and ageing stigma. Where possible, personalised care needs to replace a standardised health-care checklist mentality. Our report presents a rationale for this paradigm shift and describes the essential elements and changes that are needed to enact this shift. If the millions of people with HIV around the globe are to age well, the global health community must act to maintain access to ART and to build and strengthen the clinical and community-based structures required to support healthy ageing.

## Introduction

WHO defines healthy ageing as "the process of developing and maintaining the functional ability that enables wellbeing in older age", where functional ability relates to having the capabilities that enable people to do what they value.[1] More people are ageing with HIV than ever before and are experiencing substantial challenges to healthy ageing, including an excess burden of chronic diseases (multimorbidity), polypharmacy, and compounded stigma. As the age distribution of people living with HIV shifts upward, the challenge lies not only in extending survival but also in maintaining functional abilities, personal dignity, and social engagement—in short, ageing well. Building on a growing body of research on ageing with HIV, this *Lancet HIV* Commission has produced a scientific report recognising the universal importance of this topic and the urgent need to appraise the global situation. We offer actionable recommendations

for health policy, community programmes, clinical care, research, and for people living with HIV to support ageing well with HIV with a global perspective.

Work on the Commission began in January, 2024. ACJ and KNA co-chaired the Commission, building on momentum from *The Lancet* Series on ageing with HIV published by *The Lancet HIV* and *The Lancet Healthy Longevity*[2–5] and the *Lancet* Summit: HIV and Healthy Longevity.[6] ACJ and KNA initially invited an international panel of experts and, with this core group, developed the concept of the Commission and identified community representatives. Five writing groups were designated, each with two community representatives and additional invited experts to address the following topic domains: (1) how did we get here and where are we going; (2) HIV prevention and screening among older adults; (3) managing health care with a view to ageing well: establishing a therapeutic alliance; (4) managing health care with a view to ageing well: maintaining health despite increasing complexity; and (5) systems of care. The authors then circulated a draft to international HIV community groups to solicit feedback and ensure that the perspectives of people with lived experience were included.

Central themes and key messages in this Commission include the importance of what matters most to the individual; the problem of stigma; the overlapping and modifiable roles of HIV, inflamm-ageing, substance use, mental health, and socioeconomic disadvantage; the challenges posed by multimorbidity and polypharmacy; and appropriately considering age-associated declines in physiological reserve and physical and mental functioning. We also emphasise that health-care institutions need to move beyond their institutional setting to leverage community and digital resources if more people living with HIV are to age well.

## How did we get here and where are we going?

Understanding temporal trends in the natural and treated history of HIV is essential to understanding the complexity of ageing with HIV. The present age distribution of people with HIV has been influenced by age at HIV diagnosis, temporal changes in ART initiation guidelines and access, and increasing longevity among people receiving effective HIV treatment. As a result of these factors, the population of people ageing with HIV will continue to grow.

Most people with HIV who are older than 50 years acquired HIV in their young adulthood during the late 1990s and 2000s. At that time, CD4 thresholds for ART initiation were lower, resulting in a longer period of unsuppressed viral load. As a result, despite reaching viral suppression, many people from this population are now experiencing the consequences of residual immune dysfunction. Further, many older adults with HIV have been exposed to ART regimens that are linked to longer-term negative health outcomes (eg, protease inhibitors and metabolic syndromes).[7] In this Commission, we describe the various influences on the age distribution of people with HIV based on the timing of their HIV acquisition and receipt of treatment in young adulthood (the largest group), at birth, and at older adult ages. We

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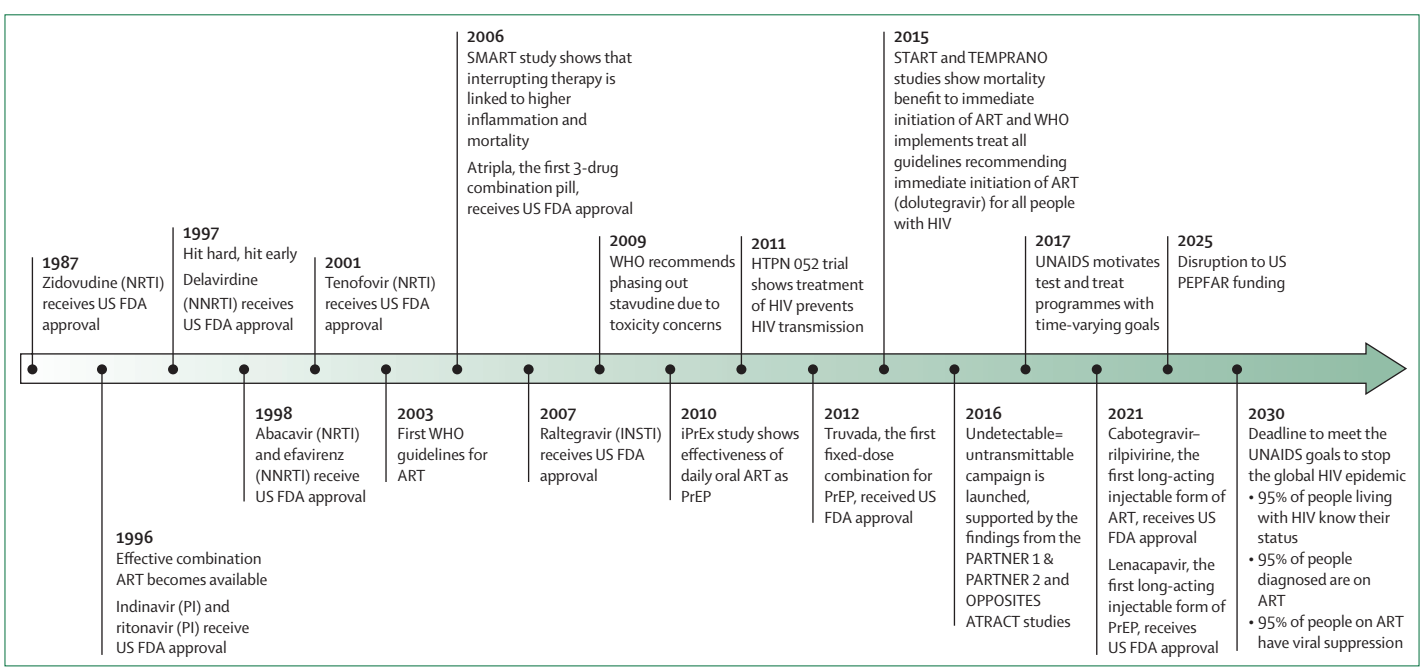


***Figure 1:*** **HIV treatment timeline**

ART=antiretroviral therapy. FDA=Food and Drug Administration. INSTI=integrase strand transfer inhibitor. NNRTI=non-nucleoside reverse transcriptase inhibitor. NRTI=nucleotide reverse transcriptase inhibitor. PEPFAR=The President's Emergency Plan for AIDS Relief. PI=protease inhibitor. PrEP=pre-exposure prophylaxis.

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forecast the global age distribution of people with HIV overall, and stratified by sex through 2040.

## Impact of ART timing and toxicity on healthy ageing

The duration of unsuppressed HIV viral load before treatment initiation is a function of the timing of the HIV diagnosis relative to infection and temporal changes in treatment (figure 1). After the initial approach advocated in the *New England Journal of Medicine*'s editorial *Time to hit HIV, early and hard* in the late 1990s,[8] guidelines restricted ART use to specific CD4 count thresholds in an effort to reduce toxicity and improve adherence.[9] Globally, between approximately 2001 and 2015, people with HIV had unsuppressed viral loads until their CD4 count dropped below a country-specified or WHO-specified threshold or they developed an AIDS-defining illness. During this 15-year period, antiretroviral drugs were developed with reduced toxicity. Studies of CD4 count guided-treatment interruptions determined that, compared with uninterrupted treatment, interrupted treatment was associated with more opportunistic infections or death.[10] In 2015, the Strategic Timing of Antiretroviral Treatment (START) study and TEMPRANO randomised trials found decreased AIDS-related events and death among participants who initiated ART without delay, ushering in the treat-all era in the mid-2010s.[11,12] Since 2015, global regions with effective test and treat programmes have been diagnosing and treating HIV closer to the timing of initial infection, resulting in a reduced duration of unsuppressed virus.

After initially reaching viral suppression on ART, HIV can become unsuppressed again due to gaps in care or, despite continued care, low-level viral replication, viral blips, or virological failure. In all these settings, unsuppressed HIV increases inflammation through immune activation and pro-coagulative effects. Even at low levels or for brief intervals, unsuppressed HIV increases inflammation and accelerates ageing according to epigenetic clocks, threatening healthy ageing. Although continued ART blunts these effects, it does not fully reverse systemic inflammation.[13]

Most older adults living with HIV (often defined as people older than 50 years) have experienced a long duration with unsuppressed HIV viraemia and have been previously exposed to antiretrovirals that are more toxic than current therapies. People who were diagnosed with HIV in the test-and-treat and treat all eras and were treated earlier or with less toxic ART have experienced shorter exposures to unsuppressed virus. For these people, the effect of unsuppressed HIV on ageing might be attenuated.

### *Panel 1:* Social prescribing: linking clinical care with community services

As people age with HIV, it is crucial that they routinely experience meaningful non-medical activities that engage their hearts, minds, and muscles. Community workers can also supplement and extend health care in important ways. HIV providers are often unaware of non-HIV-specific resources in their local community that could provide benefit, or perceive that referral to these programmes falls outside their responsibilities. Effective referral to these resources, however, could save sparse health-care resources. A social prescription is a referral from the clinical setting to a community-based programme or service made directly by the health-care provider or via a link worker who is well-versed in local resources. The UK has recently implemented a national programme that embeds link workers in primary care.[14] Early results suggest that the programme has reduced outpatient appointments, acute care visits, and hospitalisations, with a concomitant positive economic impact.[15] To maximise effectiveness, community activities should be in-person, where possible. Where this is not possible, due to geography or physical functioning, the digital community could play an important role. Whether in person or through the digital community, community actors need to become a more integral component of health care, rather than peripheral partners, with explicit roles supported by training, formal integration, and appropriate remuneration. Examples of important community-based services include:

- Social programmes (eg, general support groups, senior centres, hobby workshops, or other local community activities) can foster social connection and emotional support[16,17]
- Physical activities, such as exercise programmes or recreational outings for people older than 50 years that combine physical activity with social interaction could benefit physical and mental health
- Buddy systems and volunteer opportunities can match people ageing with HIV with volunteers (and often peers) who can offer companionship, assist them in managing their health-care and social activities, and could also suggest appropriate volunteering opportunities for the person with HIV, to create a sense of purpose and connection
- Participation in religious or cultural events can provide a sense of belonging and reduce isolation for people with religious or cultural backgrounds
- Resources are increasingly available from the internet, but people might need to be shown how to use digital tools (eg, video calls, social media, and online forums that support exercise, hobbies, and intellectual interests) to maintain social connections and enable continued physical and mental engagement, especially when in-person interactions are not possible[17]

For these general referrals to be effective, focused formal training in relevant content areas and in ways of reducing stigma towards chronic infections (eg, HIV) might be needed.

Accumulated ART toxicity is a function of the duration and the type of ART used (figure 1). Highly ART-experienced people have navigated the evolution of ART (figure 1), including changes in potency, drug classes, number of drugs per combination, available classes, tablets per day, and formulations. Some people might have switched from oral to injectable medications, and could have experienced resistance, toxicity, drug interactions, and drug intolerance.

Country-specific HIV treatment guidelines and WHO guidelines have changed over time. Although previous ART regimens have saved lives, regimens that were used before 2010 are now known to have greater toxicity than regimens used since, and the long-term toxicity of modern ART regimens is currently unknown.[18] Accumulated toxicity can result in longer-term sequelae, such as comorbidities, disability, and geriatric syndromes.[19] Unfortunately, the effects of accumulated ART toxicity are only partly reversible after switching to more modern ART regimens.[19]

The profile of healthy ageing among people with HIV who are initiating treatment currently with integrase inhibitors and potentially long-acting agents as first-line therapy will continue to unfold. In most parts of the world, the incidence of new HIV diagnoses continues to be highest in people younger than 50 years, but the median age of people living with HIV is over 40 years, and over 50 years in countries where ART has been accessible since the late 1990s and early 2000s.[3] Although the distribution of CD4 counts at ART initiation has shifted to be higher since the adoption of WHO's treat all campaign, 30% of people with HIV still initiate ART with a CD4 count of less than 200 cells per µL. The decline in the frequency of CD4 count measurements (primarily due to the transition in the US President's Emergency Plan for AIDS Relief [PEPFAR] testing priorities to viral load monitoring in 2018) have made it challenging to accurately estimate changes to these trends. By reducing the immune system assault before ART initiation, it is possible that the difference in physiological injury and multimorbidity in people with HIV versus people without HIV who are the same age might narrow. Additionally, integrase strand transfer inhibitors have superior efficacy in suppressing HIV, which could translate into less virological failure, further diminishing the difference in physiological injury in people with HIV versus people without HIV.[20] The longer-term sequelae of integrase inhibitors are still being investigated (panel 1).

## From perinatally acquired HIV to new diagnoses among older adults

HIV infection can occur at any point during the lifespan, from perinatal acquisition to older age. Since 2009, over 7 million children globally have been born with or acquired HIV before age 5 years (perinatally acquired HIV).[21] Although there have been striking reductions in the rates of perinatally acquired HIV—which has fallen from 40·6% (33·1%-51·0%) in 2000 to 10·8% (8·8%-13·6%) in 2023—gains have slowed and, as of 2023, approximately 120 000 children have perinatally acquired HIV.[21] At the other end of the age spectrum, as the proportion of people living with HIV increases among older adults, incident HIV infection has proportionately increased.

In a modelling study of simulated age-matched people with and without HIV, people with perinatally acquired HIV experience a greater burden of comorbidity and a shortened survival (decreased by 10 years for males and almost 12 years for females).[22] In high-income countries (HICs), people acquiring HIV perinatally are now entering their 30s and 40s. In low-income and middle-income countries (LMICs) where ART became widely available in the mid-2000s, children with perinatally acquired HIV are now entering adulthood.

Much can be learned from studying the lifespan of people with perinatally acquired HIV. People reaching adulthood (age 20 years or more) and early middle age (age 40 years or more) with perinatally acquired HIV have fewer traditional risk factors that influence ageing (eg, tobacco use, sedentary lifestyle, insufficient exercise, poor diet, and substance use), yet experience many of the same comorbidities.[23] Specifically, compared with age-matched people without HIV infection, children and young adults with perinatally acquired HIV experience higher rates of metabolic syndrome and cardiovascular disease, cancer, bone disease, fatty liver disease, and neurocognitive disorders.[23]

Although global guidelines recommend the immediate initiation of ART after HIV diagnosis in children, early HIV diagnosis and ART initiation remain global challenges.[24] In addition to immune dysfunction and chronic inflammation experienced by people who acquire HIV as adults,[25] people who have acquired HIV perinatally are exposed to all these factors during gestation and early development before their immune system is fully developed. Perinatal HIV infection is associated with impaired growth and musculoskeletal development, which limits bone mass accrual and can ultimately increase the risk of osteoporosis in adulthood.[26,27] People who have acquired HIV perinatally are also likely to have an increased risk of congenital cytomegalovirus infection and greater immune response impairment.[28] Alongside the effect of unsuppressed HIV viraemia on immune dysfunction, chronic inflammation, and development, children have historically had fewer ART options, and might therefore remain on older, more toxic drugs for longer than adults.

HIV and ART coupled with non-HIV-related traditional risk factors (eg, malnutrition and family context) contribute to differences in the spectrum of comorbidities experienced by people with perinatally acquired HIV compared with people who acquire HIV as adults. For example, people with perinatally acquired HIV have a higher prevalence of chronic lung diseases (including

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constrictive obliterative bronchiolitis and bronchiectasis), and also commonly have visual and hearing impairments, dental disease, and troublesome skin conditions, despite viral load suppression.[29] Moreover, compared with adults who acquire HIV, people who have perinatally acquired HIV experience poorer HIV treatment outcomes.[30] People with perinatally acquired HIV also have a greater likelihood of orphanhood, experience lifelong stigma, and might have fewer or smaller social communities.[31] A higher prevalence of mental health disorders (especially attention-deficit hyperactivity disorder) and poorer quality of life outcomes have also been documented.[32] Although a similar prevalence of mental health disorders in the siblings of people with perinatally acquired HIV—who have been exposed but not infected with HIV—suggests the importance of non-HIV traditional risk factors, poorer neurocognitive performance in people with perinatally acquired HIV compared with their siblings indicates factors outside of the family context.[33] Transitions in life such as disclosure of HIV status, transition to adult clinics, and navigating choices related to reproductive freedom and health could exacerbate feelings of anxiety and depression in these people as they age.[34–36] All these factors can contribute to poorer ageing trajectories.

Furthermore, women with perinatally acquired HIV experience increased postpartum mortality.[37] There is growing concern for maternal outcomes among these women, due to the increased prevalence of comorbidities (including hypertension, diabetes, and renal disease) in this population, which can complicate pregnancy and the postpartum period.[38] Hypertension, excess weight gain, hyperglycaemic disorders, and decreases in bone mineral density that occur during pregnancy and postpartum do not fully resolve,[39,40] and could have long-term implications for the mother's ageing. Emerging evidence from Africa on postpartum outcomes is similar to observations made in HICs.[41]

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On the other end of the age spectrum, the proportion of new HIV diagnoses occurring among older adults is increasing. Adults older than 50 years with new HIV infections are more likely to have delayed presentation for care,[3] which shortens survival.[3] This population experiences an increased risk for death with advanced HIV disease due to multiple factors, including the compounding effects of age and HIV on immunosenescence and comorbidity (panel 1).

