REVIEW

Life expectancy living with HIV: recent estimates and future implications

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Purpose of review
The life expectancy of people living with HIV has dramatically increased since effective antiretroviral therapy has been available, and still continues to improve. Here, we review the latest literature on estimates of life expectancy and consider the implications for future research.

Recent findings
With timely diagnosis, access to a variety of current drugs and good lifelong adherence, people with recently acquired infections can expect to have a life expectancy which is nearly the same as that of HIV-negative individuals. Modelling studies suggest that life expectancy could improve further if there were increased uptake of HIV testing, better antiretroviral regimens and treatment strategies, and the adoption of healthier lifestyles by those living with HIV. In particular, earlier diagnosis is one of the most important factors associated with better life expectancy. A consequence of improved survival is the increasing number of people with HIV who are aged over 50 years old, and further research into the impact of ageing on HIV-positive people will therefore become crucial. The development of age-specific HIV treatment and management guidelines is now called for.

Summary
Analyses on cohort studies and mathematical modelling studies have been used to estimate life expectancy of those with HIV, providing useful insights of importance to individuals and healthcare planning.

Keywords
antiretroviral therapy, HIV, life expectancy

INTRODUCTION

The number of people living with HIV has never been higher; UNAIDS estimates the global figure to be 34.2 million people [1]. This reflects both the increase in the number of new infections and also the rise in access to antiretroviral therapy (ART) which has dramatically reduced mortality and morbidity [2–8]. Consequently, life expectancy has substantially improved to the extent that HIV is increasingly considered as a chronic illness, in which a near-normal lifespan is achievable with successful care [9,10].

In this review, we first define 'life expectancy' and discuss the main methods of calculation. A brief overview of how life expectancy has improved over time is then given, followed by the main focus of this study, which reviews the literature on the latest estimates of life expectancy. Finally, the literature is discussed in the context of what impact it will have in the future.

DEFINITION OF LIFE EXPECTANCY AND METHODS OF CALCULATION

Life expectancy is 'the average number of years an individual of a given age is expected to live if current mortality rates continue to apply' [11]. It is commonly perceived as a useful indicator of population health and mortality and is easier to relate to than mortality rates.

Ideally, life expectancy would be calculated using data from a large cohort with very long

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KEY POINTS

- The life expectancy of someone living with HIV who achieves and maintains viral suppression on ART is approaching that of HIV-negative individuals; however, it is unlikely to be equal even if the CD4 count has been maintained at a high level.

- Earlier diagnosis is one of the most important factors associated with better life expectancy.

- Further increases in life expectancy might occur through the development of improved antiretroviral regimens and treatment strategies, increased uptake of HIV testing, and through adopting better lifestyles such as quitting smoking and recreational drug abuse.

- The effects of ageing in HIV-infected people need to be studied further, so that findings can help develop age-specific guidelines for HIV care and clinical management.

follow-up such that 50% of deaths are observed. Although this approach would directly provide the median life expectancy, it is currently infeasible. Furthermore, the estimated life expectancy would be outdated and therefore not applicable to those infected or diagnosed today.

Instead, calculation of life expectancy is often done by constructing period life tables from the mortality experiences of a cohort over a short period of time, assuming the cohort is subject to age-specific death rates in any given year. Life tables can be complete or abridged, depending on whether death rates were discrete at each year of age, or grouped for similar ages (e.g. 5-year groups), respectively. The life expectancy of an individual is then calculated using projections of these age and sex-specific death rates, assuming they apply throughout an individual's lifespan [12]. An alternative method to estimate life expectancy is to use mathematical models.

ESTIMATES OF LIFE EXPECTANCY (PUBLISHED 1980–2009)

Survival in people with HIV has progressively improved since AIDS was first seen in the United States [13]. In those early days when treatment for HIV did not yet exist, the median time of survival following an AIDS diagnosis was no longer than about 20 months [14]. Without treatment, it has been estimated that the median time from seroconversion to AIDS and death is approximately 9 and 10 years, respectively, but varies significantly by age at seroconversion [15].

