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Life expectancy after 2015 of adults with HIV on long-term antiretroviral therapy in Europe and North America: a collaborative analysis of cohort studies

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Contributions: JACS and AT conceived and designed the study. AT combined, checked, and cleaned the datasets (including dataset verification). At least two named authors have accessed and verified the data (AT and JACS). Individual cohort representatives (CAS, GB, HC, AdM, ME, MJG, SG, JG, IJ, FCL, NO, JMR, CS, TRS, RT, GT, JW, FW, LW, RZ, MJS, and AJ) contributed to the provision of cohort data. AT conducted all statistical analyses. AT and JACS drafted the manuscript. All authors contributed to the interpretation of data and critical revisions of the manuscript for important intellectual content. AT and JS had final responsibility for the decision to submit for publication.

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Summary:

Background—Life expectancy (LE) of persons with HIV (PWH) starting antiretroviral therapy (ART) has increased substantially over the last 25 years. Most previous studies were based on the first years after starting ART when mortality is highest, whereas many PWH have been successfully treated for many years and require up-to-date data on prognosis. We aimed to estimate LE among adult PWH after one year on ART in Europe and North America, from 2015 onwards.

Methods—We used data from the Antiretroviral Therapy Cohort Collaboration and the UK Collaborative HIV Cohort Study, totalling 20 European/North American cohorts of PWH on ART. Included PWH started ART from 1996–2014, when aged ≥16, and had been on ART for ≥1 year by 2015 or started ART 2015–2019 and survived ≥1 year. Associations of demographic/clinical characteristics with mortality were estimated using Poisson models. Estimated expected remaining LE for men and women, stratified by variables associated with mortality, was calculated and compared to a corresponding multi-country general population.

Findings—There were 5,780 deaths post-2015 among 206,891 PWH. For females, the standardised remaining years of LE at age 40 for those starting ART 1996–2014 was 35.8 (95% confidence interval: 35.2–36.4), versus 39.0 (38.5–39.5) for those starting post-2015 (general population: 45.8 years). For males, corresponding figures were 34.5 (33.8–35.2) and 37.0 (36.5–37.6) years respectively (general population: 40.7 years). Among females and males starting ART 1996–2014, remaining LE at age 40 was 19.4 (18.2–20.5) and 18.2 (17.1–19.4) years respectively for those with CD4 count 0–49 cells/μL at follow-up start, rising to 40.2 (39.7–40.6) and 38.0 (37.5–38.5) years respectively for those with CD4 count ≥500 cells/μL. Corresponding figures for females and males starting ART post-2015 were 24.9 (23.9–25.9) and 23.7 (22.7–24.8) years, rising to 42.0 (41.7–42.3) and 39.2 (38.7–39.7) years, respectively.

Interpretation—For PWH on ART with high CD4 counts who survived to 2015 or started ART after 2015, LE was only a few years lower than in the general population, regardless of when ART was started. However, for those with low CD4 counts in 2015, estimates of remaining LE were substantially lower than in the general population, emphasising the continuing importance of early diagnosis and sustained treatment.

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Introduction

The life expectancy of persons with HIV (PWH) starting antiretroviral therapy (ART) has increased over the last two decades(1, 2), over which period the side effect profiles of ART regimens, drug-efficacy, comorbidity care, and time to virological suppression have steadily improved(3). Previous analyses of life expectancy were mainly based on mortality rates during the first few years after starting ART(4), which may not correspond to mortality rates after several years on ART if HIV infection has a long-term impact on health despite

successful treatment. Individuals treated with ART for many years want to know their life expectancy in the era of modern ART.

Consistent with updated treatment guidelines and as recommended by the World Health Organization, in recent years PWH are starting ART earlier and with higher CD4 counts(5). Longer times between infection and effective treatment lead to lower CD4 counts at the time of starting ART and worse outcomes for some years after starting ART(6). Therefore, time from diagnosis to starting combination ART, nadir CD4 cell count and peak CD8 count as well as their rate of recovery after starting ART may all influence subsequent morbidity and mortality. Treatment in the early ART era used less-effective drugs than are now available(3), and treatment with mono- or dual-nucleoside reverse transcriptase inhibitor (NRTI) therapy before receipt of combination ART may have induced drug resistance, limiting future treatment options(7). Receipt of drugs with severe metabolic side-effects, such as stavudine (d4T)(8) and azidothymidine/zidovudine (AZT)(9), may have had long term effects.