## Age distributions among populations of people with HIV

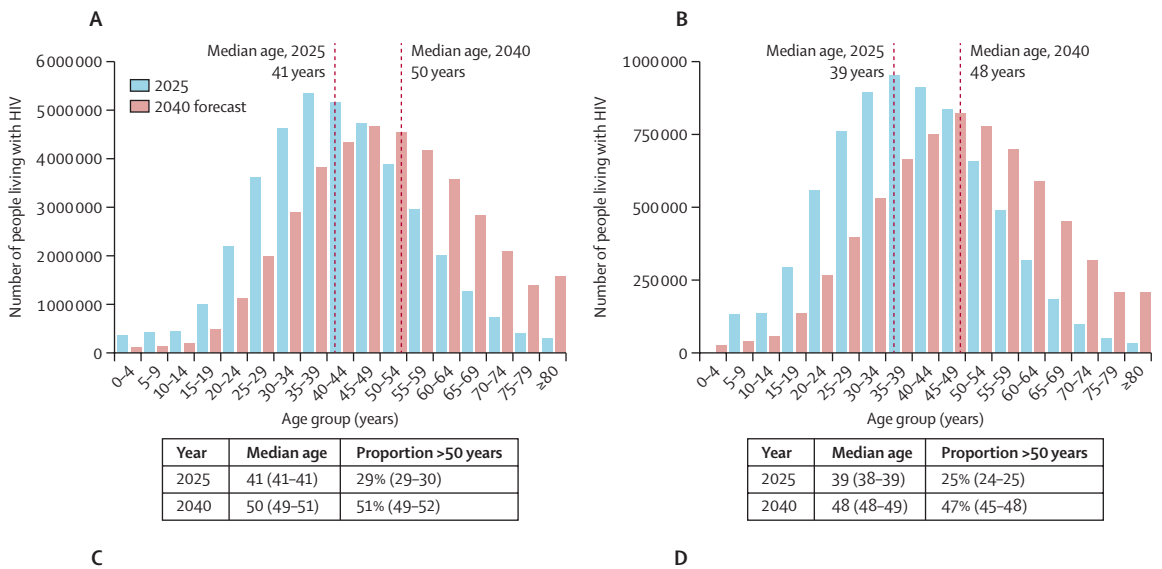
See **Online** for appendix 5

The transition of the age distribution of people with HIV can be investigated using computational models; the forecasted age distribution is valuable to care planning for people with HIV as they age. Mathematical models, although imperfect, provide an approach to synthesising dynamic interactions and generate forecasts of the shifting age distribution. These models help to quantify and analyse how transmission patterns, disease progression, and mortality influence future trends in the age distribution. Models can also evaluate the effects of various HIV prevention, testing, and treatment strategies, making mathematical models invaluable tools for forecasting future trends where data do not yet exist. Gaining insight into the changing age distribution of the population with HIV is essential to understanding the future scale of comorbidities and health-care needs of people with HIV, so that health-care resource provisions and clinical guidelines can ensure that high-quality care can be delivered.

The best use of mathematical models requires input data, assumptions, and expert knowledge of changes over time in HIV acquisition, treatment, and mortality patterns, by age group and sex and within geographical regions. Accurate data on the age-specific number of new HIV diagnoses, HIV care cascade (including treatment initiation and retention), and mortality are essential for forecasting the age distribution, which is influenced by transmission and treatment dynamics. In high-income countries, such data are often readily available from national or subnational HIV surveillance systems and longitudinal studies. However, in LMICs, obtaining robust data can be challenging and limited to case reporting, periodic population-based surveys, or non-systematic and non-electronic records. Assumptions are used to simplify the structure of the mathematical models to allow for the same model to be used in heterogeneous contexts, such as geographical regions. Decision-making on the data input, assumptions, and structure of the mathematical model needs to be based on both biology and expertise in the local epidemiology trends in HIV. Ultimately, a mathematical model can be used to recreate the age distribution of the population with HIV over time and compare it to historical age distributions to evaluate the model's calibration. Once calibrated, forecasting future changes in the age distribution is possible; although, as seen during the COVID-19 pandemic, the forecasted changes can differ widely among modelling teams.

Our goal was to estimate the 2040 global age distribution of the population with HIV, from which estimates of the proportion in age-specific categories (ie, older than 50 years or older than 70 years of age) would be possible. We adapted a peer-reviewed, dynamic, and compartmental model that forecast the effect of HIV interventions on the age distribution of people in Kenya; the full model has been previously published.[42] In brief, this compartmental model is characterised by transitions along the HIV care cascade (incidence, diagnosis, engagement in care, and viral suppression) and is stratified by age and sex (appendix 5 p 1). The model parameters are calibrated using Bayesian methods, combining previous distributions of key model parameters from available literature and survey data with calibration targets from routine HIV and demographic surveillance data (appendix 5 pp 2–11).

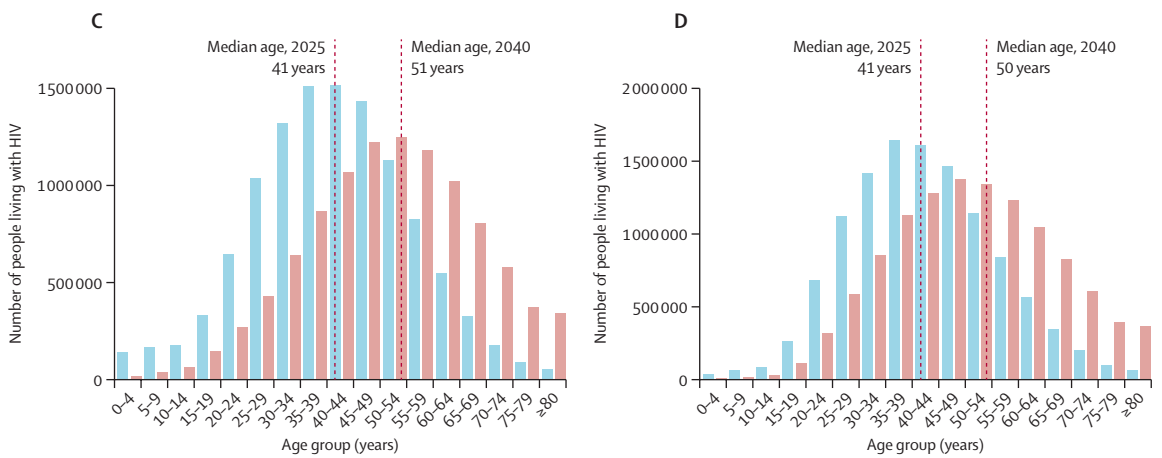
To capture local differences in HIV epidemics, global estimates were generated by calibrating nine individual




| Year | Median age | Proportion >50 years |
|---|---|---|
| 2025 | 41 (41–41) | 29% (29–30) |
| 2040 | 50 (49–51) | 51% (49–52) |



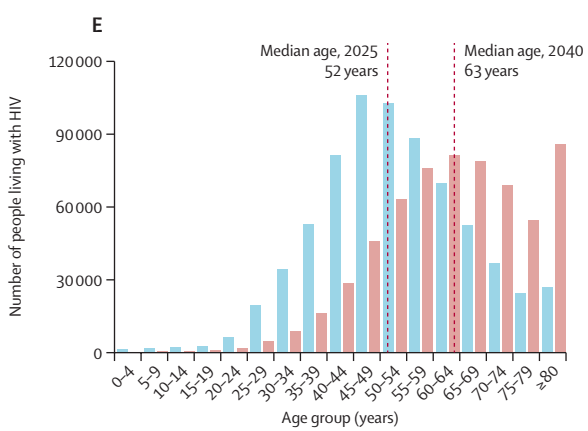

| Year | Median age | Proportion >50 years |
|---|---|---|
| 2025 | 39 (38–39) | 25% (24–25) |
| 2040 | 48 (48–49) | 47% (45–48) |




| Year | Median age | Proportion >50 years |
|---|---|---|
| 2025 | 41 (40–41) | 28% (27–28) |
| 2040 | 51 (50–52) | 54% (52–55) |




| Year | Median age | Proportion >50 years |
|---|---|---|
| 2025 | 41 (41–41) | 28% (27–29) |
| 2040 | 50 (49–50) | 50% (49–52) |




| Year | Median age | Proportion >50 years |
|---|---|---|
| 2025 | 52 (51–52) | 57% (55–58) |
| 2040 | 63 (63–64) | 82% (81–84) |

***Figure 2:*** **Forecasted global age distribution of people with HIV assuming the continuation of current trends in HIV care**
Distribution of people with HIV by age in 2025 (blue bars) and 2040, assuming the continuation of current trends in HIV care (pink, bars). Distribution is classified by country income status: (A) global, (B) low income, (C), lower-middle income, (D) upper-middle income, and (E) high income

country models (South Africa, Mozambique, Nigeria, Tanzania, Uganda, Kenya, Zambia, Zimbabwe, and Malawi), which represented about half of the global population living with HIV, and modelling the remaining countries as two aggregate models: one capturing all other countries included in UNAIDS disaggregated data reporting, and one capturing the remaining countries that are not included in the UNAIDS data. All models were calibrated to target data up to 2023, and the calibration process was run across multiple chains and thinned to a final set of 1000 simulations. The global model was constructed by aggregating outputs across all individually fitted country-level models, and outcomes were validated against UNAIDS global data on HIV incidence and prevalence (appendix 5 p 12). For our outcomes of the forecast number of people with HIV in 2040 and their age distribution, we report the median value and 95% credible interval (95% CrI) overall and stratified by UNAIDS country-level income, which uses the World Bank's income classification and country-specific HIV epidemic information to classify country-level income.

There are a forecast 39 million people living with HIV globally in 2025, with a median age of 41 (95% CrI 41–41) years (figure 2A and appendix 5 pp 13–15). An estimated 11·5 (11·2–11·7) million people with HIV are older than 50 years, representing 29% (29–30) of the total population living with HIV. Assuming the continuation of current trends in HIV care, the median age is expected to increase to 50 (49–51) years by 2040, with 20·2 (19·4–20·8) million people being older than 50 years, and accounting for 51% (49–52%) of all people living with HIV. Although the median age and proportion of people with HIV over 50 years of age increases with country-level income, 96% of people with HIV over 50 years of age are forecast to be residing in LMICs in 2040 (figure 4B–E; appendix 5 pp 16–17).

The accuracy of a model is only as reliable as the data that inform it, the appropriateness of its structure, and its assumptions regarding key dynamics. Regarding data, our use of UNAIDS data as calibration targets allowed us to standardise across countries. However, not all countries' data are included in the UNAIDS estimates. Although we individually modelled nine countries that represented approximately half of the global population living with HIV, several countries with large HIV epidemics (eg, India, China, USA, and Russia) were captured in the aggregate models, as their data are not reported by UNAIDS. Additionally, the UNAIDS estimates are generated from Spectrum/AIM, which is another modelling tool that has been validated across several settings and generates the most routinely reported and accepted estimates globally.[43,44] Structurally, the adaptation of a peer-reviewed compartmental model forecasting the age distribution in Kenya allows us to build on a more rigorous foundation. Our Bayesian calibration process is a particular strength, as handling unknown variables in HIV epidemiology allows us to approximate parameters' probability distributions and characterise uncertainty about future epidemic trajectories.

Finally, it is impossible to foresee every possible scenario or account for extraordinary events, including the abrupt withdrawal of US funding for HIV treatment in many countries with high HIV prevalence or global pandemics.[45] The forecasted age distribution we present is a starting point for understanding the magnitude of the ageing population of people with HIV, and a potential foundation to inform consideration of how to optimise care in specific geographical and country-level income contexts.

### HIV prevention and screening among older adults

Older adults often suffer substantial HIV and age-related stigma and misconceptions concerning their vulnerability to HIV acquisition. As a result, current HIV prevention interventions, screening services, and diagnostic strategies might not meet their needs.

Globally, the highest HIV incidence rates remain among people younger than 35 years, motivating the focus of HIV prevention efforts on younger adults. For example, in the USA (with a ratio of 3·6 males to 1 female among people with HIV across all ages), the estimated HIV incidence rate is highest in people aged 25–34 years (27·8 per 100 000 population), compared with 0·9 per 100 000 population among people older than 65 years.[46] In the generalised HIV epidemic in South Africa (with a ratio of 2 females to 1 male among people with HIV across all ages), the HIV incidence rate is 455 per 100 000 population for adults aged 15–49 years, and 270 per 100 000 population for adults older than 50 years.[47]

Monitoring HIV incidence in older adults is challenging when surveillance and reporting systems do not include granular age categories for people older than 50 or 65 years. Globally, most of the HIV prevention data from cohort studies comes from people younger than 50 years. A 2021 review of HIV incidence using cohort studies from southern and eastern Africa restricted data analysis to an upper age limit of 49 or 54 years, due to inadequate serosurveillance above these ages.[48] Similarly, analyses in a 2024 study on HIV prevalence and treatment among key populations in Africa (eg, sex workers, men who have sex with men, people who inject drugs, and transgender, gender diverse, and nonbinary people) focused on people aged 15–49 years.[49] Both in terms of HIV prevention efforts and data describing new HIV infections, people older than 50 years have largely been ignored.

Although HIV incidence might be higher in younger adults, HIV prevalence is increasing among older adults. In USA, the estimated prevalence of HIV infection (diagnosed and undiagnosed) is highest among people aged 55–64 years (728·1 per 100 000 population), which is 50% higher when compared with those aged 25–34 years

(487·1 per 100 000 population).[46] Similar trends have been observed in South Africa, with a 2022 study suggesting that HIV prevalence is increasing in people older than 30 years, with no noticeable change among younger women and a decline among younger men.[50] Over time, similar trends are expected in other world regions. Incidence commonly follows prevalence. We expect to see a proportionate increase in HIV incidence among older adults if prevention programmes are not targeted towards and accessible to this population. HIV prevention and screening programmes and policies have been slow to respond to this concern.[51] Although WHO guidelines do not specify an older age limit in their HIV testing recommendations, the US Centers for Disease Control and Prevention, European Centre for Disease Prevention and Control, and US Preventive Services Taskforce continue to recommend screening only up to age 64 years.[52,53]

Older adults are sexually active, and new HIV infections occur. Targeted and tailored HIV prevention and screening services for older adults are a pressing global need. In addition to many of the same barriers to accessing HIV prevention and diagnostic services faced by younger people based on gender, race, and ethnicity, older people face barriers related to their age, functional abilities, increased socioeconomic vulnerability, end of formal employment (often without financial stability in retirement or ongoing health insurance), the onset of multiple chronic diseases and polypharmacy, and caregiving responsibilities for loved ones. These factors collectively influence HIV acquisition risk for older adults in complex and dynamic ways.

## Sexual health in older adults

Although sexual activity has important physical functioning, mental, social, and cultural implications for people of all ages, there remain ageist stereotypes, stigma, and myths about sexuality among older people.[54] These notions include that, regardless of sexual orientation, older people do not have sex and, if they do, it is comical or disgusting. As a result, older people might hesitate to disclose sexual activity, which can be particularly true for older people who are not heterosexual, as they might fear additional stigma.

Although sexual frequency can decrease with age, many older adults report sexual activity well into their later years. Sexual activity in later life is influenced by the person's health and that of their partner, and partner availability.[55,56] In a 2007 study of US adults, 73% of people aged 57–64 years reported being sexually active in the past year, declining to 26% of those aged 75–85 years.[55] Older men were more likely to be sexually active and consider sex more important than women, a gap which increased with age.[55] These findings parallel studies of sex and older adults with and without HIV globally.[57] In South Africa, a 2018 study found that women aged 40–59 years reported a lower prevalence of sexual activity (73%) compared with men (88%).[58] Over 18% of women older than 60 years reported having had sex in the past two years compared with 73% of men older than 60 years, and there was little variation in the sex–age pattern of sexual activity in the past two years by HIV status.[58] Although the frequency of sexual activity can vary, sexual activity among many older adults is common and should not be overlooked by HIV prevention and screening services or health-care providers. There is a shortfall of information on sexual health in older adults who are LGBTQIA+.

Sexual function is intrinsically linked to overall health and HIV health literacy. Older people with low psychological wellbeing, depression, and alcohol or substance misuse disorders are more likely to report problems that interfere with sexual activity.[54] Among older women, disinterest in sex, anxiety about sexual performance, and other health problems are responsible for diminished sexual activity, with older lesbian and bisexual women more likely to cite health interference. A notable gap in the literature is the understanding of sexual dysfunction in women overall and especially in older women, both with and without HIV.[59] The hormonal and social conditions of older women living with HIV might increase their risk of experiencing sexual dysfunction.[60] Further research is needed due to the substantial implications of sexual dysfunction on quality of life for affected women.[61] With regard to older men, disinterest in sex, performance anxiety, and lack of sexual pleasure were prominently mentioned, regardless of sexual orientation. Older adults with HIV might not be aware that an undetectable viral load means that they will not transmit the virus to a sexual partner. Many older adults with HIV might also avoid sex to avoid transmission or due to concerns regarding disclosure of their serostatus.

Sexual inactivity could predict later health problems; older adults who are sexually active are more likely to report better self-rated health and functional ability over time.[62] For example, among older men, erectile dysfunction is the most common problem, occurring in more than 40% of men over the life course.[63] Erectile dysfunction could be a signifier of undiagnosed cardiovascular disease, and is more common in people with diabetes, hypercholesterolemia, hypertension, obesity, and those who smoke.[63] Further, sexual function is affected by changes in hormone levels and other organ systems that occur with ageing. Post-menopausal women often report disinterest in sex, problems with lubrication, inability to orgasm, or pain during intercourse.[55] Among older women, sexual functioning can be impaired by health conditions (eg, diabetes) or treatments for breast or gynaecological cancers.[64] Older women report difficulties when trying to address these issues with their health-care providers. Treatments for erectile dysfunction and menopause hormone therapy could increase older adults' potential for sexual activity and their quality of life.

The quality of relationship between patient and health-care provider is the foundation upon which a conversation

about sexual health and treatments occurs; an absence of education and training for health-care providers in these conversations can be consequential.[65] A potential result of strained patient and health-care provider conversations is older adults who are uninformed about sexual health and sexually transmitted infections.[66] Through these conversations with their patients, health-care providers play a key role in determining an older persons' vulnerability to HIV.[66] Unfortunately, fewer than 50% of people older than 50 years reported a conversation with a health-care provider about sexual health, and older women were less likely to have these conversations than older men.[55,56] Older men who self-identified as gay and bisexual are 26% more likely to talk about sexual health with a health-care provider than men who are heterosexual, who are 38% more likely to discuss sexual health with their health-care provider. A similar pattern was observed among women who are lesbian and bisexual women (8%) compared with women who are heterosexual (19%).[56]

Barriers to patient and health-care provider discussions about sexual health include older people being embarrassed to talk about sex due to stigma around sexual activity in late adulthood. These barriers could inhibit sharing relevant sexual health information with health-care providers, such as having multiple sexual partners or using dating apps to connect with sexual partners. Furthermore, health-care providers might be reluctant to address a topic that they fear could offend patients.[56] Lubricants, erectile dysfunction medications, and other interventions and medications for sexual health problems common in older adults are underused, possibly due to an absence of conversation about these problems between patient and provider.[67] Health-care providers need adequate training to take and update their older patient's sexual history, normalising these discussions and the promotion of sexual health and wellbeing as part of medical care for older patients.[68]

### Older adults' vulnerability to HIV acquisition

Several factors can increase vulnerability to HIV acquisition when exposed. In women, ovarian function is progressively lost during perimenopause, with a substantial reduction in oestrogen production.[69] This stage leads to thinning of the epithelium and reduced elasticity of the vaginal wall, which increases both the occurrence of microtears and abrasions during vaginal sex and the risk of HIV and other pathogens. Furthermore, reduced vaginal epithelial cells produce less glycogen, the substrate of lactobacilli. Lactobacilli maintain a low pH (acidic) environment, which is characteristic of a healthy microbiome. Decreased lactobacilli levels can lead to an altered microbiome and higher pH that contribute to bacterial vaginosis, which is linked to higher risk of HIV and reproductive tract infections.[70]

As adults age, there are numerous life course changes that can increase HIV exposure risk or decrease a health-care providers' inclination to test for HIV. These changes include shifts in marital relationships (eg, separation, divorce, and widowhood) and new partners (including potential casual-partnered sexual activity). In heterosexual partners, pregnancy prevention is no longer needed among postmenopausal women, resulting in condom use decisions that are based on perceptions of a new partner's HIV status or other sexually transmitted infections.[71] In concentrated epidemics, older women are not part of key population groups and lose the opportunity to be tested by their health-care provider after passing reproductive age. Older adults also move out of the workforce, might have varying levels of access to pensions or other financial means, and change familial responsibilities. These changes can affect their time and available discretionary funds, which can influence health behaviours. Living situations might also change (eg, moving into or out of housing with extended family or moving into congregate housing), and as a result, access to new sexual partners might differ.[72] Outbreaks of sexually transmitted infections have been noted in older adults residing in retirement communities.[73]

Substance use is underaddressed in older adults. A 2018 study from the Netherlands showed that around 30% of men older than 45 years who had sex with men were engaged in sexualised drug use.[74] Substance use, including alcohol and drug use, might be adopted as a coping mechanism in response to ageing,[75] and further compounds the issue by impairing judgement and increasing the likelihood of engaging in acquisition behaviours, such as unprotected sex.[76] These factors highlight the need for targeted substance use and HIV prevention strategies that are tailored to older populations.