Even after treatment was available, HIV was in the top 10 causes of deaths worldwide in 1997, partly

because ART was not very effective at first and also because it was mainly limited to resource-rich countries [16]. Numerous studies have since estimated the life expectancy of people infected with HIV and have demonstrated that survival has improved over time [17–22]. This has been a result of successful virologic suppression because of the availability of increasingly effective and tolerable treatment [23–25].

ESTIMATES OF LIFE EXPECTANCY (PUBLISHED 2010 ONWARDS)

Recently, there has been a surge in the number of research papers [9,10,26,27■■,28,29■■,30■■] which estimate life expectancy in people with HIV (Table 1). As these estimates apply to different circumstances (such as no hepatitis coinfections or injecting drug use) and to certain settings (most studies assume good access to ART and HIV care), it is difficult to directly compare the estimates against one another.

Life expectancy calculated using data from cohort studies

Life expectancy has been estimated by May *et al.* [30■■] using data from the UK Collaborative HIV Cohort study, which combines patient data from over 30 HIV clinics across the UK. Although life expectancy at age 20 increased from 30.0 years during 1996–1999 to 45.8 years during 2006–2008, the presence of HIV infection reduced average life expectancy by 13 years compared to someone without HIV. Men had lower life expectancy than women (39.5 years compared to 50.2 years) and people who started treatment later than guideline recommendations also had a worse prognosis.

Van Sighem *et al.* [9] found that life expectancy of recently diagnosed asymptomatic individuals approached that of uninfected individuals using data from the AIDS Therapy and Evaluation Netherlands cohort. The median number of years lived from age 25 was 52.7 and 57.8 years for men and women, respectively, whereas it was 53.1 and 58.1 years for men and women, respectively, in the general Dutch population. The analysis was restricted to a selective group of healthy people who were still not eligible for treatment nor had experienced a HIV-related symptomatic event (except one associated with primary HIV infection) or AIDS as of 24 weeks from HIV diagnosis. However, these estimates may be biased upwards because of losses to follow-up with consequent under-ascertainment of deaths and to keeping age fixed over follow-up.

Mills and colleagues have investigated life expectancy and survival in people receiving ART

Table 1. Estimates of life expectancy from recently published studies

Study (publication year)	Study population	Method	Main findings, life expectancy	Comments
Nakagawa et al. (2012) [10]	A simulated cohort of 10000 MSM, aged 30 years, who become HIV-positive in 2010, and have good access to HIV care and ART. Calibrated with data from UK.	Stochastic simulation model of the progression and treatment of HIV.	Assuming a high rate of HIV diagnosis (median CD4 cell count at diagnosis: 432 cells/μl): 75.0 years for overall cohort; 76.5 years if rate of ART interruption reduced to 0; assuming a low rate of HIV diagnosis (median CD4 cell count at diagnosis: 140 cells/μl): 71.5 years for overall cohort; 68.0 years if three-fold raised risk of AIDS-related deaths occurring at HIV diagnosis.	Simulation modelling makes multiple assumptions about the course of HIV and the long-term efficacy of ART. Results do not apply to people with hepatitis coinfection.
Sloan et al. (2012) [29■■]	10 Million HIV-infected individuals in each modelled scenario, with the same characteristics as the newly diagnosed French HIV-infected population in 2005.	First-order state-transition Monte Carlo simulation of the natural history, clinical management, and costs of HIV.	If cART was initiated at CD4 count <350 cells/μl: 23.8, 26.5, and 27.5 years if mean CD4 count at presentation to care was 97, 372, and 510 cells/μl, respectively. If cART was initiated at CD4 count <500 cells/μl or viral load >100000 copies/ml or if presenting with an ADC: 26.4 and 27.4 years if mean CD4 count at presentation to care was 372 and 510 cells/μl, respectively.	Simulation modelling makes multiple assumptions about the course of HIV and the long-term efficacy of ART.
May et al. (2011) [30■■]	17661 Adult patients from the UK CHIC study with CD4 count ≤350 cells/μl at start of cART between 1996 and 2008.	Construction of abridged life tables.	At age 20: 30.0 years during 1996–1999; 45.8 years during 2006–2008; 39.5 years for men (1996–2006); 50.2 years for women (1996–2006); 37.9, 41.0, and 53.4 years in those starting cART with CD4 count <100 cells/μl, 100–199 cells/μl and 200–350 cells/μl, respectively.	Study excluded patients who have ever injected drugs. Results do not apply to people who are undiagnosed, not seen for care or have not initiated ART.
Mills et al. (2011) [27■■]	22315 Patients aged 14 years or older, who initiated cART at TASO clinics in Uganda between 2000 and 2009.	Construction of abridged life tables.	At age 20: 26.7 years for overall cohort; 19.7 years for men; 30.6 years for women; 13.5 and 37.4 years for patients with baseline CD4 count <50 cells/μl and ≥250 cells/μl, respectively.	Diverse population cohort. Some missing data. Most patients treated with older and more toxic regimens than those used in developed countries.