Aiming to provide life expectancy estimates for treated PWH in the current ART-era, particularly those on long-term ART, we used follow-up from 2015 onwards to estimate life expectancy of PWH in Europe and North America who started ART during the early years of ART, conditional on survival to 2015, and in those who started ART from 2015 onwards. We also examined associations of markers of delayed or unsuccessful treatment with subsequent mortality.

Methods

Cohort collaboration

We used data from the Antiretroviral Therapy Cohort Collaboration (ART-CC), which combines data from multiple European and North American cohorts of PWH(10), and from the UK Collaborative HIV Cohort (UK CHIC) Study(11). In total 20 cohorts, which are listed in the supplementary materials, were included. Data were extracted from each cohort and sent to the ART-CC data centre in Bristol to be cleaned and combined. Ethics committees or institutional review boards approved the 20 individual cohorts, which each used standardised data collection methods, and regular follow-up of participants who had consented to be included. Cohorts gathered information on mortality through linkage with vital statistics agencies and hospitals or physician report, and active clinical follow-up of participants.

Included PWH were aged ≥16 years when starting combination ART and had: (a) started combination ART during 1996–2014 and were still on combination ART in 2015, having survived for at least a year on ART; or (b) started combination ART during 2015–2019 and survived for at least a year on ART. 2015 was chosen for stratification between these two groups because in that year treatment guidelines changed to recommend ART for all PWH regardless of CD4 count. Our definition of combination ART includes different numbers and varieties of ART drugs, but excludes mono- or dual-NRTI regimens, which were used prior to the modern ART era. For PWH who started combination ART during 1996–2014, follow-up started on the later of 01/01/2015 and one year after ART start (for those who

started ART during 2014). For PWH who started combination ART during 2015–2019, follow-up started one year after they started ART. Follow-up ended at the earliest of death, loss-to-follow-up, or administrative censoring.

The variables included in analyses, which were decided a priori through consultation with HIV clinicians and representatives of groups of PWH, were: *(a) Combination ART start year group* (1996–99, 2000–04, 2005–09, 2010–14, and 2015–19); *(b) Demographic variables:* age category, sex at birth, and mode of HIV acquisition (men having sex with men [MSM], injecting drug use [IDU], heterosexual sex, other/unknown); *(c) Characteristics measured at start of follow-up (2015 or afterwards):* AIDS status, hepatitis C virus (HCV) RNA status, CD4 count (cells/μL) category, CD8 count (cells/μL) category, and viral load (copies/mL) category; and *(d) Characteristics measured before start of follow-up:* exposure to ART drugs with more side effects pre-follow-up start (Zidovudine, Stavudine, Zalcitabine, Didanosine, and Indinavir), mono/dual-NRTI regimen exposure pre-follow-up start, pre-combination-ART start CD4 count nadir, pre-combination-ART start CD8 count peak, nadir CD4 count between combination-ART start and 2015, peak CD8 count between combination-ART start and 2015, CD4 count 1-year after combination-ART start, CD8 count 1-year after combination-ART start, and viral load 1-year after combination-ART start. Some variables were sometimes unavailable for individual PWH or cohorts. Frequencies of missing data were tabulated. Data for 20 PWH who were reported to have died but had unknown date of death were excluded from analyses.

Statistical analyses

Poisson regression models were used to estimate mortality rate ratios (MRRs) after the start of follow-up: (1) for each variable adjusting only for cohort and age; (2) for combination ART start year group and additionally adjusting for characteristics at the start of follow-up, as well as sex and transmission group; and (3) additionally adjusting for characteristics measured during earlier years. Regression models included indicator variables for categories corresponding to missing or unknown values. The variables that had the strongest associations with mortality were selected, together with age and sex, for inclusion in life expectancy calculations.