Mental health challenges and social factors play key roles in the vulnerability of older adults to HIV acquisition and delayed treatment. Conditions such as depression and anxiety can diminish motivation to seek HIV testing or engage in prevention strategies, as people can feel overwhelmed or disconnected from the ability to have their health needs met.[51,77] Social isolation[78] (common among older adults and particularly among older adults who are LGBTQIA+) exacerbates this issue by limiting access to accurate information and support networks, making it harder to learn about HIV risks or access prevention services.[79] Additionally, stigma around sexual activity in later life or the fear of being judged for having a positive HIV diagnosis can deter older adults from seeking testing or discussing prevention with health-care providers.[68,77] These combined factors create barriers to timely diagnosis and effective prevention, underscoring the need for mental health support and stigma reduction efforts in HIV prevention strategies for older adults.

Cognitive challenges in older adults can substantially influence HIV risk, diagnosis, and treatment. Cognitive functioning is influenced by level of education and degree of neuronal injury. Reduced health education and literacy

can complicate the ability of many older people to comprehend complex information about HIV prevention, diagnosis, and treatment, ultimately increasing their vulnerability to poor health outcomes. Age-related cognitive decline (eg, benign memory loss, mild cognitive impairment, or early stages of dementia) can impair a person's ability to understand HIV acquisition risk or consistently remember to take preventive measures.[80] Anecdotal experience also suggests that there is a potential increase in risk of sexual abuse among older adults with cognitive decline, due to their inability to consent to or refuse sexual activity.[81] Navigating health-care systems and understanding the importance of routine HIV testing can also be challenging for older adults with poor cognitive functioning, leading to missed opportunities for early diagnosis and care.[68] HIV services and health-care providers need to be aware of the effect of cognitive functioning on engagement with HIV prevention, testing, and diagnosis.

### HIV prevention tailored to older adults

Tailored preventive efforts for older adults begin with improved surveillance, and some efforts are underway. For example, a 2021 study collected data on HIV status in populations up to age 89 years in South Africa.[82] Older adults were also identified as a key population in a 2021 study of HIV and AIDS prevalence in older populations between 2008 and 2019 in China.[83] HIV incidence rates in adults aged 60–89 years have been estimated since 1990 by the Global Burden of Disease Study, which reported rising trends in eastern Europe, central Asia, and high-income Asia–Pacific.[84] More HIV prevention and acquisition data collection from older adults is needed. Sero-surveillance programmes, government agencies, and WHO have not consistently provided age-specific data. Setel and colleagues developed the concept of the scandal of invisibility in data collection.[85] In addition to improved surveillance data, health education and pharmacological prevention efforts need to be better tailored to older people.

Prevention education tailored to older adults needs to address the unique challenges they face in understanding and managing HIV acquisition risks. Five key aspects of tailored education should include: (1) dispelling the misconception that older adults are not at risk for HIV;[86,87] (2) integrating safe sex practices (including consistent condom use and lubrication) when promoting sexual health in later life and the necessity of routine sexual health check-ups;[88] (3) discussing pre-exposure prophylaxis (PrEP) options; (4) encouraging regular HIV testing and providing options for testing that ensure privacy and confidentiality;[89] and (5) communicating that undetectable equals untransmittable, and discussing the implications of this fact for HIV status disclosure and stigma.

Prevention information should use clear lay language and culturally and contextually sensitive materials that resonate with older adults.[90] Community-based outreach could be a key strategy, using settings such as community centres, religious groups, and social gatherings (including those within retirement communities) to distribute information and hold HIV prevention workshops tailored for older adults (see connect with community and internet). Considerations should also be given to the education of vulnerable older adults on harm reduction measures concerning drug and alcohol use and needle sharing.[91]

Support and counselling are essential components of HIV prevention for older adults, providing the emotional and social support needed to navigate health challenges. Age-appropriate peer-led support groups can offer a safe and stigma-free environment where adults share experiences and receive education on HIV prevention, as shown in a 2025 scoping review on peer-led adjunctive interventions in Latino men who have sex with men.[92] These groups empower people by creating a sense of community and reducing feelings of isolation, which can often hinder access to care. Additionally, stigma reduction programmes that target health-care providers and the broader community can dismantle misconceptions and judgements about older adults' sexual activity and HIV status. By promoting empathy and understanding, stigma reduction efforts ensure that older adults feel comfortable discussing their sexual health openly with health-care professionals and seeking HIV prevention services.[93] This holistic approach to support and counselling is key to improving HIV prevention and care outcomes for older adults.

The integration of HIV prevention into routine health-care for older adults is crucial to improving diagnosis, care, and overall health outcomes. The offer of routine HIV testing should be incorporated into regular health assessments, particularly for older adults receiving care for chronic conditions that include mental health.[94] By normalising HIV testing, stigma can be reduced and early diagnosis becomes more attainable.[95] Comprehensive sexual health services should also be integrated into primary care, offering education, counselling, and access to preventive measures (eg, condoms, PrEP, and post-exposure prophylaxis [PEP]).[96,97] This approach, especially within geriatric and primary care clinics, ensures that older adults have easier access to these essential services.

### PrEP, PEP, and undetectable=untransmittable

ART is now a key component of HIV prevention strategies, including PrEP, PEP, and ensuring sustained viral suppression in couples with different HIV serostatus (undetectable equals untransmittable). The use of PrEP and PEP as an effective means for HIV prevention is important across the age spectrum, including in older adults who might be at risk of HIV acquisition.[98] As older adults were either not included or minimally recruited in key ART HIV-prevention trials,[99] there are important

considerations when implementing these prevention approaches in older populations.

Whether ART medications are used to treat or prevent HIV acquisition, due to age-related loss of organ reserve, comorbidities, and medications, older adults are more vulnerable to toxicity and need careful consideration of PrEP regimen and more intensive clinical monitoring when taking PrEP. As with ART (see where possible, individualise ART regimen), nuanced prescribing is important when implementing PrEP in older populations. Event-driven PrEP with tenofovir disoproxil fumarate–emtricitabine can also be considered to minimise exposure and potential toxicities. Finally, hepatitis B infection status should be known before tenofovir initiation to avoid reactivation upon discontinuation of PrEP.

Long-acting PrEP could have particular benefits for older adults, including lower pill burden in those with polypharmacy, improving adherence in people with cognitive decline, and avoiding oral pills in people with dysphagia. However, drug–drug interactions, potential toxicities, injection site reactions, and the risk of resistance in older adults require further studies. Cabotegravir was the first long-acting agent to be rolled out as PrEP, and lenacapavir (another long-acting agent) has also recently been shown to be effective for PrEP,[100] yet neither drug has been well studied in older adults.[100,101] Lenacapavir is metabolised via the CYP3A4 pathway, which could limit its use with tuberculosis treatment.[102] Specific to older women, the dapivirine ring is a localised form of PrEP that does not induce systemic toxicities. The dapivirine ring is a highly acceptable method of HIV prevention that is perceived to be more suitable than condoms among postmenopausal women, with worries about ring insertion and discomfort decreasing after use.[103]

There are some real-world data of PrEP use that include older adults. The uptake of PrEP among older people is generally low, and is affected by sociodemographic factors and stigma (both HIV-related and age-related).[104,105] There is no evidence of lower effectiveness of PrEP among older people, and adherence to PrEP and retention to PrEP programmes are reported to be higher in older adults.[104,106]

Older adults are unlikely to ask for or be offered PrEP or PEP due to fear of stigma or the possibility that their health-care provider might be unlikely to offer it due to ageism. However, older adults who are at risk of HIV acquisition should be encouraged to consider PrEP, with further strategies to improve PrEP uptake among older adults needed. The choice of PrEP agents and consideration of event-driven PrEP (with less toxicity) should be discussed according to each person's underlying comorbidities, health needs, and cost concerns.

PEP for HIV prevention is an underused strategy that could offer substantial advantages for some older adults. For people with infrequent sexual activity or for whom event-driven PrEP is not effective, PEP could be an attractive alternative. There are notable barriers to PEP use, which include unawareness of the effectiveness of PEP from both health-care providers and patients. There are also structural factors that limit the use of PEP generally, such as the narrow window of time post-HIV exposure where initiation needs to occur, the inaccessibility to centres that provide ART, and incomplete adherence to the current recommended 28-day course. A modelling analysis suggested that community availability of PEP with tenofovir, lamivudine, and dolutegravir would be cost-effective in eastern, central, southern and western Africa, although results were not age-specific.[107,108]

The disruption in US foreign aid presents a key challenge to HIV prevention, regardless of age. Although a waiver was made available for lifesaving products and activities, HIV prevention was not included in this category. Regardless of whether HIV prevention services are reinstated through foreign assistance, uninterrupted and sustainable support for HIV prevention is essential for acceptance, uptake, and consistent use.

Older adults are often excluded from clinical trials of new technologies and pharmacological HIV prevention strategies. Chronic disease burden, polypharmacy, and other age-related complexities are cited as reasons for exclusion. The exclusion of older adults from clinical trials has reduced health-care providers' ability to appropriately use these medications in this population. We need to better understand potential contraindications in medically complex older adults, how to identify those most appropriate to receive these medications, and how to maximise acceptance. Real-world data from observational studies can partly fill this gap by evaluating acceptability, enablers, and barriers for accessing PrEP and PEP in older adults. However, older people also need to be included in randomised trials to produce evidence-based HIV prevention strategies that are acceptable and effective in older adults who are at risk of HIV acquisition.

### HIV testing

Globally, older people are more likely to be diagnosed, enter into HIV care, and initiate ART at a later stage of disease compared with people in younger age groups. A review of 40 peer-reviewed studies of late presentation for HIV care from Africa, Asia, Australia, Europe, the Middle East, North America, and South America included data from 1984 to 2018.[3] 32 of the 40 included studies defined late presentation as having a CD4 count of fewer than 350 cells per µL or an AIDS diagnosis at or near the time of presentation for care. Older age was most often defined as being older than 50 years. In 39 of the 40 studies, older age was associated with delayed diagnosis and treatment (odds ratio 1·1–7·4). These authors also conducted an additional analysis with the International Epidemiology Databases to Evaluate AIDS consortium, encompassing data from 2000 to 2019.[3] In 2019, a greater number of people age 50–64 years versus people younger than 50 years presented with CD4 counts below 350 cells

per µL (in North America 42% *vs* 38%; in Central and South America 61% *vs* 49%; in central Africa 57% *vs* 52%; in East Africa 67% *vs* 54%; and in Asia–Pacific 81% *vs* 69%). Delays in HIV diagnosis, entry into HIV care, and ART initiation increase the risk of severe illness and mortality, and increase HIV transmission in the population due to unsuppressed viral load. The perception of low HIV vulnerability both in older adults and from their health-care providers is likely a driver of delayed HIV diagnosis and subsequent ART initiation.

In many settings, particularly in LMICs or generalised HIV epidemic contexts, HIV testing recommendations and community or home-based testing programmes are focused on risk profiles (risk-based testing), or identified key populations (eg, pregnant women, female sex workers and their clients, people who inject drugs, and men who have sex with men). Many recommendations for testing do not include people older than 50 or 65 years. In universal HIV testing programmes in LMICs, HIV testing is conducted in collaboration with reproductive health services (eg, contraception services and antenatal care), reducing access to adults who are over reproductive age. Periodic national population-based surveys, which often focus on populations aged 15–49 years (although sometimes up to age 54 years for men), are a common approach to serosurveillance in generalised HIV epidemics. Although there are differential barriers to testing among older adults, PEPFAR data from 2022 showed almost 10% (approximately 5% men and approximately 5% women) of new positive tests were from older adults, showing the need for the inclusion of older adults in HIV testing programmes.[109]

Health-care provider-initiated HIV testing and counselling is a common approach to HIV testing in

***Panel 2:* Provider fundamentals for supporting healthy ageing with HIV**

**Phase 1: establish a therapeutic alliance (initial 6–12 months of care)**
Two primary goals are to: (1) promote a lifestyle supportive of ageing well; and (2) initiate a regimen that is well tolerated with minimal side-effects.

*Promote self-care*
- Address stigma, social isolation, and mental health (table 1)
- Screen for and address substance misuse (table 1)
- Address other challenges to self-care
- Encourage physical activity (aerobic and resistance) based on WHO guidelines
- Discuss diet and the risk of ART-related excess weight gain
- Connect with community resources, support networks, or internet resources

*ART initiation*
- When possible, individualise ART regimen
- Consider long-acting agents
- Deliver routine vaccinations and test for and treat common co-infections
- Monitor for gaps in care, side-effects, viral breakthrough, and resistance

**Phase 2: maintain health despite increasing complexity (expected survival of more than 10 years)**
This phase is likely the longest stage of care. During this time, monitor the person's health, preventing, detecting and intervening on modifiable alterations in health in a timely manner, based on established screening and treatment guidelines. Where possible, guidelines should be followed that explicitly consider the increased risk that is associated with HIV infection. It is important to monitor the person's vision, hearing, and physical activity in phase 2, as these are common addressable issues that might cause or exacerbate serious functional compromise in phase 3.

*Monitor physiological age*
- After reaching viral suppression, monitor for modifiable physiological changes and intervene appropriately
- Survival expectation should be assessed based on physiology rather than chronological age

*Follow guidelines for screening and treating of common comorbid disease*
- These guidelines might require adjustment in light of the increased risk associated with HIV

*Minimise harms from polypharmacy*
- Conduct complete medication reconciliation at every visit
- Look for evidence-based non-pharmacological treatments
- Avoid or discontinue potentially inappropriate medications where possible
- Adjust medications if evidence of hepatic or renal injury is present
- Consider medications in the differential diagnosis of problematic symptoms

**Phase 3: focus on patient prioritised function (expected survival of less than 10 years)**
At this juncture, adhering to disease-specific guidelines might be counterproductive and a more formal geriatric assessment (table 1) is indicated. Shift to maintaining cognitive and functional capacities that matter to the person. This is particularly important in the last two years of life.

*Perform geriatric assessment and address geriatric syndromes*
- Formally evaluate cognitive and functional capacities (table 1)

*Palliative care*
- Have recurrent goals of care conversations
- Address emotional and spiritual distress
- Carefully manage pain and other problematic symptoms

*Plan for transitions in care and end of life*
- Ensure that ART and other essential medications are maintained during transitions from home, hospital, skilled nursing facilities, and assisted living arrangements
- Help the person and their caregivers anticipate the need to transition to assisted living to avoid interruption in ART or other essential medications
- Normalise discussions of preferences for end of life and provide supportive measures to protect dignity as end-of-life approaches
- If possible, be available to surviving loved ones during the bereavement period

ART=antiretroviral therapy.

| | Self-report | Internet tool available |
|---|---|---|
| **Diet and exercise** | | |
| WHO Diet Quality Questionnaire | Yes | Yes |
| WHO Global Physical Activity Questionnaire | Yes | Yes |
| **Physical health** | | |
| Cardiovascular disease | | |
| Framingham risk score | Yes | Yes |
| ACC and AHA Guideline on the Primary Prevention of Cardiovascular Disease | Yes | Yes |
| AHA Predicting Risk of Cardiovascular Disease EVENTs online calculator | Yes | Yes |
| Systematic Coronary Risk Evaulation 2 (<70 years) and Systematic Coronary Risk Evaulation 2-Older Persons ( ≥70 years) | Yes | Yes |
| WHO cardiovascular disease risk | Yes | Yes |
| Renal disease | | |
| Estimated glomerular filtration rate | No | No |
| Urine protein | No | No |
| Liver disease | | |
| Fibrosis-4 index, APRI, and non-alcoholic fatty liver disease fibrosis score | No | No |
| Model for end-stage liver disease | No | No |
| CT (steatosis) | No | No |
| Ultrasound (steatosis) | No | No |
| Transient elastography (steatosis) | No | No |
| Lung disease | | |
| Spirometry | No | No |
| Cancer | | |
| Mammogram or ultrasound (breast cancer) | No | No |
| Pap smear (cervical cancer) | No | No |
| Digital rectal exam or pap smear (anal cancer) | No | No |
| Serum α-fetoprotein levels test or ultrasound (liver cancer) | No | No |
| Hearing | | |
| Johns Hopkins Hearing Number smartphone app | No | Yes |
| Vision | | |
| Snellen eye chart or WHOeyes smartphone app | No | Yes |
| **Cognitive health** | | |
| Montreal cognitive assessment | Yes | Yes |
| International HIV dementia scale | Yes | Yes |
| **Mental and behavioural health** | | |
| Substance use | | |
| Self-reported alcohol use disorders identification test-C | Yes | Yes |
| Phosphatidylethanol dried blood spot testing for alcohol | No | No |
| Self-reported pack years tobacco smoking history | Yes | Yes |
| Sputum cotinine analysis for tobacco smoking | No | No |
| Self-reported cannabis use | Yes | Yes |
| Hair or nail analysis for cannabis | No | No |
| Drug misuse screening test | Yes | Yes |
| Depression | | |
| Patient health questionnaire-2 or patient health questionnaire-9 | Yes | Yes |
| **Falls or fractures risk** | | |
| Fracture risk assessment tool | Yes | Yes |
| Dual-energy x-ray absorptiometry | No | No |
| **Polypharmacy** | | |
| Medication reconciliation | Yes | Yes |
| Anticholinergic medications | Yes | Yes |

(Table 1 continues on the next page)

most global settings. Health-care providers who understood the specific health needs of older adults in key populations and engaged in respectful communication were more likely to test for HIV.[110] Assessing HIV acquisition risk among older adults using simple tools to guide the approach could increase uptake of HIV testing.[104] Universal testing using an opt-out approach is another method for health-care provider-initiated HIV testing and counselling, and can reduce the likelihood of delayed diagnosis, improve the timeliness of HIV treatment, and help re-engage people previously diagnosed in HIV care.[111] In emergency departments in the UK, universal HIV testing with an opt-out option was shown to be cost-effective, particularly when identifying people at higher risk of late diagnosis, including older adults.[112]

HIV self-testing has been shown to be acceptable and even preferred in countries of all income levels (although access in rural settings can be poor), with greater uptake in older adults than in younger adults.[113] Privacy and convenience drive HIV self-testing as a preferred mode of testing in some older populations; in a 2021 study in Malawi, door-to-door distribution of self-testing kits was preferred.[114] Supportive services (eg, on-site or online home-based counselling services) could enhance confidence and accuracy of HIV self-testing and improve linkage to HIV care or prevention services, particularly for older adults who might perceive self-testing as a complex process. Lessons learned from SARS-CoV-2 self-testing could inform the greater emphasis, enhancement, or roll-out of HIV self-testing programmes that include a focus on older adults.