(Continued)

Table 1 (Continued)

Study (publication year)	Study population	Method	Main findings, life expectancy	Comments
Harrison et al. (2010) [28]	U.S. surveillance data from 25 States, includes 220 646 people who were diagnosed with HIV between 1996 and 2005.	Construction of life tables	At HIV diagnosis: 10.5 years in 1996; 22.5 years in 2005; 22.0, 25.5, 19.9, and 22.6 years for men overall, white, black and Hispanic men, respectively; 23.6, 21.4, 24.2, and 21.2 years for women overall, white, black and Hispanic women, respectively; 19.4 and 21.1 years in 2005, with a first CD4 count <200 and <500 cells/μl, respectively, at or within 6 months after diagnosis.	Data not nationally representative. Surveillance data subject to local variations in reporting and data quality. Results not adjusted for coinfections or for treatment.
Van Sighem et al. (2010) [9]	8717 adult patients from the ATHENA cohort (Netherlands), diagnosed with HIV during 1998–2007, and who were ART-naïve as of 24 weeks after diagnosis.	Time-dependent multivariate hazards model to predict median survival.	At age 25: 52.7 years for men; 57.8 years for women.	Analysis restricted to a selective group of healthy people who were still not eligible for treatment nor had experienced a CDC-B or CDC-C[a] event as of 24 weeks from HIV diagnosis.
Braithwaite et al. (2009) [31]	A simulated cohort of HIV-infected individuals calibrated and validated with data from CHORUS and ART-CC cohorts.	Probabilistic, second-order Monte Carlo simulation model of the progression and treatment of HIV.	At age 30, assuming minimal toxicity and if cART initiated at CD4 count <350 cells/μl: 23.3, 26.0, and 32.2 years if proportion of antiretroviral doses taken was 50, 80, and 100%, respectively. At age 30, assuming maximum toxicity and if cART initiated at CD4 count <350 cells/μl: 15.5, 17.0, and 18.5 years if proportion of antiretroviral doses taken was 50, 80, and 100%, respectively.	Results based on data from a cohort with low prevalence of injecting drug use and hepatic diseases. The simulation does not consider the potential correlation of age with the mode of HIV transmission.