Life expectancy from age 40 was estimated for various sex-stratified population groups, with the expected age at death then calculated from this. In brief, for each combination ART start year group, mortality rates in 5-year age bands (up to 80–84, and then ≥85) were calculated from Poisson model coefficients and then entered into a life table to produce estimated expected remaining years of life for each age group. The variables selected for inclusion in the life expectancy calculations were chosen through assessment of the magnitude of associations and consideration of what data are commonly available across cohorts, as well as to PWH and their clinicians. The methods for estimating life expectancy are described in more detail in the supplementary materials (supplementary tables 1 and 2). The same methods were used to estimate life expectancy from age 20, for comparison with previous literature.

There are few patients in the oldest age groups (≥85 years), and so there is only limited follow-up time and few deaths in these groups. Therefore, we calculated the ratio of the

mortality rates comparing PWH and the general population in each of the age-groups above 20 and then the average of these rate ratios, to produce an estimated rate ratio for PWH compared with the general population, separately for PWH who started ART during 1996–2014 and 2015–2019. Only the ratios from age-groups where the mortality rates among PWH were higher than in the general population are included in the overall rate ratio calculation due to low numbers of events in some age-groups. This rate ratio was used to multiply the general population mortality rate in the oldest age groups (≥85 years). In the age-groups where the mortality rate estimates among PWH were less than in the general population, the general population rate was used instead. An example of this process is shown in supplementary tables 1 and 2.

Standardised estimates of remaining years of life at ages 40 and 20 were derived by weighting the life expectancy estimates in each population group by the proportion of the sample in that group starting ART 2015–19. This was done for each sex, as well as after stratification by CD4 count at follow-up start. General population comparator mortality rates and life expectancies were taken from mortality.org for 2015(12). Sex-specific rates were calculated for each country and then weighted to correspond to the countries of residence of the PWH in our dataset. Analyses were performed using Stata version 16.1.

Role of the funding source

The funders had no role in the collection, analysis or interpretation of data, report writing, or the decision to submit this study for publication.

Results

Among 206,891 included PWH, there were 5,780 deaths in 619,356 person-years of follow-up post-2015. PWH starting combination ART in later calendar years tended to be younger, with lower CD4 counts and higher viral loads, at the time of follow-up start (table 1). A smaller proportion of those starting ART in later calendar years had received an AIDS diagnosis, been exposed to ART drugs with more side-effects, or been treated with mono/dual-NRTI regimens. The median time between starting ART and the start of follow-up was 7.8 years (IQR 3.4–13.9) for people who started ART between 1996 and 2014. For people who started ART between 2015 and 2019, follow-up started 1 year after treatment initiation.

In analyses adjusted for age and cohort, all the variables examined were associated with mortality from 2015 onwards (table 2). Compared with those who started ART in 1996–99, those who started ART more recently had lower mortality, with MRRs similar for those who started in 2010–14 (0.51: 95%CI 0.47–0.56) and in 2015–19 (0.58: 0.52–0.66). In the analysis additionally adjusted for sex, transmission route, and characteristics at follow-up start, females had lower mortality rates than males, and PWH who had acquired HIV via sexual contact between males had lower mortality rates than those acquiring HIV through other routes, particularly IDU. For most variables, MRRs were attenuated somewhat after additional adjustment for characteristics at follow-up start, but with similar patterns as after adjustment for age and cohort. However, for those starting in 2015–19 compared with 1996–99 the MRR was reduced after adjustment: from 0.58 (95%CI: 0.52–0.66) to 0.47 (0.41–0.53). Compared to those with CD4 counts of ≥500 cells/μL at follow-up start, lower CD4

counts were strongly associated with higher mortality. Those with viral loads ≥50 copies/mL at follow-up start had higher mortality than those with viral loads of <50 copies/mL, whilst PWH who had been diagnosed with AIDS by follow-up start had higher mortality rates than those without AIDS, and those diagnosed with chronic HCV infection at follow-up start had higher mortality than those without HCV. Compared to those with CD8 counts of 0–399 cells/μL at follow-up start, those with CD8 counts of 400–799, and 800–1199 cells/μL had lower mortality rates, although the associations were weaker than for the characteristics at follow-up start.