HIV and age stigma are often encountered, and could be even greater for older men, who are less likely to test overall.[113,114] Meeting older adults where they are with access to HIV self-testing and home-based testing could result in increased uptake. Accessible, confidential, and non-judgemental HIV testing services at community facilities—particularly facilities linked to health-care or community services—are needed.

## Managing health care with a view to healthy ageing

Healthy ageing for people with HIV requires numerous fundamental considerations that can be organised into sequential phases of health care (panel 2). The first phase focuses on establishing a therapeutic alliance, beginning with ART initiation and ending once a well tolerated and effective regimen is established (typically 6–12 months). The second (ie, maintain health despite increasing complexity) and third (ie, focus on maintaining function) phases build on phase 1. In all phases it is important to support excellent ART adherence, good mental health, a healthy lifestyle, and self-care. Furthermore, phases 2 and 3 overlap with a gradual shift in emphasis over time (figure 3). The beginning of phase 2 starts with a strong focus on guideline directed screening and treatment for

specific ageing associated comorbid conditions, which later shifts to focus on maintaining cognitive and functional abilities that are important to the individual in phase 3. Throughout all phases, consideration needs to be given to what matters most to the individual and identifying modifiable threats to cognitive and functional capabilities. For example, polypharmacy is uncommon at ART initiation in phase 1, but an increasing challenge in phases 2 and 3. Nevertheless, health-care providers should consider what other medications the person is taking when initiating ART. Similarly, it is important to monitor vision and hearing in phase 2, as these are common addressable limitations that could cause or exacerbate serious cognitive compromise in phase 3. The balance between priorities in phases 2 and 3 shifts as increasing functional limitations or multimorbidity are noted, or the person is unlikely to live more than 10 years. Although we show this as a linear shift over time (figure 3), transient conditions (eg, acute illness) can temporarily alter priorities. For people who are experiencing a substantial burden of physiological injury, multimorbidity, or pre-existing functional compromise at diagnosis, issues addressed in phases 2 and 3 will likely require more immediate attention.

### Phase 1: establishing a therapeutic alliance

ART initiation can be a pivotal point in a person's life, where they might be uniquely receptive to abandoning unhealthy behaviours and adopting healthy ones, and could be a foundational moment for establishing a healthier lifestyle, regardless of the person's age. Thoughtful discussions that address how people with HIV can live full and productive lives if they adopt healthy behaviours, engage in their care, and take antiretroviral medication are needed. In these discussions, health-care providers need to avoid blaming the individual for behaviours that might negatively impact healthy ageing, and encourage change where needed to improve health. The behavioural changes that are needed for a person with HIV to age well might seem daunting and require substantial effort on the part of the health-care provider, the person, and the community, who must all work together to provide the factors required for behavioural change (eg, personal motivation, understanding the need for change, creating a defined plan with achievable goals, consistent self-monitoring, social support, managing barriers and setbacks, and addressing factors that could hinder change).

To optimise care, health-care providers need to encourage ART adherence and elicit individual preferences and priorities for their care more generally. To fully capitalise on this pivotal point in health care (ART intitiation), health-care providers should assess the person's understanding, concerns, and readiness to learn. Communication needs to be clear, concise, and easily understood, with information that is directly relevant to the person's concerns and their specific situation. The person's questions should also be responded to directly and clearly, and the health-care provider should also ask questions to ensure both their own understanding and an understanding of the person's life. The health-care provider's goal is to establish a health trajectory that will help to ensure healthy ageing, regardless of the person's

| | Self-report | Internet tool available |
|---|---|---|
| (Continued from previous page) | | |
| Neurocognitively active medications | Yes | Yes |
| Beers or STOPP-START Criterion | Yes | Yes |
| Clinical Pharmacogenetics Implementation Consortium grade A medications | No | No |
| **Functional ability including mobility** | | |
| Activities of daily living | Yes | Yes |
| Instrumental activities of daily living | Yes | Yes |
| Karnofsky or palliative performance scale | Yes | Yes |
| Gait speed | Yes | No |
| Grip strength | Yes | No |
| Chair stand | Yes | No |
| **Social and structural supports or barriers** | | |
| Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences | Yes | Yes |
| American Academy of Family Physicians' EveryoneONE Project screening tool | Yes | Yes |
| Accountable Health Communities health-related social needs screening tool | Yes | Yes |
| **Vulnerability to physiological or functional injury** | | |
| WHO Integrated Care for Older People intrinsic capacity | Yes | Yes |
| FRAIL scale (self-assessment) | Yes | Yes |
| Clinical Frailty Scale (physician assessment) | No | No |
| Frailty phenotype | No | No |
| VACS index | No | Yes |
| VACS–CCI | No | Yes |

ACC=American College of Cardiology. AHA=American Heart Association. APRI=aspartate aminotransferases to platelet ratio index. CCI=Charlson Comorbidity Index. STOPP–START=Screening Tool of Older Persons' Prescriptions–Screening Tool to Alert to Right Treatment. VACS=Veterans Aging Cohort Study.

***Table 1:*** **Examples of screening tools by geriatric domain**

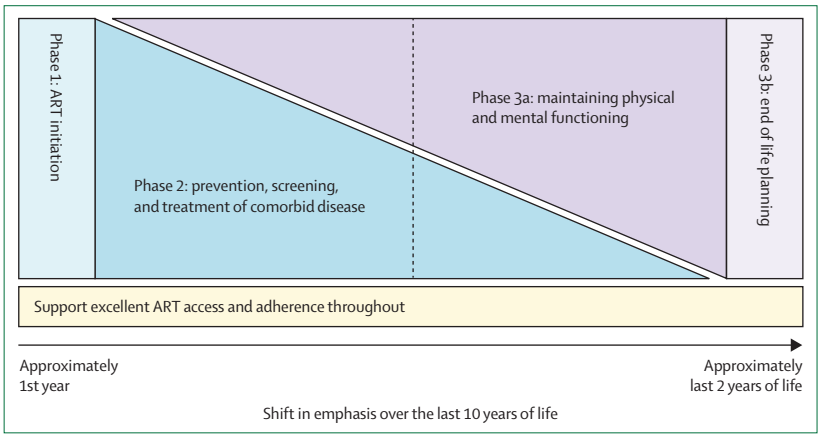



***Figure 3:*** **Phases of health care and their emphasis to optimise ageing with HIV**
Phase 1 focuses on initiating ART and establishing a therapeutic alliance. Phases 2 and 3 build on phase 1 and overlap with each other, with a gradual shift in emphasis away from screening and treatment and toward maintaining physical and mental functioning. ART=antiretroviral therapy.

age when treatment is initiated. Although it might not be possible to cover all these issues in one visit, the person and their health-care provider should establish a therapeutic alliance that includes a system of follow-up and acknowledged progress, covering these issues over time (table 1, panel 2).

From the beginning of HIV care, it is crucial to empower the person to participate fully, including addressing necessary components of self-care. We use the term self-care to refer to the proactive steps that a person takes to preserve and improve their physical, mental, and emotional wellbeing. Healthy ageing for people with HIV relies heavily on the relationships between the person beginning HIV care and their family or chosen family members, partners, health-care providers, and community, and on the person's own capacity for self-care. In some settings, health-care providers might partner with a community member who is trained to provide health education and facilitate connection with community resources (panel 1).[115]

People with HIV need to be empowered to take charge of their health by accessing available resources with ongoing guidance and support from their health-care provider. As people reach an undetectable viral load with ART, they might feel further empowered to tackle issues regarding diet, exercise, and substance use, and avoiding excess weight gain after ART initiation.

### *Stigma, social isolation, and mental health*

Stigma, whether internalised, anticipated, or experienced, can affect mental and physical health, treatment adherence, sense of social isolation, and overall quality of life.[116] Stigma is linked to increased psychological distress and decreased engagement with health-care service.[117,118] Effective counselling and support aims to mitigate the psychological and social effect of HIV, which are often exacerbated by stigma.[117]

Age and HIV can also be associated with intersectional stigma and discrimination with negative effects on diagnosis and treatment (see HIV testing). Ageism (assuming that older people are not at risk for HIV) can result in delayed diagnoses and suboptimal care in the older population based on the misconceptions that HIV predominantly affects the younger population and that older people are no longer sexually active.[117,119] Older people might have internalised stigma regarding their age and sexual practices and be reticent to seek HIV testing and treatment.[120] Addressing ageism and stigma requires a comprehensive approach.

Counselling should include interventions that are designed to reduce internalised stigma and promote resilience, and simultaneously challenge discriminatory attitudes and practices within health-care environments.[121] This approach involves creating inclusive and non-judgemental spaces where people of all ages feel valued and understood. Peer groups and counsellors can play a crucial role in providing emotional support by normalising individual experiences and helping people to navigate the social and psychological barriers that are associated with HIV in different settings (panel 3). Peer groups can also facilitate coping strategies to manage the adverse effects of stigma,[116,121] particularly its effects on social isolation, by offering a sense of belonging. Understanding that undetectable=untransmittable can both promote adherence to ART and help dismantle

### *Panel 3:* Community voices

The recommendations of this Commission are based on current evidence, which is not inclusive of all topics that people living and ageing with HIV globally would like to be addressed. The perspective of people ageing with HIV remains essential to guiding the direction of research, clinical care, and policies. In addition to including two representatives from communities of people living with HIV in each of the five writing groups that created this report, we also solicited feedback from communities with HIV across the globe after this Commission was drafted by circulating a community summary of the report and its findings and an early draft. Based on global community feedback, we summarise the following suggested future directions for research and care that is meaningful to people ageing with HIV:

- Case-study reports of successful patient, provider, health system, and community organisation collaborations meeting the needs of those ageing with HIV (country-level or programme-specific)
- Recognition that ageing well encompasses more than clinical outcomes to include belonging, thriving, and dignity
- Harm-reduction strategies for substance use that are tailored to people older than 50 years should be used when abstinence strategies do not work
- Mechanistic studies delineating how ageism, HIV, and sexual orientation stigma result in negative health outcomes
- Interventions to reduce stigma towards people older than 50 years with HIV, specifically targeting these interventions at clinicians in health-care and residential care settings
- Characterisation and effective interventions that address non-adherence due to treatment exhaustion, which is likely common among adults who have aged with HIV
- Caregiver's roles are often essential to ageing well. For people ageing with HIV, caregivers are commonly members of their chosen family, rather than their family of origin. The international health-care community understand little about how to support them, and their needs likely differ from those caring for people ageing without HIV
- Characterisation of the many challenges to secure care for people with HIV who are navigating nursing home placement or disability
- Longer-term, larger sample size studies of the influence of gender-affirming hormone therapy in transgender men and transgender women, particularly the use of oestrogen in transgender women and cardiovascular risks
- Increased awareness and studies of risks that disproportionately impact ageing transgender and gender diverse populations, such as the negative health outcomes associated with liquid silicone injections
- A consistent focus on language to reduce stigma, blame, and othering, and build trust, deepen empathy, and improve mental, emotional, and physical health

This feedback provides crucial insight into the challenges faced by people ageing with HIV and the topics that this population would like to be addressed to age well and meet end of life with dignity. We encourage the community of people with HIV, their loved ones, their care providers, researchers, and policy makers to move collaboratively to address the challenges that are most meaningful to people who are ageing with HIV.

internalised stigma, fostering self-worth and reducing feelings of shame.[120]

A notable gap in the literature is the insufficient exploration of how stigma influences the ageing process. Although substantial progress has been made in understanding the medical and psychosocial aspects of ageing with HIV, the role of stigma—both external (from society and health-care systems) and internalised (self-stigma)—has not been adequately examined in relation to ageing outcomes.

Social isolation, or the retreat from social obligations, can be caused by or result in depression and difficulties in adhering to medication and self-care practices. Older people living with HIV should be encouraged to participate in social activities and maintain social ties and obligations within their communities; panel 1 suggests ways to do so.[14–17] Such interventions have many positive effects, ranging from reduction in HIV stigma, loneliness, marginalisation, distress, depression, anger, and anxiety to increase in self-esteem, self-efficacy, coping skills, and quality of life.[16]

Poor mental health can lead to non-adherence to ART and substance use with lasting consequences.[124] Depression is the most frequently reported mental health condition among people with HIV and occurs at all ages and stages of HIV infection.[125,126] Depression is associated with suboptimal retention in care and ART adherence, and is a risk factor for cardiovascular disease, geriatric syndromes (eg, frailty and falls), and cognitive decline in older people with HIV. Anxiety disorders are also widely prevalent, and symptoms can increase in response to being diagnosed with HIV. Both non-pharmacological (particularly exercise and talk therapy)[127] and pharmacological interventions can effectively reduce anxiety and depression,[128] but the use of pharmacological agents needs to be balanced against potential adverse effects (eg, an increased risk for falls or cognitive compromise).[129,130]

### *Screen for and address substance use*

Substance use is common among people ageing with HIV and can change over time, interact with prescription medications, and severely compromise healthy ageing.[131] Screening for and addressing legal and illegal substance use is crucial (table 1), although harm reduction might be more achievable than outright abstinence. Alcohol is the most common substance used among people with HIV across ages and geographical settings,[132] often in combination with other substance use, such as smoking tobacco. Due to the increased risk of numerous comorbidities, people with HIV should be encouraged to stop using alcohol and other substances and to quit smoking. If abstinence is not attainable, harm reduction can be emphasised. Where available, support networks and rehabilitation care should be offered. Heavy alcohol consumption is strongly associated with poor ART adherence and could also result in liver disease, exacerbation of cardiac disease, cognitive decline, and drug–drug interactions.[133] Long-term alcohol use is associated with ageing-related morbid effects on cognition, sarcopenia, and risk of falls.[134–136] Cigarette smoking is more common in people with HIV than in people without HIV across various settings and ages.[137,138] Smoking is also associated with future risk of several ageing-related morbidities in people with HIV, including cardiovascular diseases, pulmonary disease, cancers, frailty, and cognitive decline.[139–141] Cannabis use is also prevalent in this population, but its associations with the HIV care continuum and ageing outcomes are poorly defined.[142] Further research is needed to understand the use patterns and effects of cannabis among people with HIV, particularly as these factors could influence ageing outcomes. However, early evidence has documented a rapid increase in diagnoses of cannabis use disorder among older people with and without HIV following widespread legalisation in the USA.[143] The use of other substances—including cocaine, opioids, and amphetamines—is also seen in people older than 50 years and people experiencing polypharmacy;[144] however, approaches to treatment for substance use are rarely tailored to older adults.

### *Address self-care challenges, including exercise, diet, and excess weight gain, on ART*

Challenges to self-care can arise from social and economic vulnerabilities, depression, struggles with changing social roles, treatment fatigue, and difficulties managing an ageing body.[145] Pathways to overcome these challenges could become clearer from the acknowledgment of the individual's priorities, personal empowerment, and capitalising on community and internet resources. In addition to providing financial and social resources for self-care when needed, training health-care providers to address self-care will legitimise this approach as a part of treatment. Models of self-care that draw from an individual's preferences have the potential for better outcomes. It is crucial to recognise when an individual is not able to engage in self-care, as care-giving is then required.

Self-care might also be limited by the individual's environment.[146] Social and structural determinants of health affect physical exercise and diet and the risk of coinfections and non-communicable disease vulnerability among people with HIV.[119] At the individual level, social and structural determinants have been associated with heightened levels of stress, malnutrition, increased measures of systemic inflammation, and ageing-associated morbidities (eg, frailty and cognitive decline).[147,148] Health-care providers should ask about housing, food security, income, and personal safety to better understand their patients' environment when advising them on feasible self-care actions and resources through social prescribing (table 1, panel 1).

The positive effect of physical activity on all older people and those with HIV is well documented, with clear

benefits for physical health, psychological wellbeing, and overall quality of life.[149] The type of exercise should be individualised based on functional capacity and available resources. The 2020 WHO guidelines on physical activity and sedentary behaviour[150] highlight that almost any level of physical activity compared with a sedentary lifestyle improves cardiorespiratory fitness, lipids values, glucose levels, health-related quality of life, lean body mass, and muscle mass. For people ageing with chronic diseases including HIV, WHO recommends a minimum of 150 m per week of moderate-intensity aerobic activity, muscle-strengthening activities of at least moderate intensity on two separate days, and balance training on three separate days. When not able to meet the above recommendations, people with HIV should aim to engage in physical activity according to their functional abilities. Previous research in other populations suggests that diet and exercise interventions can be effective.[150]

All older people, and especially those ageing with HIV, need a balanced diet to help maintain immunity,[151] avoid inappropriate weight gain after ART initiation, and maintain muscle mass for optimal functioning. Consuming fruits and vegetables and the recommended amount of proteins, carbohydrates, and fats to maintain a healthy weight and facilitate nutrient absorption is important. Health-care providers should give guidance concerning herbs, natural medicines, and foods that interact with ART. A diet plan should be customised based on the availability of resources, presence of other comorbidities, and availability of particular foods, with a focus on minimising the consumption of ultraprocessed foods, excess salt, saturated fat, and added sugar.[152] For people with low CD4 counts and reduced immunity, it is better to avoid uncooked foods (eg, raw meat or fish and unpasteurised milk) to prevent the risk of parasitic and zoonotic diseases such as bovine tuberculosis and brucellosis.[152] Furthermore, although calorie requirements depend on activity levels, calorie requirements are generally reduced with age, whereas nutrient requirements are not. These changes might be particularly challenging for people who live in places where highly processed and calorie-dense foods are more accessible and more affordable than nutrient-rich alternatives. Where possible, consulting a dietitian should be advised. Dental health is also a factor that can greatly influence nutrition.