ART, antiretroviral therapy; ADC, AIDS-defining condition; ART-CC, Antiretroviral Therapy Cohort Collaboration; ATHENA, AIDS Therapy and Evaluation Netherlands; cART, combination antiretroviral therapy; CHORUS, Collaborations in HIV Outcomes Research-US; MSM, men who have sex with men; TASO, The AIDS Support Organization; UK CHIC, UK Collaborative HIV Cohort; .
[a]The Centers for Disease Control and Prevention (CDC) in the USA has developed a classification system for HIV infection, in which a clinical event can be classified as category A, B, or C (i.e. CDC-A, CDC-B, or CDC-C). In brief, category A consists of asymptomatic or primary HIV infection, category B consists of symptomatic HIV infection, but not including AIDS-defining conditions, and category C consists of AIDS-defining conditions.

in Uganda [27■■,32,33]. In one study, they found that life expectancy was 26.7 years at age 20, approaching the overall rate for all young adults in Uganda [27■■]. Similar to the observations seen in resource-rich settings, there was substantial variability in the life expectancy depending on the patient's age, sex, and CD4 count at baseline [27■■]. Most of these patients were treated with older regimens than those currently used in the USA and Western Europe.

Since the roll out of ART, adult life expectancy has increased in a South African population cohort, where 28% of adults are infected with HIV [34]. In 2003, the expected age at death was 52 years, but by 2011, this figure was 61. In this study, Bor *et al.* also found that treatment costs were far outweighed by the economic value of gain in life expectancy.

Life expectancy calculated using other methods

Harrison *et al.* [28] used U.S. surveillance data to find that the average life expectancy following diagnosis increased from 10.5 years in 1996 to 22.5 years in 2005. However, according to these estimates, HIV-positive people still have a lifespan 21 years shorter compared to HIV-negative people. Women had a better life expectancy compared to men, but this difference lessened by 2005. The researchers also found that life expectancy was shortest for black men, followed by Hispanic men and white men. This racial disparity was also found by Losina *et al.* [35].

Although developed primarily for cost-effectiveness analyses, the CEPAC model (a state-transition Monte Carlo simulation of HIV-infected individuals) has been used extensively to answer many research questions [17,18,29■■,35,36]. In one study, Sloan *et al.* [29■■] estimated the mean life expectancy for a simulated cohort with mean age of 38 years to be 26.5 years, assuming ART was initiated when CD4 counts fell below a threshold of 350 cells/µl. If patients presented earlier and ART was assumed to be initiated when CD4 counts fell below 500 cells/µl or if the HIV viral load was over 100 000 copies/ml, life expectancy increased slightly to 27.4 years.

Another well validated simulation model of HIV, developed by Braithwaite *et al.* [37], has been used to consider the impact of adherence interventions on cost-effectiveness by comparing the increase in life expectancy with increase in costs (mainly from the intervention itself). Although this study did not explicitly state the estimated life expectancy, results from previous studies have done [31,38,39]. For example, in one study they estimated that life expectancy for a 30 year old, assuming minimal toxicity from antiretrovirals, ranged from 19.3 to 33.5 years depending on the CD4 count at treatment initiation and adherence [31].

Nakagawa and colleagues used their previously developed stochastic simulation model of HIV progression to project the life expectancy of men who have sex with men (MSM) in the UK [10,40,41]. The median life expectancy for MSM infected in 2010 at age 30 was estimated to be 45 years [10]. This assumed that no one had hepatitis coinfection, 40% were lifelong smokers and the median CD4 count at diagnosis was 432 cells/µl. If the median CD4 count at diagnosis declined to 140 cells/µl, the median life expectancy dropped to 41.5 years. The authors suggest that their estimates of life expectancy are much higher than in most other studies because the model takes into account the long-term durable effects of therapy using current estimates of rates of virologic failure and resistance emergence and, therefore, over time the CD4 count increases and mortality rates decrease.

INTERPRETATION OF LIFE EXPECTANCY ESTIMATES

The major assumption made in all life expectancy calculations is that age-specific mortality rates estimated at a given point in time will apply throughout the individual's entire lifespan. This does not allow for potential improvements in mortality rates over time, which has been observed in both the HIV-infected population and the general population [42,43], and any estimates may therefore be an underestimation. Some studies [10] have taken into account that relative to HIV-negative populations, there is a late fall in survival because of increased mortality associated with several non-AIDS-related causes.