The MRRs for demographic and ART start characteristics remained similar after additionally adjusting for characteristics measured before the start of follow-up. However, mortality rates for those starting in 2000–04, 2005–09, 2010–14 and 2015–19 were more similar to those starting in 1996–99 (MRRs 0.91 [95%CI: 0.84–0.98], 0.88 [0.81–0.97], 0.88 [0.79–0.99], and 0.70 [0.58–0.84] respectively). Exposure to ART drugs with more side effects, mono/dual-NRTI regimens, to pre-ART start CD8 count peak, lower nadir CD4 count between ART start and 2015, and higher viral load 1-year after ART start were all associated with higher mortality after adjustment for other characteristics. However, the associations of characteristics measured before the start of follow up with mortality were generally weaker than for characteristics measured at follow-up start.

For the life expectancy analyses, combination ART start year group was re-categorised as pre- or post-2015 due to due to the modest differences between the adjusted MRRs for the pre-2015 groups. The other variables included were HIV acquisition category, viral load at follow-up start, AIDS at follow-up start, and CD4 count at follow-up start. Estimated MRRs from the Poisson model including these variables that were used for the life expectancy calculations are shown in supplementary table 3.

For females, the standardised expected remaining years of life at age 40 for those starting ART in 1996–2014 and 2015–19 were 35.8 (35.2–36.4) and 39.0 (38.5–39.5), respectively (table 3 and figure 1a). For females starting ART 1996–2014 and with CD4 count 0–49 cells/μL at follow-up start, remaining life expectancy at age 40 was 19.4 (18.2–20.5) years, increasing with each CD4 count category to 40.2 (39.7–40.6) years for those with CD4 count ≥500 cells/μL at follow-up start. Among females starting ART post-2015, life expectancy at age 40 increased from 24.9 (23.9–25.9) to 42.0 (41.7–42.3) years for those starting follow-up with CD4 counts of 0–49 and ≥500 cells/μL, respectively. The expected remaining years of life at age 40 for women in the comparator general population was 45.8.

For males, the standardised expected remaining years of life at age 40 for those starting ART in 1996–2014 and 2015–19 were 34.5 (33.8–35.2) and 37.0 (36.5–37.6), respectively (table 4 and figure 1b). For males starting ART 1996–2014 that had a CD4 count of 0–49 cells/μL at follow-up start, remaining life expectancy at age 40 was 18.2 (17.1–19.4) years, increasing with each CD4 count category to 38.0 (37.5–38.5) years for those with a CD4 ≥500 cells/μL at follow-up start. Among males starting ART post-2015, life expectancy at age 40 increased from 23.7 (22.7–24.8) and 39.2 (38.7–39.7) years for those with CD4 counts at follow-up start of 0–49 and ≥500 cells/μL, respectively. For men in the comparator general population, the expected remaining years of life at age 40 was 40.7.

Females at age 20 who started ART during 1996–2014 had, on average, a remaining life expectancy of 52.3 (51.7–52.9) years, whilst those starting ART during 2015–19 had, on average, a remaining life expectancy of 56.6 (56.2–57.1) years (supplementary table 4). The corresponding figures were 50.8 (50.1–51.4) and 54.5 (54.0–55.1) years for males at age 20 that started ART in 1996–2014 and 2015–19, respectively (supplementary table 5).

Discussion

Life expectancy of PWH from 2015 onwards was 5.6 and 3.8 years lower than in the general population for women who had started ART between 1996–2014 and 2015 onwards, respectively, had survived for at least one year on ART and had CD4 counts ≥500 cells/μL. Corresponding differences in life expectancy for men were 2.7 and 1.5 years, respectively. However, for PWH with lower CD4 counts one year after starting ART, estimated life expectancy is up to 30 years lower than in the general population. Life expectancy is lowest for PWH who acquired HIV through IDU and who have had prior AIDS events. PWH starting ART during 2015–19 had slightly higher estimated life expectancy those who started ART earlier. However, the differences between these groups were smaller when CD4 counts at start of follow up were high. Mortality rates were higher among PWH who were exposed to early ART drugs with more side-effects, and for other adverse characteristics before the start of follow-up. However, age and CD4 count at the start of follow up were those factors most strongly associated with mortality from 2015 onwards.