As ART has become more effective and tolerable and administered earlier in the disease course, excess weight gain after ART initiation has substantially increased.[153] Uncontrolled HIV and other viral infections influence caloric requirements[154] and, after reaching viral load suppression, resting energy metabolism decreases.[155] If the person does not decrease their habitual pre-treatment caloric intake or increase their physical activity to compensate, they will gain weight. An expert panel reviewed the evidence regarding weight gain after ART initiation in 2023 and concluded that tenofovir disoproxil fumarate-based regimens—particularly when given with efavirenz—reduced weight gain, likely due to side-effects such as nausea.[153] Sax and colleagues suggested that observed associations between dolutegravir, bictegravir, and tenofovir alafenamide fumarate-based regimens (which generally have few gastrointestinal side-effects and greater weight gain) and weight gain occur only in comparison to tenofovir disoproxil fumarate and tenofovir disoproxil fumarate with efavirenz regimens.[153] Nevertheless, due to proven clinical benefit and antiretroviral effectiveness, integrase strand transfer inhibitor-based regimens are recommended in all ART initiation clinical guidelines. However, clinically significant weight gain occurs in a subgroup of people who take integrase strand transfer inhibitors, with Black women and older people at greater risk for clinically significant weight gain.[157] Further investigations of the multifactorial pathways to weight gain after ART initiation are needed.

Health-care providers need to discuss the risk of weight gain at the time of ART initiation in a similar manner as to how obstetricians counsel pregnant women on diet and exercise to avoid excessive weight gain during pregnancy.[158] This discussion is of paramount importance, as it is easier to prevent weight gain than to lose weight and maintain weight loss, and safer for the person, as weight loss in older age typically includes the loss of both fat and muscle. However, if weight is regained, the lost muscle is replaced with fat, which is also true for regained weight after the discontinuation of GLP-1 receptor agonists.[159] Notably, although BMI is an imprecise metric, it can be combined with waist circumference to offer basic guidelines. Although these guidelines should be adjusted based on gender, race, and ethnicity, more research is needed.

*Connect with community and internet resources*

Neither the individual nor their health-care providers can easily manage healthy ageing with HIV alone. Health-care providers and people ageing with HIV need to engage with their local and digital communities. Given that clinics often do not have the ability to fully address the social aspects, structural barriers, and intersectional challenges that people might face, referring patients to community (panel 1) and digital resources (see digital health and artificial intelligence [AI]) can provide substantial assistance and reinforcement.

Fortunately, people with HIV and their communities are eager to effectively engage with health care. As stated in the Denver Principles (1983),[160] which addressed HIV generally, and echoed in the San Francisco Principles (2020),[161] which addressed ageing and HIV, "nothing about us, without us". In 2022, the Glasgow Manifesto[162] was developed by the founding members of the International Coalition of Older People with HIV, European AIDS Treatment Group, National AIDS Treatment Advocacy Project, Realise, and UTOPIA_BXL.

The Glasgow Manifesto was supported by over 100 HIV community organisations, and emphasised the importance of working together to improve the lives of people ageing with HIV by capitalising on human and community resources both within and outside of the clinical setting. HIV peer groups and counsellors can play a crucial role in providing emotional support, normalising individual experiences, and helping people with HIV to navigate social and psychological barriers associated with HIV in different settings.

Community members have already played an important role in HIV care, including health promotion and education; HIV prevention, testing, treatment, care, and clinical management support; integrating activities across health conditions; addressing stigma, discrimination, and education; and providing counselling.[163] The education, designated roles, and remuneration of these community members might need to be adjusted to accommodate the growing and evolving needs of people ageing with HIV.[164] Additionally, there are multiple programmes for older people to build community and combat loneliness that also encourage exercise through group activities.[165] Exercise activities that are tailored to older people (group or individual), support groups for dietary changes and tobacco and alcohol cessation,[91] and social and religious organisations can be essential in the empowerment of older people to practice self-care. These resources are important in environments where health-care resources are sparse and in LMICs, where formal support for these activities is rarely available, and should be made a part of the overall landscape of care.

Community and internet resources need to be adapted to be welcoming to people with HIV and combat stigma that might discourage them from taking full advantage of these resources.[165] Health-care providers should become familiar with a wide range of local resources and refer where appropriate, which can be facilitated through social prescribing (panel 1). Self-care supported through community-based programmes, social networks, and, when available, internet resources, can be greatly facilitated. However, it is important to acknowledge that the varying capacities and personal resources of individuals might mediate effective engagement in self-care, particularly as they might require some help in identifying community activities, social organisations, and internet resources that support self-care.

*Where possible, individualise ART regimen*

Whether the person is young or old at the time of their initial HIV diagnosis, early ART initiation and consistent adherence facilitates ageing well. The adverse effects of antiretroviral drugs are a common reason for a change in treatment regimens. Clinical trials commonly underestimate long-term complications of ART, as they can use highly selective inclusion criteria that exclude people with underlying comorbidities. Clinical trials can also be time-constrained and end before most long-term effects can be observed. Additionally, older people are often excluded from clinical trials. Appropriate ART regimen choice at initiation could reduce adverse effects and comorbidity-related individual and programme-related costs. Establishing an appropriate ART regimen from the start of care could also prevent additional unreimbursed care costs.

Approaches to optimising a person's HIV treatment regimen will vary by health-care setting, available formulary, and supply chain, and external factors such as guideline and payor considerations. In settings with multiple options, assistance from AI-based clinical decision tools could be useful. The following factors should also be considered: (1) individual-level demographic, psychological, social, behavioural, and financial factors; (2) biological factors including ART history, drug resistance profiles, and comorbidities (eg, kidney disease, cardiovascular disease, metabolic syndromes, liver disease, cognitive impairment, and bone health); and (3) non-antiretroviral medications, including non-prescription drugs, supplements, and herbal treatments.

People who initially received nucleoside reverse transcriptase inhibitors, didanosine, stavudine, and zidovudine might have experienced mitochondrial toxicity—associated with atypical body fat distribution—and higher rates of myocardial infarction.[166] Nucleoside reverse transcriptase inhibitors are known to have substantial and—in some cases—long lasting and toxic effects on human mitochondria.[166] Tenofovir disoproxil fumarate has been associated with bone and kidney toxicities,[167,168] and abacavir was linked to increased cardiovascular risk.[169] Boosted protease inhibitors interact with many non-ART medications and have been causally linked to metabolic toxicities (eg, insulin resistance and dyslipidaemia) and produce senescence in endothelial arterial cells.[170] Protease inhibitors also have the potential to induce oxidative stress. Importantly, indinavir, nelfinavir, ritonavir, lopinavir, atazanavir, and darunavir have been linked to endothelial oxidative stress, which exacerbates inflammation, vascular complications, and insulin resistance.[171] Other mechanisms proposed for the link between protease inhibitors and metabolic atypicalities are the suppression of the activity of the glucose transporter GLUT-4 in adipose and muscular tissues, reduced leptin expression, and increased secretion of triglyceride-rich lipoproteins by disrupting the processing of sterol regulatory element-binding proteins and the alteration of the apolipoprotein B metabolism, which are believed to be responsible for atypical body fat distribution, and the higher rates of myocardial infarction associated with protease inhibitors.[171] Many of the adverse effects of these older and more problematic regimens have long-term sequelae, even after they have been discontinued. Currently used regimens (including integrase inhibitors) have less short-term toxicities, but continued monitoring for long-term toxicities using real-world data is essential.

Ageing reduces hepatic and renal function, which alters the metabolism and clearance of many medications, including antiretrovirals (see minimise harm from polypharmacy),[172,173] and could increase drug toxicity. A 2023 systematic review[172] looked at 97 studies, of which only 20 examined pharmacokinetics in people older than 50 years. Only seven studies compared pharmacokinetics between younger and older adults. These data do not include the currently preferred ART regimens.

*Consider long-acting agents*

Long-acting injectable ART formulations (administered on a monthly or once every two months basis) can offer new approaches to drug delivery to improve adherence and overcome some of the limitations of daily oral therapy. Older people with HIV frequently experience higher pill burdens, drug interactions, and side-effects,[144] and long-acting injectable ART can reduce dosing frequency, pill burden, and stigma. Long-acting injectable ART can also offer pharmacological benefits by avoiding gastrointestinal absorption issues. For people undergoing major surgery or who have other difficulties with swallowing, these medications could be beneficial. The benefits, risks, and applications of long-acting injectable ART for ageing populations and the distinct needs of these populations remain under-researched, but a 2026 real-world sub-analysis of a Spanish cohort suggests that long-acting injectable cabotegravir–rilpivirine has good tolerability and maintains virological suppression in adults older than 60 years.[174] There are also structural challenges to implementing long-acting injectable ART in older people with HIV, which include clinical capacity, insurance issues, cost, and availability, especially in LMICs. More research is needed on the long-term efficacy, pharmacokinetics, and acceptability of long-acting injectable ART—or long-acting orally administered ART—in older populations. Despite substantial pharmacokinetic data in younger adults, knowledge gaps persist regarding the effects of ageing on antiretroviral pharmacokinetics. Furthermore, clinicians need to be knowledgeable about a patient's history of ART side-effects and toxicities (which increases in complexity with increasing duration of ART use) and contraindications for use of specific antiretrovirals in people with certain comorbidities. Where possible, an ART regimen should be carefully selected, particularly if the person is older, already taking other medications, and has pre-existing or risk factors for renal insufficiency.

*Deliver routine vaccinations, test for and treat co-infections*

People with HIV who are ageing have an increased susceptibility to co-infections and greater need for routine vaccinations. From the outset of care, regular monitoring of co-infections and timely vaccination is crucial to their comprehensive management. Well established recommendations have been previously published, and will likely be updated over time.[175] There are substantial gaps in knowledge regarding vaccinations for people ageing with HIV; primarily, the long-term effectiveness and safety of vaccines that are likely influenced by both HIV-related and age-related immune senescence. The immune response to vaccines in older populations with HIV—especially those with lower CD4 counts or incomplete viral suppression—remains unclear. The effect of chronic co-infections (eg, hepatitis B virus, hepatitis C virus, or cytomegalovirus) on vaccine response requires further investigation, as does the role of common comorbidities in influencing vaccine efficacy for older adults with HIV. Continued research and advocacy regarding older people with HIV in vaccine trials is needed to make guidelines more inclusive and refine these recommendations to provide the best possible care for this population.

*Monitor for gaps in care, viral breakthrough, and resistance*

Gaps in care can have serious and well documented consequences. In a programmatic cohort from Homa Bay (Kenya), 18% of people with advanced HIV disease had previously received ART.[176] Notably, the median age of participants was 46 years, and 991 (54%) participants were older than 45 years, reinforcing the relevance of this issue in older adults.[176] People who had previously received ART had worse outcomes, with 124 (38%) participants dead or lost to follow-up compared with 105 (7%) participants who had been newly diagnosed at the time of the study.[176] Gaps in care occur for multiple reasons, including unexpected life events, socioeconomic issues (panel 1), ART tolerance challenges, and low perceived benefit of treatment.[177] Among older people, additional factors contribute to these gaps, such as multimorbidity requiring multiple clinic visits, changes in residence or caregiving responsibilities, treatment fatigue, and interruptions occurring during care transitions.[178] Older adults also frequently report difficulty with transportation and scheduling and poor digital literacy, which add further barriers to continuous engagement. The most common causes of viral breakthrough are service delivery interruptions or personal non-adherence. ART resistance is less common, but should also be considered.

## Phase 2: maintain health despite increasing complexity

Managing the health care of people as they age with HIV can be challenging. A weakened immune system due to HIV and ageing increases their susceptibility to communicable diseases, including tuberculosis and diverse viral, fungal, and bacterial infections.[179] Compared with people ageing without HIV, people ageing with HIV are also at increased risk for non-communicable and ageing-associated conditions, such as hypertension, diabetes, chronic kidney disease, cardiovascular diseases, and cancers. Menopause in people with HIV occurs earlier than in people without HIV, can be more symptomatic, and is associated with higher levels of inflammation compared with premenopausal people.[180,181]

Additionally, menopausal people with HIV show higher inflammation levels compared with menopausal people without HIV.[181] However, the effect of these findings on clinical outcomes, quality of life, and appropriate management strategies remains underexplored.[182,183] Therefore, although HIV health-care providers are familiar with infectious diseases, managing menopause, non-communicable diseases, cancers, and eventually, geriatric syndromes over the life course could be less familiar and require thoughtful prioritisation among competing—and sometimes contradictory—goals.

With increasing complexity, prioritising care according to the individual's health goals becomes increasingly important. Although extensive primary care guidelines for people with HIV have been published,[184–186] the numerous screening, monitoring tests, and treatment recommendations suggested can be overwhelming. These guidelines often presume clinical resources that might not be available in many settings, especially in LMICs. These guidelines also offer age-based recommendations typically developed for a general population, and not specifically for people ageing with HIV.

*Monitor physiological age*

Age-based screening and treatment guidelines often underestimate risks derived from HIV, its treatments, or cumulative multimorbidity, polypharmacy, and physiological frailty. At any given age, depending on these factors, people living with HIV have widely differing vulnerabilities. Using chronological age rather than personalised estimates of remaining survival (physiological age) likely contributes to underscreening and overscreening. Underscreening leads to delayed diagnoses, compromising the effectiveness of treatment and, in some cases, the possibility of a cure. Overscreening means that health-care providers assign a diagnosis and possibly initiate treatment for a person who would never experience symptoms, thereby incurring unnecessary anxiety, expense, and exposure to potentially unpleasant or toxic side-effects of treatment.

In the era of electronic medical records, genomics, advanced analytic methods, and high-performance computing, we can accurately estimate physiological age, and many approaches have been reported in the general literature on geriatric care.[187,188] However, HIV care providers do not know how well these indices generalise to people ageing with HIV. Furthermore, many of these indices are not easily applied in real time in clinical settings. Approaches that have been validated among people living with HIV include epigenetic clocks, the Veterans Aging Cohort Study Risk (VACS) index, and the Veterans Aging Cohort Study–Charlson Comorbidity Index (VACS–CCI).

Epigenetic clocks are algorithms that incorporate information from DNA methylation to estimate age acceleration, defined as the difference between epigenetic and chronological age.[189] Epigenetic clocks can predict age-related comorbidities, healthspan (ie, healthy survival), and mortality in people with and without HIV.[190,191] People with (*vs* without) HIV had, on average, a 5·2 year increase in their epigenetic age (measured in whole blood) compared with their chronological age.[191] Among men with HIV in the multicentre AIDS cohort study, epigenetic age was 3·6 years older on average in participants with (*vs* without) detectable HIV RNA.[191] Evidence from people with HIV in the Swiss HIV cohort showed epigenetic age acceleration was greater before ART initiation and decelerated after ART initiation.[192] Cumulative HIV viral load after ART initiation was modestly associated with epigenetic age acceleration in the multicentre AIDS cohort study.[193] However, epigenetic age is not readily available in clinical settings.

The Veterans Aging Cohort Study 2.0 (VACS 2.0) index was developed using routine clinical data to predict survival among people with HIV. A continuous measure, the index includes measures for age; CD4 count; viral load; haemoglobin, aminotransferases, creatinine, albumin, and platelet concentrations; hepatitis C virus status; white blood cell count; and BMI.[194] VACS 2.0 has been validated with good to excellent discrimination and calibration in over 30 HIV cohorts from North America and Europe participating in the ART Cohort Collaboration and North American AIDS Cohort Collaboration on Research and Design.[195,196] Among people ageing with HIV, the VACS index is strongly associated with a future risk of adverse health outcomes, including hospitalisation, falls, fractures, and cognitive compromise.[194]

However, the performance of VACS 2.0 is not as strong among people older than 50 years. VACS–CCI combines VACS 2.0 and diagnostic groups from the Charlson comorbidity index.[197] Among 6·5 million veterans without HIV in care, VACS–CCI showed excellent discrimination and calibration. Of 30 539 veterans with HIV, the C statistic was the same as for VACS 2.0 (0·77). VACS Index and VACS–CCI are two potential tools with which to measure physiological age, and have been implemented in electronic health records as decision support through MDCalc.[198] By identifying which organ systems and medical diagnoses contribute most to a person's mortality risk, complex care requirements can be prioritised and appropriate follow-up determined. Although the components of the VACS Index and of VACS–CCI are commonly available in settings with high amounts of health-care resources and are important for clinical management in the context of multimorbidity and ageing (table 1). Other approaches might be required in settings that have fewer health-care resources.

Epigenetic clocks and VACS–CCI both suggest that chronological age is a poor indicator of a person's physiological age, particularly in people with HIV. Among adults who are age 65 years with HIV, the gap in expected survival using the VACS–CCI (11·6 to 13·5 years; figure 4) is more than twice that estimated using methylation age

(3–6 years).[190,191] This is unsurprising, given that the VACS–CCI relies on measures of organ system function and medical diagnoses, which are likely downstream effects of DNA methylation. More research is needed on women and people in LMICs.

*Follow guidelines for screening and treatment of common comorbid diseases*

Comorbid disease takes many forms among people ageing with HIV and has multiple causes, which include co-occurring infections (eg, tuberculosis, malaria, and viral hepatitis), obesity and metabolic syndrome, ongoing substance use,[200] and physical inactivity.[201] ART toxicity and polypharmacy also contribute to organ system injury.[144,202] However, most manifestations of comorbid disease among people ageing with HIV show a dose–response association with CD4 count and HIV-1 RNA,[203–205] which is thought to be due to accentuated chronic inflammation and immune dysfunction caused by HIV that persists at a lower level after viral suppression.[206] Because HIV itself can drive these conditions, early and sustained ART is essential.

Our focus is healthy ageing with HIV around the world, in widely different social, economic, and health-care settings. It is beyond the scope of this Commission to summarise regional guidelines for common comorbid diseases. Furthermore, guidelines from different agencies and regions vary and will evolve over time. In this Commission, we offer a brief review of common health conditions among people ageing with HIV and their unifying risk factors. Our goal is less to delve into each of these conditions than to highlight consistent underlying and unifying causes, which, if addressed, would decrease risk for multiple conditions.

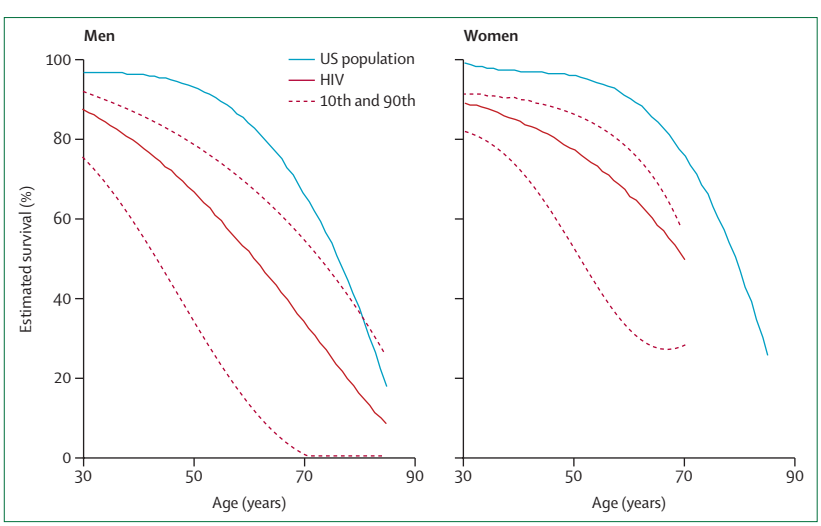



***Figure 4:*** **Chronological versus physiological age of people with HIV**

The figure illustrates smoothed median expected survival by age and sex at birth using VACS–CCI (a prognostic index based on routine laboratory data and diagnostic codes) for 30 539 US veterans with HIV (solid and dashed red lines), and life table-based US population estimates (black line) for males (left) and females (right). VACS–CCI estimates for women with HIV are truncated at age 70 years due to insufficient numbers. To illustrate the limitations of chronological age in estimating survival among people ageing with HIV, we compared expected 10-year survival by age and sex based on 2021 United States Social Security life tables to estimates based on actual clinical data applying VACS–CCI in a national cohort of 6 588 688 US veterans in care within the Veterans Healthcare Administration. At age 65 years, physiological age based on VACS–CCI estimates exceeded chronological age based on population life tables by 13·5 years for males with HIV and by 11·6 years for females with HIV. Reproduced from Justice et al.[199] VACS–CCI=Veterans Aging Cohort Study–Charlson Comorbidity Index.