Methods to estimate life expectancy can be broadly split into two approaches: life table approach and use of mathematical models. Both approaches rely on data from cohort studies to either construct life tables or to inform the models, but there are some limitations inherently associated with the use of cohort studies. For example, patients followed up in cohort studies may have better HIV care and therefore better overall prognosis because of their participation in various research studies, although this is not always the case as in some cohorts data is collected as part of routine care. Under-ascertainment of deaths can also occur, which would lead to an overestimation of life expectancy.

The main limitation when using the life table approach is the under-ascertaining of death, combined with the lack of mortality data in older age groups, where the majority of the deaths occur in

the comparator background population. Also unlike regression analyses, life tables do not adjust for covariates and therefore results need to be interpreted carefully.

One advantage of mathematical models is the ability to account for the long-term durability of ART and the subsequent decrease in mortality rates, which should ensure that life expectancy is not underestimated in people with HIV. However, it is important to note that mathematical models make many assumptions about the natural course of HIV progression as well as the effect of ART. Additionally, in the case of estimating life expectancy, considerable uncertainty is introduced by simulating very long periods of time.

IMPLICATIONS OF INCREASED LIFE EXPECTANCY

A consequence of increased life expectancy is that the number of deaths from non-AIDS-related conditions now considerably exceeds the number of AIDS deaths in resource-rich settings [44]. In particular, non-AIDS malignancies, cardiovascular disease, and hepatic disease (in those with hepatitis coinfection) are now amongst the leading causes of deaths [44,45]. HIV infection itself, as well as long-term use of ART, is also thought to increase the risk of non-AIDS-related diseases, probably, although to a lesser degree, even in people with viral suppression [45–51]. These data support the need for enhanced preventive measures more akin to those used in older people in the general population, such as screening programmes.

Another direct implication of increased life expectancy is that younger patients nowadays will expect to be on treatment for at least three or four decades. Results from the ongoing Strategic Timing of AntiRetroviral Treatment study, which is evaluating the risk/benefit of ART initiation in people with CD4 count greater than 500 cells/µl, compared with deferral to 350 cells/µl, could lead to patients being on treatment earlier [52]. If 'treatment as prevention' strategies, such as 'test-and-treat' and preexposure prophylaxis (PrEP) regimens, are to be used widely, these could also add to the length of time people are on ART. A large proportion of the lifetime costs related to the care of HIV-infected patients is ascribed to antiretroviral drugs [29■■]. Therefore, further cost-effectiveness studies of different regimens need to be done [53] and it is vital for cheaper, generic drugs to be made available.

As a result of longer life expectancy, HIV will be more prevalent in older people. Ageing in HIV is not yet well studied as it is a relatively new occurrence [54]; however, the presence of HIV infection may accelerate ageing [55]. The development of age-specific guidelines for HIV is now called for [56■■]. Other than guidance on HIV care and clinical management, the guidelines should provide recommendations on screening programmes and additional monitoring of biomarkers, especially for common comorbidities which occur more frequently with increasing age. Therefore, a more integrated approach to managing HIV-related and non-HIV-related diseases may be appropriate, such that people with HIV are seen in general practice and only referred to HIV specialist clinics when viral loads are unsuppressed. This could include lifestyle support, managing cardiovascular risk factors and other chronic diseases, as well as dealing with ART-associated complications such as drug–drug interactions.

As there is now sufficient evidence that the life expectancy of someone with HIV is nearly the same as that of an HIV-negative person, access to life insurance should be more widely available. The improved survival needs to be reflected in premium prices, particularly as survival often improves with age, which is unlike most other chronic diseases such as diabetes, because it takes several years of ART to restore CD4 counts to normal levels.

FURTHER IMPROVEMENTS IN LIFE EXPECTANCY?