We estimated that females and males aged 20 who started ART over the period 1996–2014 had estimated ages of death of 72.3 and 70.8 years, respectively, whilst the corresponding figures for females and males starting ART post-2015 were 76.6 and 74.5 years, respectively. A meta-analysis of life-expectancies for PWH starting ART aged 20-years with any CD4 count in high-income countries, estimated an age at death of 63.3 years(5). However, most studies that estimated life-expectancy among PWH in North America and Western Europe using follow-up after the first year of ART or who started ART with high CD4 counts(1, 2, 13–20) estimated higher life expectancies that were similar to those reported here. These estimates varied by country, but were mostly between 70 and 77 years, with higher estimates generally seen using more recent follow-up, follow-up taken longer after ART start, and when limiting estimates to PWH starting ART with the highest CD4 counts.

Studies estimating age of death for PWH aged 20 who started ART with CD4 counts ≥500 cells/μL included analyses by Kaiser Permanente California (74.5 years during 2008–11(2), and 77.4 years during 2011–16(13)). Studies estimating life expectancy for PWH aged 20 who started ART with CD4 counts ≥350 cells/μL included a collaboration of Canadian cohorts (70.8 years)(19), a US collaboration (74.6 years)(20), and a study in British Columbia, Canada (73.1 years)(18). The highest estimate was from the Swiss HIV cohort study (83.9 years)(16). The UK CHIC study estimated life expectancy for PWH aged 20 starting ART with CD4 counts of 200–350 cells/μL to be 73.4 years(21).

Studies estimating life expectancy from age 20 using follow-up not starting at ART initiation included a previous ART-CC analysis using follow-up data from the 2nd and 3rd years after

starting ART between 1996–2013 (76.0 and 73.1 for females and males, respectively)(1). The UK CHIC Study used follow-up from 2000–2012 from 5-years after ART start (72 years in males and 77 in females)(14). The lowest estimate was from a study in British Columbia, Canada, using follow-up after 1-year on ART (68.7 years)(18). An Italian study estimated that a 25-year-old on ART who had immunologically recovered (high CD4 counts at the censoring date) would live to 75.6 years, on average(17), whilst the Danish Cohort Study estimated an age at death of 73.9 years for PWH aged 25 (including those not on ART), using follow-up between 2010 and 2015(22). Differences in estimated remaining life expectancy between these studies and ours could be due to differing durations on ART before follow-up start, differing calendar years of follow-up, differing cohort mix regarding modes of HIV acquisition (particularly IDU), differing background mortality rates in each setting, or methodological differences.

This analysis utilised a large, detailed longitudinal dataset containing data on over 200,000 adult PWH on ART across cohorts in multiple countries in Europe and North America. The findings should therefore be generalisable to adults on ART in other high-income countries, though they may not apply to resource-limited settings, or to settings where access to antiretroviral therapy is restricted or costly. We were able to produce life-expectancy estimates for subgroups defined by sex, HIV acquisition mode, viral suppression status, prior AIDS events, ART start year, and CD4 count, and this study is, therefore, one of the most detailed analyses of life expectancy among PWH treated in the modern ART era. Possible limitations include that there was only limited follow up and therefore few deaths in the oldest age-groups. This means that estimated life expectancy depends on assumptions regarding mortality rate ratios comparing PWH with the general population, extrapolated from younger age groups. This limitation is common to all existing analyses of life-expectancy among PWH. Under ascertainment of deaths is also a possible limitation. However, over half of the included cohorts have linkage to death registries to ascertain deaths, whilst several others link to local death registries, and several of the remaining cohorts utilise procedures to track patients that have been lost to follow-up(15). We compared our findings with general population data from mortality.org, but characteristics of included PWH will differ from those in the general population regarding behaviours and demographics. Missing data were dealt with by including indicators for missing data in each variable in regression models. Although the proportions of missing data were small, this implies imperfect adjustment for these variables. Whilst we were able to estimate life expectancy, we could not estimate the quality of the remaining years of life. Previous studies found that PWH have proportionally fewer remaining years of life without disability than general population comparator groups(13). Another limitation was the lack of available data on variables linked to socio-economic status, such as education. Our analysis did not include PWH who started ART as children or adolescents – these groups are at high-risk of adverse events.