Chronic inflammation is a major root cause of physiological injury and geriatric syndromes in people ageing with and without HIV, but it is more pronounced in people with HIV.[206] Besides prescribing ART as soon as possible, timely treatment of co-occurring chronic infections is important to decrease the inflammatory load, to prevent organ system disease progression, and to prevent complications. Common non-ART treatments, including antihypertensives, statins (eg, pitavastatin or atorvastatin),[207] metformin, or other medications for obesity and diabetes (eg, SGLT2 inhibitors and GLP-1 receptor agonists), decrease inflammation and address pathophysiological pathways that could lead to geriatric syndromes. However, balancing the risks and benefits of each new medication requires careful consideration in light of growing polypharmacy.

We summarise screening tools for common organ system diseases (table 1). This summary is meant to be illustrative and not exhaustive. It is important to consider tools that have been validated in the relevant health-care setting that are feasible and culturally and linguistically appropriate.

Compared with age-matched people without HIV, older people with HIV face higher rates of cardiovascular disease, including myocardial infarction, heart failure, thrombotic stroke, and sudden cardiac death.[203] Weight gain after ART initiation, resultant diabetes, dyslipidaemia, and hypertension all contribute to metabolic syndrome, which increases the risk of cardiovascular disease. Smoking, alcohol, and cocaine use also increase risk, as does anaemia and depression.[203,208,209] Many tools predict the risk of cardiovascular and cerebrovascular events and can be used for screening in people who are at high risk for HIV. In most cases, these tools were not designed for people with HIV and have been primarily validated in high-income countries. These tools might be less accurate among people with HIV or people living in LMICs.

Hepatic injury is common among people ageing with HIV. Steatosis, acute and chronic hepatitis, fibrosis, cirrhosis, and hepatocellular cancer are associated with HIV infection, and risk for these conditions is increased by alcohol use, smoking, viral hepatitis, malaria, obesity, and metabolic syndrome. Hepatic injury is also associated with ART toxicity and non-ART polypharmacy.[210,211] Common screening tools include the Fibrosis-4 index for liver fibrosis and transient elastography.

People ageing with HIV are at increased risk of acute and chronic kidney disease. Although the initial driver of risk was HIV-associated nephropathy, for which people with African ancestry were more susceptible, HIV-associated nephropathy is uncommon among people on ART with suppressed virus. Factors that now commonly

contribute to excess kidney disease among people with HIV on ART include viral hepatitis, metabolic syndrome, vascular disease, and ART toxicity.[204] Common initial screening tools include measuring serum creatinine, calculating estimated glomerular filtration rate to determine chronic kidney disease stage, and checking for proteinuria in urine.

Pulmonary complications include infectious and non-infectious aetiologies. In addition to excess risk of bacterial pneumonia, tuberculosis, and lung cancer, people ageing with HIV have increased risk for chronic obstructive pulmonary disease, diffusion capacity impairment, asthma, and pulmonary hypertension. Smoking (tobacco or cannabis) contributes to increased risk, as does smoke inhalation and air pollution, including indoor air pollution, which might be common in LMICs, and households where smokers reside.[205,212,213] Common initial screening is based on pulmonary function tests to measure forced expiratory volume in 1 s, forced vital capacity, diffusing capacity of the lungs for $CO_2$, and chest x-ray. For people with extensive smoking history (100 pack-years), depending on resources, CT scan screening might be appropriate.

Osteopenia and osteoporosis are becoming common in people ageing with HIV. Physical inactivity, suboptimal intake of calcium and vitamin D, cigarette smoking, alcohol and opiate use, low testosterone levels, and coinfection with hepatitis C virus are all common risk factors. ART might also be associated with decreased bone mineral density (see where possible, individualise ART regimen). During perimenopause, bone density declines rapidly. The cumulative effect of tenofovir exposure, obstetric history, and breastfeeding is unknown at present, but could be clinically important. In addition to addressing the risk factors shared with other non-communicable diseases—namely, smoking, alcohol, and opioid use and hepatitis C infection—health-care providers should encourage weight bearing exercise and adequate intake of calcium and vitamin D. The decision to treat people with low bone mineral density with bisphosphonates needs to be carefully weighed against the costs, risk of jaw necrosis (which declines with good oral hygiene),[214] and increased polypharmacy. A common initial test is to measure bone mineral density with a dual-energy x-ray absorptiometry scan.

It is important to take a health promotion approach to address shared risk factors for the non-communicable diseases noted above, including smoking, substance use, physical inactivity, hepatitis C virus infection, obesity, hypertension, dyslipidaemia, and diabetes. Primary and secondary prevention of non-communicable diseases can also delay the onset of geriatric syndromes.

### *Minimise harms from polypharmacy*

People ageing with HIV should maintain a list of all their medications. Health-care providers should question all prescription and over-the-counter medications, herbal supplements and treatments, and recreational drugs (including alcohol) that have been taken by the patient. As non-HIV medications and substance use are commonly involved in polypharmacy complications, a complete medication reconciliation is needed at every clinical visit.[144,215] In addition to ensuring that a single health-care provider is monitoring all medications taken, it is also wise for the person to fill their medications at a single pharmacy (where possible). Treatment parsimony, which can emphasise synergistic treatments and question whether symptoms and conditions might be addressed by other means than additional medication, is particularly appropriate.

Polypharmacy is defined as the concomitant use of five or more medications. This threshold is based on the association of polypharmacy with the increased risks of physical decline, cognitive impairment, falls, hospitalisation, and mortality.[215] If ART is included, 89% of older people with HIV experience polypharmacy; if excluded, 60% of people with HIV older than 50 years experience polypharmacy.[216] In patients with multiple comorbidities, polypharmacy is often necessary, but needs to be carefully considered. Increasing numbers of medications increase the risk of drug–drug and pharmacogenetic interactions. When multiple drugs use the same cytochrome P450, P-glycoprotein, and uridine diphosphate-glucuronosyltransferase pathways, the risk of drug–drug interactions increases. Antiretrovirals can influence co-medications (as seen in boosted regimens), or co-medications can alter antiretrovirals exposure (as with strong inducers, such as rifampicin). Protease inhibitors, booster agents such as ritonavir and cobicistat, and non-nucleoside reverse transcriptase inhibitors often interact with commonly prescribed medications, including statins, anticoagulants, and antihypertensives. Moreover, many antiretroviral drugs are either metabolised by or affect cytochrome P450 enzymes, which are also key to the metabolism of many non-antiretroviral medications.

Controlling for the number of medications, older people and people with HIV infection are both at increased risk from polypharmacy.[217] Age-related changes that affect body composition, gastrointestinal function, renal and hepatic clearance, and plasma protein binding contribute to unpredictable prescription and recreational drug exposures in older people. The loss of skeletal muscle and increases in adiposity can lead to a lower lean body mass relative to total bodyweight, thereby reducing the volume of distribution and resulting in higher drug concentrations. The gastrointestinal tract also undergoes physiological changes with age, potentially affecting drug absorption.

Changes in liver and renal function are highly relevant to understanding the metabolism and clearance of medications and effects from alcohol, nicotine, and other substances that can increase toxicity.[218] 30–40% of reduction in hepatic clearance in older adults results from a decline in liver mass and blood flow. Furthermore, lower serum albumin levels result in higher concentrations of

unbound drugs, increasing uptake in peripheral tissues.[218] Reduced glomerular filtration rate results in decreased elimination of drugs excreted through the kidneys.

Age-related changes in pharmacodynamics due to alterations in receptor affinity, receptor density, and the decline of homeostatic mechanisms can cause heightened or diminished drug effects, particularly for cardiovascular and CNS medications. A key example is the reduction in cholinergic receptors in the brain, which increases susceptibility to central anticholinergic adverse effects such as cognitive impairment and delirium among older people with HIV.[219] Commonly used anticholinergic medications include diphenhydramine and most antidepressants (eg, tricyclic, selective serotonin reuptake inhibitors, and selective serotonin–norepinephrine reuptake inhibitors). As people ageing with HIV are physiologically older than people without HIV, their susceptibility to harm from polypharmacy is even greater.

Inappropriate prescribing occurs when the prescription of a medication does not comply with recognised medical standards or is likely to have a higher risk than benefit. Polypharmacy and inappropriate prescribing are closely linked. As the total number of medications increases, so does inappropriate prescribing. Several criteria have been developed and validated to determine whether a prescription is appropriate for an older patient. These include Beer's criteria and the Screening Tool for Older Person's Prescriptions–Screening Tool to Alert Physicians to the Right Treatment criteria.[220,221] Free tools that evaluate the pharmacological interactions of antiretroviral treatments, alcohol and other substance use, natural remedies, and non-antiretroviral medications are also readily available.[222,223]

### Phase 3: focus on patient-prioritised function

Patient priorities should be considered in all phases of care, but these priorities are particularly relevant in phase 3. When prognostic indicators suggest that the person has less than 10 years of survival remaining or in settings that have fewer health-care resources, if a decline in physical or cognitive function is noticed (by care givers, health-care providers, or the person with HIV themselves), phase 3 priorities become central. Although these health declines might be transitory, health-care providers should consider a pivot towards end-of-life planning (if not yet completed) and the geriatric approach of patient-centred care (panel 2).

At this juncture, disease-specific guidelines could be counterproductive, and a more formal geriatric assessment (table 1) is indicated. The focus in phase 3 shifts to maintaining cognitive and physical capacities that matter most to the person, which is particularly relevant in the last two years of life.

#### *Geriatric assessment*

Geriatric assessment is a misnomer, as geriatric assessment includes assessment, specific management plans targeted at underlying causes, and implementation of these plans. Comprehensive geriatric assessment extends the focus from isolated medical concerns to a multidimensional assessment of intrinsic capacity and functional ability that covers psychological, cognitive, social, financial, spiritual, physical, and environmental components.

The WHO Integrated Care for Older People (ICOPE) framework[224] defines intrinsic capacity as the composite of all physical and mental capabilities a person can draw upon. Functional ability is defined as the ability to actually perform valued activities, and encompasses intrinsic capacity and the way in which this capacity interacts with the lived environment.

Even in settings that are rich in health-care resources, there is an insufficient supply of geriatricians. Importantly, geriatric concepts become relevant as multimorbidity increases at any age. It is therefore crucial that HIV health-care providers, community members, and digital resources facilitate the enactment of geriatric concepts of patient prioritised care and maximise functional abilities. The WHO ICOPE model was designed to include empowering community members to assess at least initial components of functional ability. The ICOPE framework has been studied in people with HIV in southeast Asia and is a reasonable measure of age-related concerns in people ageing with HIV.[225]

We prefer to emphasise intrinsic capacity over frailty (ie, a state of increased vulnerability to stressors), because intrinsic capacity emphasises the interaction between physical and mental capabilities and the environment and helps to identify specific targets for intervention. The 5Ms framework of multicomplexity, mind, mobility, medications, and what matters most (in this case, to the person with HIV) is an alternative way of conceptualising geriatric assessment and targeting intervention. Geriatric assessment has been shown to reduce mortality and increase independence.[226]

For people with and without HIV, geriatric assessment includes an assessment of functional ability by domains of cognition, locomotor capacity (mobility), vitality (nutrition), sensory (eg, vision and hearing), and psychological capacity and environmental factors such as social support, support for carers, and incontinence (table 1). Health-care providers should ask about the patient's ability to perform basic life functions, observe their ability to walk easily or to rise from a sitting position, and monitor their overall functional ability. Similarly, health-care providers need to review potential threats to independence as functional ability declines. This assessment includes evaluating vision and hearing; asking about diet, exercise, falls and fractures, perceived cognition, and functional performance; and intervening where necessary. A careful medication reconciliation is essential.

For people ageing with HIV, geriatric assessment should also include screening for recreational drug use,

including alcohol, tobacco, and cannabis, and, where resources allow, laboratory assessment of physiological capacity and expected survival with a validated index such as the VACS index or the VACS–CCI. This examination should include tests for complete blood count; creatinine, aspartate aminotransferase, alanine aminotransferase, and albumin concentrations; CD4 count; HIV-1 RNA; and viral hepatitis (B and C).

Geriatric assessment is often performed by an interdisciplinary team composed of a physician, social worker, and pharmacist, who each contribute their expertise to developing a treatment plan. Access to such a team is uncommon in HICs and almost universally absent in LMICs; it is therefore essential to incorporate key components into primary care and community resources. Simple pathways and means to address these conditions in settings without specialists in ageing have already been proposed by the European AIDS Clinical Society guidelines[227] and WHO ICOPE.[224]

Debate exists regarding when to begin geriatric assessments for people with HIV. Although guidelines and literature on ageing and HIV often consider anyone over age 50 years as older, it is important to recognise that substantial diversity exists in terms of physiological age and expected survival at any given age. As the person ages, monitoring their physiological compromise and functional ability can identify areas to target for intervention, which goes well beyond simply following viral load or CD4 count.

Few guidelines mention the frequency of geriatric assessment. The International AIDS Society–USA guidelines recommend mobility and frailty assessments in patients older than 50 years who have HIV; patients who are frail or pre-frail should undergo assessments every one to two years.[228] The routine assessment of cognitive function every other year is recommended for people older than 60 years who have HIV. It is important to note that ideal intervals for geriatric assessment have not been determined for older adults more generally. For people with multimorbidity or decreased functional ability, annual screening is reasonable. Similarly, assessment after substantial changes in health, such as any acute illness or transitions of care (eg, hospitalisation or transfer to assisted living or a nursing home), should also be considered.

### *Geriatric syndromes*

Geriatric assessment is partly designed to minimise the effect of geriatric syndromes. Geriatric syndromes are associated with ageing, multifactorial in cause, do not fit easily into organ-based categories, and substantially affect functional ability. Common geriatric syndromes among people ageing with and without HIV include cognitive impairment, sarcopenia, falls and fractures, and urinary incontinence. We do not list frailty as a separate geriatric syndrome, as frailty and intrinsic capacity are closely related concepts and this Commission focuses on minimising harmful effects on intrinsic capacity to perform physical and mental functioning by geriatric syndromes. When geriatric syndromes emerge, often in the last 10 years of life or when multimorbidity occurs, a shift in focus is needed from guideline-driven care for individual health conditions to a unified approach focused on maintaining functional ability.[229]

Once driven by HIV-associated neurocognitive disorder, cognitive impairment among people ageing with HIV who are virally suppressed is influenced by many factors. Most of these factors are also relevant among people ageing without HIV, including ongoing substance use, vascular disease, age-associated neurodegenerative disorders, and polypharmacy (particularly anticholinergic medications and other neurocognitively active medications), and can be exacerbated by vision and hearing loss, social isolation, and depression.[230] Generally, women are at greater risk than men for cognitive compromise as they age, and women with HIV are at even greater risk than men with HIV.[231] The role of viral reservoirs in the CNS should be considered, but is not the most common cause.[232] The first step in addressing neurocognitive compromise is considering modifiable factors, including medication.

Sarcopenia is the age-associated loss of muscle mass that results in progressively decreased strength and physical function.[233] Sarcopenia is thought to be due to the atrophy of muscle fibres, which are replaced with fat. Women are at greater risk of sarcopenia than men in the general population, but it remains unclear as to whether this is true among people with HIV. Nevertheless, people ageing with HIV are at greater risk of sarcopenia than age-matched people without HIV.[231,233] Regular physical exercise is the most effective treatment.

Urinary incontinence or the involuntary loss of urine is common in older adults, particularly among people who are postmenopausal, and is also prevalent among people ageing with HIV.[231] The most common form is stress incontinence, which occurs when increased pressure is put on the bladder due to activities such as coughing, sneezing, or physical exercise. Although not a life-threatening condition, stress incontinence can be addressed with pelvic floor exercises, bladder training, and surgery, and has a large effect on quality of life.

Although the risk of falls that require medical attention increases in all people as they age, women are at an even greater risk, as are people with HIV experiencing polypharmacy, neurocognitive active medications, substance use, cognitive impairment, neuropathy, and physical inactivity leading to deconditioning.[129] Some forms of urinary incontinence (eg, rushing to use the toilet to avoid leakage or urge rushing) can increase the risk of a fall. Sarcopenia and osteoporosis increase the risk of debilitating injury in the event of a fall. It is essential to address modifiable risks of serious falls.[129] The strongest predictor of a clinically significant fall is a history of previous falls,[129] and health-care providers

should ask whether the patient has previously had a fall to determine who might require intervention.

*Palliative care*

Palliative care is one of the most recognisable forms of people-centred care. Offering palliative care to people with HIV has sometimes been perceived as giving up at the end of life. However, palliative care is not limited to the end-of-life period, but can be provided at any stage of serious illness, alongside curative treatments. Palliative care provides focus on and expertise in managing symptoms such as pain, nausea, fatigue, and shortness of breath, and addresses emotional and spiritual distress. Each year, half of the people living with HIV without access to treatment and 15% of those accessing ART experience serious health-related suffering, which is often most pronounced in the last year of life.[234]

Palliative care calls for an interdisciplinary and culturally sensitive approach to ensure that people with HIV and their families are at the centre of care and, as far as possible, guide direct care delivery. As in patient-centred care generally, palliative care calls for a focus on establishing and reaching personalised goals, providing holistic care that includes a care plan for physical, psychological, social, spiritual, and practical concerns. For example, it is important to address religious, spiritual, or existential concerns; support and care for families so they can give care; and involve traditional healers or other providers of complementary therapies.[235] In addition to pain and symptom management and the provision of essential medicines, care could include personal care, building a wheelchair ramp, or shopping for food.

*Plan ahead for transitions in care and end of life*

For people with HIV, transitions in care are especially vulnerable times (eg, from home to hospital or from independent living to assisted living or nursing home placement). Potential exacerbations in illness should be anticipated and prepared for as the burden of physiological injury, multimorbidity, and functional compromise on this population grows. Nevertheless, unexpected crises occur, and can be managed when caregivers are accessible and can provide oversight during transitions. Care managers should monitor patients who are in hospital and ensure that discharge plans are established and carried out effectively. It is crucial to avoid ART disruptions during these transitions.[236]

Care should be closely aligned with the person's priorities, which could change. Realising individual priorities and goals for care requires frequent and effective communication, which is a core component of palliative care. It is also crucial to help people and their loved ones to plan ahead. Understanding the family or chosen family's system and the person's values is key. Using existing legal documents, including advance directives, and other methods of documenting the person's wishes will help, along with the identification of a trusted person with authority to make decisions on the person's behalf when they are incapacitated (health-care proxy).