Many of the studies considered above have shown that life expectancy is longer in people who have a higher CD4 count at HIV diagnosis [10,28,29■■]. In the UK, approximately 50% of people are diagnosed late (defined as a CD4 count <350 cells/µl within 3 months of diagnosis) [57] and there is strong evidence that late diagnosis is associated with poorer prognosis including worse response to treatment and an increased risk for HIV-related morbidity and mortality [58–61]. Therefore, one way to further increase life expectancy of people with HIV is to improve HIV testing rates, particularly in high prevalence areas and perhaps in nontraditional settings. Early diagnosis of HIV will result in individuals starting ART in accordance with guideline recommendations and people being be in care and routinely monitored, both of which will improve life expectancy.

In general, it is recognized that HIV-positive people have an inferior profile of lifestyle risk factors compared to the general population [62–67]. Many of these risk factors, whether HIV-related or not, and which include smoking, alcohol abuse, and recreational drug use, are associated with an increased risk of death [46,62,68■,69■■], and hence investment into support programmes may help to reduce the

Table 2. Main findings and conclusions

	Findings and conclusions
Estimates of life expectancy	Without antiretroviral treatment: Estimated median time from seroconversion to death is approximately 10 years
	With antiretroviral treatment: Someone with recently acquired HIV infection has nearly the same life expectancy as that of an HIV-negative person, providing they are diagnosed early, have extensive access to HIV care and treatment and maintain good adherence
Implications of increased life expectancy	HIV will be more prevalent in older people
	Development of age-specific guidelines for HIV is now called for
	The need for enhanced preventive measures more akin to those used in older people in the general population, because of a larger proportion of deaths attributed to non-AIDS-related conditions
	Increase in demand for cheaper generic drugs
	Access to life insurance should be more widely available for people with HIV
Ways in which life expectancy could improve further	Higher rates of HIV testing
	Earlier HIV diagnosis and enrolment into care
	Better antiretroviral regimens and treatment strategies
	Adoption of healthier lifestyles (reduction in rates of smoking, alcohol abuse, and recreational drug use)

mortality rates more. The effect of hepatitis C coinfection on HIV is also important to consider, because HIV immunosuppression is associated with faster progression of liver disease in people with hepatitis C [70].

The risk factors for acquiring HIV are also associated with lower life expectancy [71]. Studies comparing mortality rates in people with HIV and on ART to people without HIV have reported conflicting results [9,72■,73], although there is some evidence of an increased death rate in individuals who are not yet on treatment because of high CD4 counts compared with the general population (with the exception of MSM with CD4 count >500 cells/μl) [74]. Even if the life expectancy of an HIV-infected person were found to be equal to that of an HIV-negative person, the quality-adjusted life years would probably be less, mostly because of the potential harm resulting from long-term ART usage [75], but also because of the psychological aspects for some of carrying a lifelong virus, despite it being controlled at very low levels. More research is required on ways in which quality of life could be improved.

CONCLUSION

The life expectancy of someone living with HIV, especially if they are diagnosed before ART is indicated, is approaching that of HIV-negative individuals; however, it is still not equal (Table 2). Even if life expectancy were to improve further such that it did not differ by HIV status, quality-adjusted life years would almost certainly be less.

The improvement in life expectancy will mean that the number of people with HIV increases and there will be a shift in the age distribution. Further research into the impact of ageing on HIV-positive people will become crucial. Therefore, age-specific HIV treatment guidelines may need to be developed and introduced. Screening programmes and more comprehensive patient management are also required to address comorbidities and risk factors associated with HIV that increasingly occur as people age.

Modelling studies suggest that life expectancy could potentially rise further. Ways in which this could be possible include increased uptake of HIV testing, better antiretroviral regimens and treatment strategies and the adoption of healthier lifestyles by those living with HIV. In particular, earlier diagnosis and enrolment into care is one of the most important factors associated with better life expectancy.

Conflicts of interest

A.P. has received consultancy fees or funds for research from Johnson and Johnson, Gilead, Bristol-Myers Squibb and ViiV.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 100).

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