Whilst our analyses showed that factors related to HIV history are less important than current age and CD4 count, comorbidities occurring while on ART are an important predictor of mortality: most mortality among PWH on ART in high-income countries is now due to non-AIDS causes such as cancer and cardiovascular disease(23) that are more common among PWH than the HIV-negative population(24), and whose importance will

increase as the population of PWH continues to age(25). Communicable diseases such as HCV are also more common among PWH than the HIV-negative population, particularly among those who acquired HIV through IDU, although the prevalence of HCV among PWH is decreasing due to the availability of curative treatment(26, 27). The prevalence of persons with a history of IDU is decreasing in Europe(28), but not in North America(29). Meanwhile, conditions such as cytomegalovirus (CMV) infection, which are linked with ageing(30), are more common in among PWH(31). Therefore, treatment and prevention of comorbidities among PWH is particularly important when considering not just the remaining years of life, but the quality of these remaining years(13, 32).

Life expectancy among PWH in North America and Europe who have been on ART for many years is lower than, but close to, that in the general population. This finding will be reassuring for PWH who have been on ART for many years. Life expectancy estimates are useful for both patients and clinicians and can enable improved access to affordable life insurance policies for PWH(33). Adverse markers related to HIV history, such as very low CD4 counts before ART start and exposure to regimens that are no longer available due to their side-effects or lower effectiveness, continue to predict mortality rates much later on. Exposure to ART regimens with more side-effects may have caused unplanned treatment interruptions that lead to higher long-term mortality rates. However, associations of these adverse markers with mortality from 2015 onwards were modest after accounting for factors at the start of follow up. Age and current CD4 count remain the most important factors for predicting subsequent mortality, confirming the importance of ongoing adherence to effective modern ART regimens. Further research should focus on the quality as well as number of expected remaining years of life for PWH, and how these are affected by comorbidities that occur more commonly in PWH on ART than in the general population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data sharing statement:

Due to the data sharing agreements between individual cohorts and ART-CC, the data collected for this study cannot be shared. Data are owned by the individual cohorts and those wishing to access these data should contact the individual cohorts, details of which are given in the appendix.

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Research in context

Evidence before this study

We searched PubMed for studies published up to 30th March 2022 for English-language studies that had estimated life expectancy for persons with HIV (PWH) on antiretroviral therapy (ART) in Europe or North America, using the terms “life expectancy” and “HIV”. Several studies found that the life expectancy of PWH starting ART has increased over the last two decades, corresponding to increased and earlier access to ART and improved side effect profiles of ART regimens. These studies all used follow-up from the first few years after starting ART. A meta-analysis estimated an age at death of 63.3 years when starting ART with any CD4 count, whilst our previous analysis, using follow-up data on the 2nd and 3rd years after starting ART between 1996 and 2013, estimated ages of death of 76.0 and 73.1 for women and men aged 20, respectively. Analyses by the Kaiser Permanente California cohort, UK CHIC Study, the Swiss HIV Cohort Study, and by collaborations of North American cohorts, estimated ages at death for 20-year-olds using follow-up 1-year after ART initiation or among PWH starting ART with high CD4 counts. Estimated ages at death varied from around 69 to 83, and these studies found that some subgroups of PWH on ART had life expectancy similar to that of the general population.