For people who are nearer the end-of-life, the level of care should increase commensurate with need. In most cases, it makes sense to continue ART to prevent symptoms associated with unsuppressed virus. This step will help carers to understand the relevant signs and symptoms and the supportive measures that can ensure a peaceful transition and as easy a death as possible. Support for carers and loved ones should continue during the bereavement period as needed and to the extent that resources allow; community-based resources should be included in bereavement support.

## Special populations

*Women*

Women represent the majority of people living with HIV globally, yet, despite efforts, remain under-represented in most clinical trials, especially at older ages.[237] Most HIV care guidelines have focused on women of reproductive age, emphasising pregnancy, birth, and lactation, with less attention given to women ageing with HIV.[59,182] The literature on women living with HIV beyond their reproductive years is sparse.[238,239] Women are often not considered nor perceive themselves to be an at-risk population, despite prevalent inequities and gender-based violence that can put them at risk of HIV acquisition. Consequently, once women pass their reproductive years, they often have fewer opportunities to be tested for HIV.[240]

According to the UNAIDS 2024 report, although mortality attributed to advanced HIV disease has decreased across all risk groups in the Latin American region, it has concerningly increased among women in Costa Rica, El Salvador, Mexico, Panama, Paraguay, and Peru.[241] Women in these countries are less likely to seek out HIV testing, access prevention counselling, use PrEP, or insist on the use of condoms.[241]

*Migrants*

There are several typologies of older migrants, including: (1) migrants who aged in the host country, have long settlement histories, and face issues of pension access, legal recognition, and access to care; (2) people who return to their country of origin after working abroad and face fragmented social protection systems and health-care gaps, especially when their pension rights are not portable; (3) older adults who migrate later in life, usually for family reunification, care needs, or economic reasons, and face legal or residency challenges and are often dependent on family networks for support; (4) people who are displaced from their country due to war, persecution, natural disaster, or famine; and (5) older people that go back to rural areas after working in urban areas most of their lives or older people that move to urban areas to live with their children. These internal migrants could also face an absence of care or ART discontinuation, as they might not be familiar with the

health-care systems in the destination areas, despite moving within their country.

Older migrants often have poor access to health services, especially those without regularised status. This inaccessibility is aggravated by bureaucratic obstacles, absence of portability of entitlements, and age-related vulnerabilities (eg, chronic diseases or reduced mobility). Although some countries (eg, Uruguay and Argentina) offer inclusive health-care access regardless of migration status, other countries present barriers tied to documentation or nationality. These barriers can result in an increased risk of reactivation and long-term complications of infectious diseases among migrants coming from areas with higher endemicity for conditions such as tuberculosis, strongyloidiasis, and chagas disease. The psychosocial stressors of ageing in displacement (eg, loneliness, loss of cultural belonging, and fragmented social networks) can have mental health repercussions that are often overlooked.

*People who are transgender, gender diverse, or non-binary*

The ageing process in people with HIV who are transgender, gender diverse, or non-binary presents unique and understudied challenges. These populations face substantially reduced expected survival outcomes due to high rates of violence, discrimination, and adverse social determinants of health.[242] For people who reach older than 50 years, there have been few studies on the pharmacological interactions between ART and gender-affirming hormone therapy, particularly feminising hormone therapy.[243] The effect of gender-affirming hormone therapy on long-term cardiovascular risk in people who are transgender remains under-researched, and longer-term follow-up, more detailed measurements of gender-affirming hormone therapy (ie, formulation, dose, and duration of exposure), and larger sample sizes are needed to understand these relationships.[244] Early evidence has signalled unfavourable lipid changes and an increase in Framingham 30-year cardiovascular risk score among transgender men; higher haematocrit and increased blood pressure could also influence an increased risk of cardiovascular disease.[245] An increase in cardiovascular risk in transgender women using gender-affirming hormone therapy could be influenced by higher fat mass, insulin resistance, pro-coagulation changes, and lower high-density lipoprotein cholesterol.[246] People who are transgender, gender diverse, or non-binary remain under-represented in clinical trials, resulting in an absence of evidence-based guidelines for their long-term health care.[185,247] Additionally, people who are transgender, gender diverse, or non-binary could undergo body modification procedures (eg, silicone or other soft-tissue fillers), which might introduce further health complications that remain poorly characterised in the context of ageing with HIV.[248]

Beyond ART and gender-affirming hormone therapy interactions, little is known about the prevalence and severity of age-related comorbidities in older people who have HIV and are transgender, gender diverse, or non-binary. Conditions such as cardiovascular disease, osteoporosis, and metabolic disorders are concerns for people living with HIV in general, but it remains unclear whether people who are transgender, gender diverse, and non-binary face a heightened risk due to hormonal and lifestyle factors.[243,249] Moreover, social determinants—including barriers to health-care access, economic instability, and stigma—might further exacerbate health disparities in this ageing population.[247,250] Without targeted research and inclusion in longitudinal studies, the medical community remains ill equipped to provide optimal care for people ageing with HIV who are transgender, gender diverse, or non-binary.

*Indigenous people*

Numerous studies have characterised HIV among Indigenous populations, both in HICs and in LMICs.[251] Although a scoping review has highlighted particular challenges among Indigenous populations, strengths and opportunities related to culturally tailored community care, self-determination, and solidarity have been noted.[252,253] Little has been written specifically about HIV among older Indigenous adults, but a few studies have noted HIV among Indigenous people older than 40 years and sometimes in Indigenous people older than 50 years.[252] Care systems for older Indigenous people need to be sensitively designed and build on cultural strengths, and should show a deep understanding of Indigenous perceptions of disease, sexuality, and wellbeing.

*People who are incarcerated*

Currently, one in four adults who are incarcerated in the USA are older than 50 years. Adults who have been formerly incarcerated are approximately 10–15 years older physiologically than people who have not been incarcerated, and develop geriatric syndromes earlier in their life course.[254] In part due to legal systems in which people with HIV are prosecuted under laws that criminalise their actions (often related to exposure rather than actual HIV transmission), the prevalence of HIV in the criminal justice system is substantially higher than in country-level populations. These vulnerabilities likely add to those due to HIV, making those who have been incarcerated at particularly high risk of adverse ageing.

## Systems of care

Possibly the single greatest challenge to supporting healthy ageing with HIV is transforming current systems of care from vertical disease-specific programmes to well integrated health-care service delivery networks. For our purposes, a system of care can be described as an organised, inclusive framework of health and social services that delivers a continuum of coordinated interventions in a network of connected institutions to people across their lifespan, encompassing healthy lifestyle

promotion, disease prevention, acute care, rehabilitation, chronic disease management, and supportive services.[255] Such a system can include centralised points of care, distributed community-based networks, and support for supervised or self-directed care practices, preferentially personalised to the needs of the person.

Historically, the HIV response was built around vertical programmes that focused on diagnostics, antiretroviral therapy, and viral load suppression.[256] This design proved indispensable in rapidly scaling access during epidemic growth and drastically reducing HIV-related morbidity and mortality. These vertical structures were originally designed to target people who had been most affected, with a primary focus on viral containment and survival rather than a holistic approach to wellness and longevity. As a result, many health-care systems—especially those in settings with low health-care resources—are only now beginning to integrate chronic disease screening and treatment into HIV services.

In practice, integrated health networks consist of multiple vertical services nominally connected through referral pathways. These services often remain fragmented, requiring users to navigate physically distant facilities that have separate queues, forms, schedules, and insufficient data-sharing agreements, particularly in countries that do not have electronic medical records or universal health systems. Each referral step often introduces additional logistical and bureaucratic friction, frequently involving repeated travel, unreimbursed expenses, duplicated testing, and extended waiting periods.[257] For older adults living with HIV who might have restricted mobility, lower autonomy, or financial constraints, these obstacles can become prohibitive, leading to disengagement and dangerous gaps in care. These health-care systems stand to benefit substantially from a more integrated and differentiated approach.[258]

Although the management of uncomplicated HIV is increasingly straightforward, it is unlikely that any singular care provider is an expert in all care domains that are relevant to ageing well with HIV. In some countries, including the USA, primary care is typically provided by an HIV specialist (often an infectious disease physician). These care providers might be skilled at managing health conditions that are common in younger people with HIV (eg, mental health conditions, substance use, and gender affirming care), but much less experienced at managing conditions associated with ageing. In the UK, Canada, and Australia, generalist physicians provide HIV care and might be more experienced with ageing, but might not appreciate how HIV can interact with ageing. In Honduras, El Salvador, Guatemala, and Bolivia, HIV care is provided in specific HIV clinics that do not have the capacity to provide care domains beyond that required for uncomplicated HIV. As the population of people with HIV becomes increasingly older, and as capacity allows, it makes sense for health-care providers to undergo additional targeted training. In settings where additional training is not feasible, coordinated referral might be more appropriate. If management is to be based on referrals, at a minimum, health-care providers need to learn how to determine when a referral is indicated.

Complexity-competent approaches could better link or integrate existing HIV programmes into broader chronic disease management, or develop specialised HIV services that incorporate geriatric expertise and wellness programmes.[255] In settings with low health-care resources, digital and data-driven innovations can help to extend care outside of the clinical setting and empower people with self-monitoring tools, guide health-care workers with standardised protocols, and enhance community-based follow-up. However, digital tools need to be paired with offline or SMS options to mitigate the digital divide seen in many LMICs. Although challenging to implement, these complexity-based models promise more comprehensive care coordination and greater efficiency—goals that are increasingly urgent as more people with HIV reach older age.

The key challenge lies in ensuring feasibility and sustainability. Health systems originally built around vertical models or age-based geriatric thresholds need to evolve to meet the multifaceted needs of people with HIV, particularly in contexts where financial and human resources are constrained. We explore practical strategies—ranging from reconfiguring referral pathways to incorporating community resources to implementing digital innovations—that can strengthen the continuum of care. By charting realistic pathways, care can move beyond only survival outcomes toward comprehensive, long-term wellbeing for an ageing population.

### Demand and resource-based diagonalisation of health systems

In contrast to vertical health systems, horizontal systems are integrated and demand-driven, using resource-sharing and primary care services to address a broad range of health needs (figure 5). Geriatric care exists in many settings as a horizontal system, addressing a wide range of ageing-related conditions to improve quality of life and functional health for older adults.

Diagonal health systems exist on a gradient between these two frameworks, leveraging vertical programmes to scale-up primary health-care or other horizontal systems. In the early 2000s, Sepúlveda and colleagues introduced the diagonal approach to health system reform in Mexico.[259] This approach—described as the proactive and supply-driven provision of highly cost-effective interventions spanning health clinics and homes—leverages elements of vertical programmes to strengthen health systems. For example, interventions for vitamin A supplementation, oral rehydration therapy, and deworming were incrementally built onto vertical immunisation programmes as a means of scaling up primary health care.[259] When applied to HIV care, a diagonal approach allows for the integration of services

based on epidemiological burden and available programmes,[260] offering a pragmatic pathway for LMICs to address the increasing incidence of chronic diseases and multimorbidity among people with HIV.[261] In the field of HIV care, diagonalisation can be harnessed to integrate HIV services with screening for diseases such as hypertension, diabetes, hypercholesterolaemia, mental health conditions, and early markers of functional compromise. Indeed, pilot initiatives in sub-Saharan Africa show that integrating HIV clinics into broader chronic care services can improve adherence and reduce duplicative visits.[262] Similarly, a 2021 policy review in east Africa showed that HIV programmes were evolving to integrate non-communicable disease services.[263]

Diagonalisation of systems for people with HIV can be achieved in two ways: either by broadening existing vertical HIV resources through the integration of services (dedicated care) or by strengthening referrals to and provision of HIV interventions in services shared for the general public (designated care, figure 5). For example, Kenya's Academic Model Providing Access to Healthcare is a dedicated HIV and chronic disease service,[264] whereas South Africa's Ideal Clinic framework is a designated, referral-driven model.[265] To ensure that this process is sustainable, these choices could be seen on a gradient that can be adapted to both local demand and available resources. In contexts with high HIV prevalence and well established treatment programmes (and consequently, contexts with an expected growth of people ageing with HIV), a dedicated service might be more appropriate, where an expanded vertical system incorporates specialised geriatric and other complementary services. In this scenario, creating a dedicated HIV–geriatrics subspecialty could address the unique needs of people ageing with HIV. By contrast, in settings with lower HIV prevalence, it could be more practical to focus on strengthening referral pathways between existing HIV clinics and other health-care services, rather than building new specialised structures and incorporating foundational HIV services in the general system (eg, the provision of HIV information and testing, PrEP, and PEP). A trial in South Africa comparing the efficacy of dedicated versus designated delivery of mental health care had similar outcomes, indicating that the choice is largely a question of resources and preference.[266] However, evaluation of the cost-effectiveness of these approaches in settings with low health-care resources is rare.[267]

Although neither approach is simple to implement in settings with low health-care resources, digital tools can help reduce referral burdens and enhance individual self-management. For instance, mobile applications and telemedicine platforms can empower older adults to monitor their conditions at home and enable fragmented systems to share clinical information, thereby improving overall continuity of care. The promise of digital technologies—even in settings with low health-care resources—emerged over a decade ago with ART self-management programmes based on telephone SMS systems, such as the WelTel Kenya1 trial[268] and the Cameroon Mobile Phone SMS programme.[269] However, digital interventions designed for people ageing with HIV are exceedingly rare. A systematic review of more modern smartphone interventions for chronic disease management in older adults suggest promising results, although evidence remains sparse.[270]

Similarly, in regions where HIV prevalence is low and where clinicians might not routinely treat older adults with HIV, digital education and decision-support tools can help bridge skill gaps. These tools ensure that health-care workers remain updated on best practices for HIV management in older populations, even where patient volumes are small. Ultimately, an adaptable and gradient-based approach that is supported by digital innovations can offer a pragmatic way to shape diagonal care models for people with HIV, regardless of local prevalence or resource constraints.

## Digital health and AI

As digital health and AI capabilities have grown, these technologies are evolving from a supporting role into an

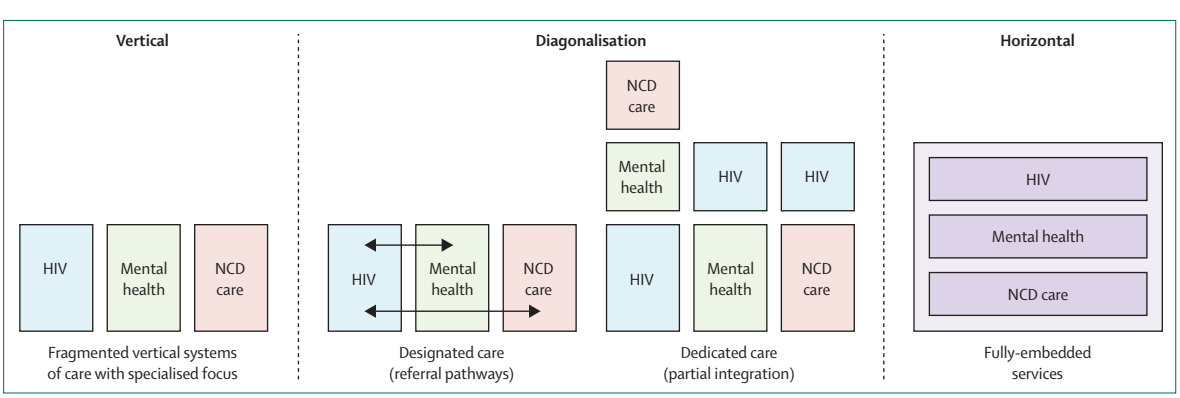



***Figure 5:*** **Diagonalisation of health care**
Vertical systems of care target people who have been most affected by HIV, with a focus on HIV treatment. Horizontal systems are integrated and demand-driven, using resource sharing and primary care services to address a broader range of health needs. Diagonal systems can either expand vertical programmes to include primary care or add expertise in HIV management to an existing horizontal system. NCDs=non-communicable diseases.

autonomous system of health. As shown by WHO guidelines on digital health interventions,[271] telemedicine, remote diagnostics, and virtual monitoring can now deliver, document, and coordinate care along a self-contained continuum of services, transcending traditional facility-based boundaries. In contrast to services that are bound by the scope of the specific qualification of the health-care worker, digital health and AI can combine disparate human skillsets and act as a coordinating layer for existing services.

Generative AI systems (including large language models and specialised chatbots) have reshaped how crucial health information is accessed and delivered.[272] Unlike traditional single-purpose digital tools that target specific tasks, generative AI systems can address a broad range of needs, from preventive advice and diagnostic support to treatment planning and mental health counselling. By functioning as inherently horizontal technologies that bridge patient knowledge gaps, AI-driven tools have the potential to empower people and their caregivers to manage their own care more effectively, particularly in contexts marked by clinical complexity or poor health-care access.[273,274]

Recent pilot programmes have highlighted the potential of chatbots to enhance the continuity of care in diverse populations, including older adults. A small-scale US study found that older adults with multiple chronic diseases who used a chatbot for medication reminders and symptom tracking reported improved self-efficacy and more consistent follow-up visits.[275] These findings suggest that AI not only enhances patient engagement but can also improve communication channels between clinicians and patients, potentially easing the strain on overburdened health-care workers.

Beyond informational support, AI-driven applications are being used to detect and manage age-related conditions more proactively. Several projects have explored passive monitoring of cognitive function through keystroke pattern and language analysis, noting correlations between subtle shifts in typing behaviour and early cognitive decline.[276] Similarly, speech-based tools have shown promise in identifying cognitive decline and other geriatric syndromes, substantially reducing diagnostic barriers in settings that do not have access to geriatric specialists.[277] Crucially, these technologies do not rely on active engagement with an application or smartphone literacy, meaning that they are potentially better adapted to bridge the age-related digital divide. Mental health chatbots, which were initially deployed to combat stigma and provide psychosocial support among younger populations with HIV, are now being adapted to address loneliness, depression, and anxiety in older adults, delivering real-time emotional support without requiring clinic-based interventions.[278]

Over two-thirds of the world's population subscribe to mobile services, with 73% of all mobile subscribers living in LMICs, showing that mobile phone accessibility is high.[279] Leveraging existing electronic health records to deploy decision-support modules aligns well with WHO-recommended digital decision support.[280] Although digital health approaches (eg, mobile phone devices, telemedicine, and digital tracking) offer great advantages, there are barriers to their widespread use, such as uneven access to smartphones, internet connectivity, and digital literacy. Furthermore, the age-related digital divide is a barrier to active engagement with an application. The accessibility and reliability of AI tools have raised crucial concerns. Many advanced large language models depend on robust internet connections and proprietary cloud hosting services, which can be prohibitively expensive or simply unavailable in remote areas. Open-source alternatives (eg, DeepSeek and LLaMA) mitigate some of these challenges by allowing models to be downloaded and customised locally, although hardware requirements and data-governance questions persist. In low-bandwidth environments, SMS-based workflows (such as the one deployed by Jacaranda Health in Kenya) show that chatbots can still function effectively on basic feature telephones, and voice interfaces can help to address literacy barriers and vision impairments that are more prevalent in older adults.[281]

Further, the black box nature of generative AI has also drawn scrutiny. Although chain-of-thought or retrieval-augmented approaches can improve transparency by revealing partial reasoning steps, studies consistently show that AI models can still fabricate evidence or hallucinate data, emphasising the need for stringent clinical oversight.[282] Furthermore, realising the potential of digital health and AI technologies requires the careful alignment of these technologies with local epidemiological, linguistic, and cultural contexts to avoid misguidance, inequitable inaccuracy, or exclusion.

Recognising these barriers should not discourage efforts to explore the use of digital health technologies, but instead underscores the urgency of initially validating these tools and then embedding mechanisms for ongoing validation in routine use. Despite uncertainties, the robust adoption of generative tools in health care is well underway. The 2026 American Medical Association Physician Survey on Augmented Intelligence was conducted from January 15 to February 2, 2026, and surveyed 1692 physicians across specialities, practice settings, and career stages to assess their adoptions, perceptions, and anticipated impacts of AI in medical practice.[283] Over 80% of physicians respondents confirmed that they used AI in a professional context at that time, which is double the number reported in the 2023 American Medical Association's previous AI survey.[284] Similar trends are emerging globally, often outpacing regulatory frameworks.[285]

The Massive Open Online Validation and Evaluation framework exemplifies how a global community of clinicians can probe these chatbots across linguistic and

For more on the **Massive Open Online Validation and Evaluation framework** see https://jointhemoove.org/

epidemiological contexts. Seeking critical feedback and expert consensus from health-care providers can not only reinforce vigilance and critical reflection during real-world deployment, but also provides a sense of co-ownership and shared stewardship of the governance of these tools.

As large language models evolve to better handle local adaptation and to articulate their reasoning processes, they could serve as a powerful integrative layer in diagonalised health systems, particularly for older adults with HIV who require multifaceted support. However, realising this potential necessitates robust infrastructure that ensures access, inclusive design, and policy frameworks that guarantee sustainability, data privacy, and clinical accountability.

The digital determinants of health (eg, literacy in information and communication technologies and access to equipment, broadband, and the internet) have become more important as digital health technologies becomes more prevalent. The WHO global strategy on digital health[286] underscores the need to ground digital health foundations within national strategies and work with different sectors and stakeholders at all levels.

## Realities of integrated HIV care models

Previous studies have highlighted both the opportunities and challenges of the integration concept, which challenges health-care systems to treat the whole person rather than focusing on individual diseases.[266] Under this person-centred framework, HIV care delivered through accessible and universal primary care systems would integrate interventions from other health programmes, including sexual and reproductive health, tuberculosis, mental health, and non-communicable diseases. Such integration could improve quality of care and potentially optimise the use of finite resources.[287] Although unprecedented financial shortfalls in 2025 have led to drastic changes in HIV programming in LMICs, 25 of 60 countries included in the 2025 UNAIDS report have found ways to increase HIV spending from domestic resources in 2026.[45] HIV care infrastructure (including electronic health records) and reporting tools provide a strong foundation upon which to build chronic disease management systems.[288]

In practice, integrated care can either ingrate HIV services into other health-care services or vice versa (tables 2 and 3, figure 2).[289–305] The studies in tables 2 and 3 generally reported improved care outcomes.[262] Other health-care service integrations into HIV services are typically well suited to high HIV prevalence areas (eg, chronic disease care incorporated into dedicated HIV clinics), and HIV service integrations into other health-care services are typically better adapted to low prevalence settings (eg, HIV screening integrated into maternal and child health or primary care programmes).[306] Key enablers of integration include person-centred

| | Setting | Type of study | Sample | Key findings |
|---|---|---|---|---|
| HIV testing in primary care (2015)[289] | General practices (London, UK) | Cluster RCT | 40 participating general practices and 83 435 participants | Increased new HIV diagnoses versus standard care; increased cost-effectiveness due to earlier diagnosis |
| HIV services in rural primary care facilities (2013)[290] | Rural health centres (Kenya) | Pilot or quasi-experimental | 343 participants | Increased patient satisfaction and privacy (decreased wait times and stigma) |
| Facility-based HIV self-testing in outpatient departments (2020)[291] | High-burden outpatient departments (Malawi) | Cluster RCT | 5885 outpatients | Increased HIV testing uptake; feasible in large-volume outpatient department settings |
| Routine HIV testing in adult emergency departments (2010)[292] | Urban emergency department (USA) | Implementation pilot | 25% of 28 043 eligible patients completed HIV testing in the opt-out phase; 0·8% of 29 925 eligible patients completed HIV testing in the diagnostic phase | Increased detection of undiagnosed HIV; earlier linkage to HIV care through emergency departments |
| Routine HIV testing in adult emergency department (2016)[293] | Urban emergency department (USA) | Implementation pilot | 46 385 screening tests performed; 0·5% confirmed HIV-positive | Increased detection of undiagnosed HIV; earlier linkage to HIV care through emergency departments |
| HIV testing in inpatient wards (2015)[294] | Adult inpatient wards (Malawi) | Prospective implementation | 3154 inpatients | Increased acceptance with provider-initiated approach; decreased missed opportunities for diagnosis; counselor-initiated testing increased rates of testing by 79% |
| HIV testing integrated into mobile health interventions (2025)[295] | 21 separate studies including the USA, China, South Africa, Brazil, Malaysia, Kenya, and Zimbabwe | Systematic review | 12 studies focused on men who have sex with men, four on general adult populations, three on cisgender men and youth, one on female sex workers, and one on women | Mobile health approaches appeared a promising way to expand access to HIV self-testing |
| HIV testing in outpatient mental health care (2011)[296] | Community mental health facilities (South Africa) | Feasibility and cross-sectional | 514 patients, with 467 patients available for outcome analysis | Increased testing among people with mental illness; coordinated referral for antiretroviral therapy following diagnosis |
| HIV testing at home-based visits (2010)[297] | Rural community households (Uganda) | Implementation and mixed methods | 264 966 people accepted testing; 4·3% were positive for HIV | Of people who tested positive, 90% had never been tested before; 12% of people tested were older than 49 years |

RCT=randomised controlled trial.

***Table 2:*** **Studies the integration of HIV care into other health services**

programmes, effective collaboration, a skilled and incentivised workforce, supportive institutional structures, dedicated resources, and strong political leadership. Telemedicine, particularly after COVID-19, has also emerged as a key facilitator.[307,308]

Substantial barriers persist, including a perceived increase in costs, inadequate resources (eg, infrastructure, medicines, and trained professionals), weak data systems, and fragile health financing mechanisms.[304,309] Standardising the documentation and reporting of integration approaches—especially regarding access, coverage, continuity of care, and service quality—is essential to ensure equitable outcomes across diverse settings.[310]

Questions also remain over how far to integrate systems without compromising the quality of specialised HIV care. Some fear that broadening clinic mandates might dilute HIV-specific expertise or overwhelm existing staff. Resource constraints are also present; in many LMICs, prime bottlenecks include shortages of pharmaceuticals for chronic diseases, insufficient diagnostic labs, and weak supply chains.[311] As a result, context-specific integration is often recommended, which involves scaling up integrated services gradually and in alignment with local epidemiology and available financing.

### Implementing an essential package of services for people with HIV

An essential package of services for people with HIV needs to prioritise complexity over specific services dictated by chronological age, reflecting the multifaceted challenges posed by ageing in this population and the need to extend care outside of clinical settings (panel 2). In settings with low availability of health-care resources, implementing such a package requires careful adaptation. Task sharing involving the community, coupled with targeted training, can mitigate workforce shortages in geriatrics and mental health without compromising quality of care.[266] Governments and donors should integrate costs for chronic diseases (including mental health services) into national HIV budgets or broader universal health coverage frameworks.[261] Phased implementation strategies allow for iterative refinement before scaling, and cost-effectiveness analyses can provide evidence to support investments. Complexity-based care aligns with the evolving needs of people ageing with HIV and could reduce hospitalisations and late-stage complications, enhancing long-term sustainability.

### Empowering community approaches

Community-driven care has been integral to global HIV responses, particularly in sub-Saharan Africa. Peer

| | Setting | Type of Study | Sample | Key findings |
|---|---|---|---|---|
| Cardiovascular risk screening in HIV clinics (2020)[298] | Public HIV clinics (Uganda) | Modelling and implementation | NA | Decreased 10-year cardiovascular disease risk with hypertension and diabetes screening; increased cost-effectiveness if scaled |
| Mental health screening in HIV clinics (2018)[299] | Urban and semi-urban ART clinics (Malawi) | Implementation and feasibility | 2067 people consented, 96% were screened, and 25% had mild to severe depression | Increased onsite management of depression and alcohol; increased ART adherence |
| NCDs screening in home-based HIV testing (2018)[300] | Community households (home-based; South Africa) | Cost-effectiveness and programme evaluation | NA | Decreased cost versus standalone NCDs screening; increased early detection of hypertension and diabetes |
| Primary care-based mental health in HIV care (Friendship Bench; 2016)[301] | Primary care clinics (Harare, Zimbabwe) | Randomised controlled trial | 573 people with common mental disorders | Increased improvement in depression versus usual care (typical care provided) for mental health; facilitated ART linkage for people with HIV and comorbidities |
| Geriatric assessments in HIV clinics (2019)[302] | Urban HIV clinics (USA) | Observational and quality improvement | 76 patients | Increased detection of frailty or cognitive issues; increased patient satisfaction |
| Tuberculosis in HIV care (2015)[303] | District hospitals (Kenya) | Programmatic integration | 501 patients with HIV and tuberculosis | Integration of tuberculosis and HIV services enhanced uptake and reduced delay in instituting preventative tuberculosis treatment and ART |
| NCDs services in rural HIV clinics (2023)[304] | Rural clinics with low access to health-care resources (Ethiopia) | Prospective cohort pilot | 15 key informant interviews with health-care providers and managers | Increased detection of hypertension and diabetes; feasible nurse-led triage (although supply chain limits) |
| NCDs screening in community-based HIV campaigns (2019)[305] | Urban and peri-urban community camps (India) | Pilot and cross-sectional | 6994 participants screened | Increased detection of undiagnosed hypertension and diabetes; feasible door-to-door approach |

ART=antiretroviral therapy. NA=not available. NCDs=non-communicable disease.

*Table 3:* **Studies evaluating the integration of other health services into HIV services**

support networks can increase access to information, promote HIV testing and prevention options, distribute certain medicines, facilitate adherence and re-engagement, reduce stigma and mental health challenges (particularly for people with HIV), and identify early signs of frailty or functional decline.[16] In many regions, community health workers and community organisations can deliver home-based services, which could be adapted to include screening for non-communicable diseases and mental health conditions and basic clinical assessments for older adults who might not have access to traditional health-care facilities (panel 1).

However, a consistent challenge is the potential overextension of community cadres in task-sharing models. The expansion of responsibilities can strain workers who are already responsible for HIV testing and ART adherence support. To mitigate this strain, simplified screening protocols and accessible digital tools can guide community health workers in identifying red flags and making timely referrals.[312] In-service training and supervision can also reduce burnout and strengthen skills. Strong referral mechanisms should link community services with higher-level clinical settings, ensuring continuity for complex presentations.

Within this broader community ecosystem, traditional medicine has a notable role. Across all settings with differing levels of access to health-care resources, traditional medicine is an important source of care, including for people with HIV facing chronic pain or psychological distress,[313] and is often their initial point of entry to the health-care system. Although some herbal remedies and spiritual practices can conflict with biomedical treatment, collaborative approaches can improve trust and early referral rates. Training traditional healers to identify HIV-related symptoms (eg, cognitive changes or non-response to traditional approaches) can expedite people's linkages to care.[255] Global policy frameworks and practical approaches for integrating traditional healing into national health systems have been recommended to help ensure that older people with HIV receive both culturally acceptable and clinically effective care.[314] Ensuring the safety and evidence base of traditional medicine is crucial. Standardised referral systems need to clarify when people should seek biomedical treatment.[259] Partnerships between formal health facilities and traditional healers can enhance cultural competence and reduce stigma, but requires ongoing research, capacity building, and ethical oversight.[256]

### Policy implications and financial sustainability of integrated care

Shifting from vertical HIV programmes to integrated, complexity-encompassing care requires clinical innovation, system adaptability, and sustainable financing.[261] ART scale-up has been largely funded by external donors, national governments, and philanthropic actors, often with narrow mandates. Expanding these mandates to include mental health care, non-communicable disease management, and palliative services will strain budgets. However, economic modelling suggests that the early detection and intervention of comorbidities can avert expensive hospitalisations or late-stage complications, rendering integrated models cost-effective in the long run.[266] These short-term costs are therefore better positioned as long-term investments.

Public–private partnerships, pooled procurement, and cross-programme resource-sharing offer potential avenues to finance a broader care package for people ageing with HIV.[261] Digital health technologies, although incurring upfront costs, could reduce longer-term expenses by streamlining visits and improving adherence.[312] Ultimately, advocating for complexity-based and digitally enabled care requires robust health economic studies that highlight how comprehensive management can be cost-effective.

Complexity-driven care models are designed to deliver care in a way that accounts for the diverse needs of people ageing with HIV. Delivering complexity-driven care requires a multidisciplinary approach that includes primary, specialised, and social care delivered across the health system. Complexity-driven care models require flexibility to adapt to the evolving needs of patients. The intended benefits are improved outcomes due to better management, and increased patient and health-care provider acceptance. There is also an emphasis on early intervention and health promotion to prevent disease progression.

An example is WHO's Integrated People-Centred Health Services (IPCHS) framework,[315] which promotes reorienting care models to meet individual and community needs across the life course. In 2016, WHO member states approved—with overwhelming support—the resolution on strengthening integrated, people-centred health services, which supports the IPCHS framework. During the adoption of this framework, it was noted that longer lifespans and the growing burden of long-term chronic diseases that require complex interventions over many years are putting increased pressure on health systems globally. Another example aligned to the specific needs of people with HIV was the consensus statement on person-centred care in the HIV response, which underscores the essential role of community health workers.[316]

Developing policies to support complexity-encompassing care models is challenging. Existing methods for developing evidence-informed policies were originally designed for single and well-defined clinical interventions. These approaches are often inadequate for responding to highly context-dependent public health and health system interventions, which require the nuanced consideration of local factors and system-wide dynamics. Recently, methods have been developed to support evidence assessment and recommendation

formulation for complex interventions.[317] This field is still emerging and evolving. As new evidence becomes available, innovative methods to address complexity in evidence reviews and guidelines need to be continuously assessed and refined.

## Conclusion

Since effective antiretroviral therapy became available, the global community's understanding of the multifaceted relationships between HIV infection, disease progression, and treatment and comorbid disease has expanded our understanding of ageing with and without HIV. As HIV prevalence increases in older adults, HIV incidence is also likely to increase among older adults. Public health HIV prevention messages about safe sex, HIV screening, and early HIV diagnosis need to be better tailored to older people. People older than 50 years are 200–400% more likely to experience a delayed HIV diagnosis and treatment than people younger than 50 years, which can endanger their health, prolong the period in which their viral load is detectable, and expose other people to infection. Older people might face synergistic stigma from ageing and HIV infection and therefore avoid HIV testing, even when they suspect that they have HIV. Health-care providers should ask older people about sexual health, consider HIV as a possible explanation for symptoms commonly associated with acute or chronic HIV infection, and ask about substance use.

If healthy ageing is to be achieved for the increasing number of people living with HIV, HIV care needs to be reconfigured in multiple ways. Prevention and screening efforts should be extended and tailored to older adults. Regardless of age at HIV diagnosis, care should be initiated with a focus on ageing well. Building a therapeutic relationship between the person and their health-care provider starts with selecting a highly tolerable initial ART regimen and addressing immediate threats to health and ART adherence. In addition to screening and vaccinations for infectious disease, behavioural and social threats to an optimised health trajectory need to be identified and addressed. Mental disorder and substance use can compromise retention in HIV care and adherence to treatment. Weight gain is particularly common in the first 12–24 months after ART initiation, which can result in people of typical or higher bodyweight experiencing a suboptimal ageing trajectory. Health-care providers need to offer counselling on how to avoid weight gain through diet and exercise, and should facilitate social prescriptions to connect patients with community resources that facilitate healthy lifestyles and provide social support. Finally, unnecessary medication (polypharmacy) should be avoided to reduce exposure to ineffective or harmful medications.

Although age is a major risk factor for diseases that reduce lifespan and healthspan (healthy survival), chronological age is a poor indicator of risk for people ageing with HIV. Health-care provisions in the years following successful ART initiation and initial health threats should include monitoring for physiological injury and multimorbidity at earlier ages than people ageing without HIV. As a result, people ageing with HIV might require screening at earlier chronological ages for cardiovascular disease, bone health, and some cancers. Women with HIV also often begin menopause at an earlier age. When survival is expected to be less than 10 years (regardless of chronological age), shifting towards integrating geriatric principles of care that are focused on managing multimorbidity, person-centred care, and end-of-life planning are essential to preserve function and dignity for the remainder of life.

By basing care on local epidemiological burden and available programmes (based on demand and resources or diagonalisation), vertical and horizontal system can be transformed to better support ageing well. Diagonalisation offers a pragmatic pathway for LMICs to address the increasing incidence of chronic disease and multimorbidity and continue to treat HIV. Importantly, within the limits of available technology, digital and data-driven innovations can help scale diagonalisation approaches by empowering people with self-monitoring tools, guiding health-care workers with standardised protocols, and enhancing community-based follow-up.

Healthy ageing with HIV is only possible if partnerships extend outside of clinical settings. Partnerships are required between the person with HIV and their caregivers, health-care providers, health-care system, community, and digital resources to meet the needs of the global population ageing with HIV and reduce HIV transmission (panel 1). Incorporating community perspectives is crucial to inform this work (panel 3). More generally, the global population is ageing with and without HIV, and training programmes for health-care providers have failed to adapt to the needs of an ageing population. Worldwide, opportunities for training in foundational geriatric competencies remain inadequate. Supporting healthy ageing for people with HIV from ART initiation to end-of-life planning will require HIV health-care providers to develop new foundational competencies. Programmes need to upgrade training in relevant core disciplines of geriatrics, family and internal medicine, palliative care, and psychiatry to be able to understand and meet these complex clinical needs. Although this educational issue goes well beyond HIV and ageing, without curricular reforms, practitioners will struggle to cope with the complex clinical scenarios resulting for people ageing with HIV.

**Contributors**

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**Declaration of interests**
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