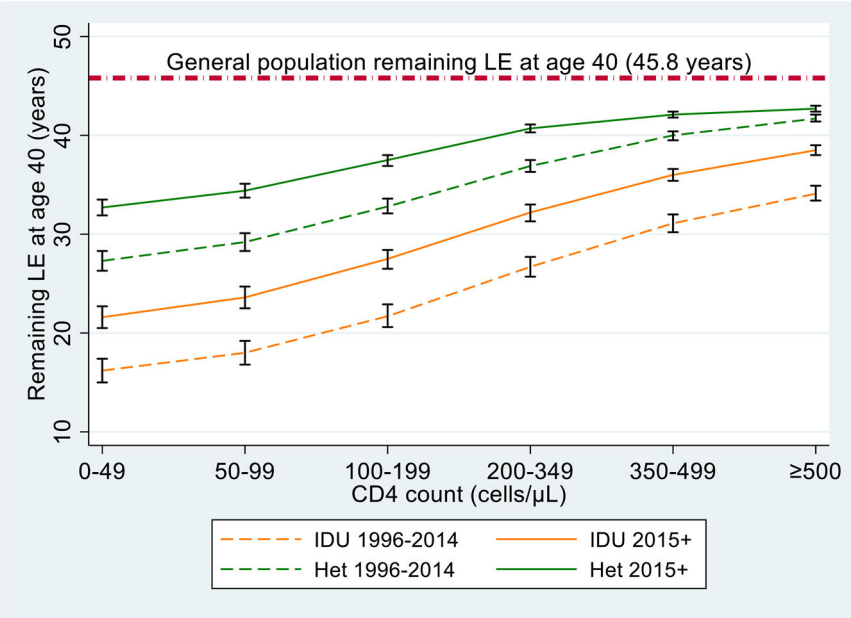
Added value of this study

Most previous analyses were mainly based on mortality rates calculated from or soon after ART start, and may therefore not be applicable to most PWH in high-income countries. Our study included follow-up data from 2015 (when treatment guidelines changed) on over 200,000 PWH from 20 cohorts in North America and Europe who had started ART up to 20 years previously, and investigated whether current prognosis was affected by markers of previous delayed or unsuccessful treatment. Various aspects of HIV history, such as exposure to ART regimens no longer recommended due to side effects, were associated with rates of mortality after 2015. However, the strongest associations were with age and current CD4 count. For females, the standardised expected remaining years of life at age 40 for those starting ART 1996–2014 were 35.8 (95% confidence interval: 35.2–36.4), versus 39.0 (38.5–39.5) for those starting post-2015; general population comparator: 45.8 years. Corresponding figures for males were 34.5 (33.8–35.2) and 37.0 (36.5–37.6) years respectively; population comparator 40.7 years.

Implications of all the available evidence

Life expectancy for PWH on long-term ART with high CD4 counts is estimated to be only a few years lower than in the general population, regardless of when ART was started. PWH starting ART since 2015 are estimated to have slightly higher life expectancy than those who started ART between 1996 and 2014. Past exposure to low CD4 counts and ART regimens with more side effects has less influence on prognosis than current CD4 counts. These results indicate the continuing importance of early and sustained treatment with ART.

a)



b)

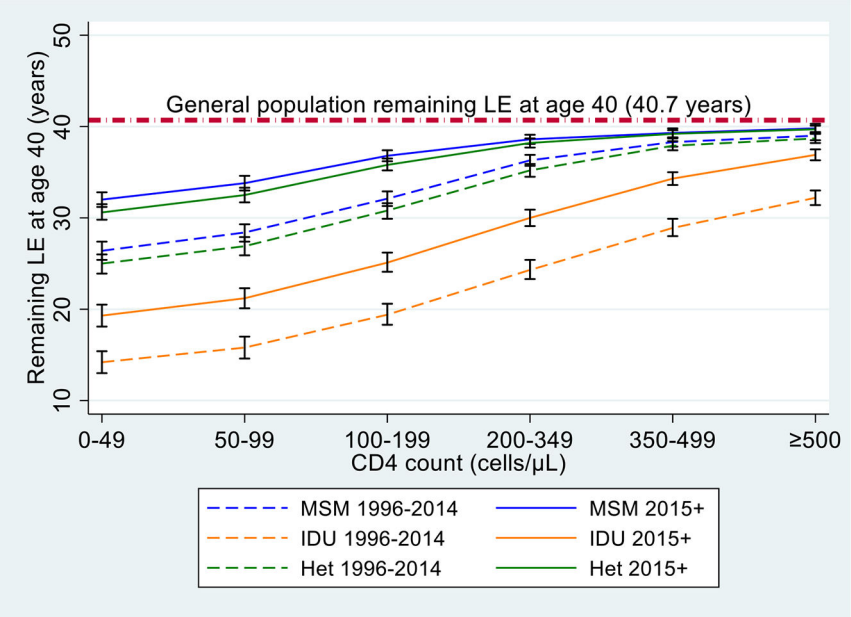


Figure 1:

Remaining life expectancy at age 40 for a) females and b) males with suppressed viral load (<50 cells/ml) and no prior AIDS at follow-up start, stratified by CD4 count, HIV acquisition route, and ART start year.

Table 1:

Characteristics of PWH by combination ART start year group, provided at the follow-up start unless otherwise specified ψ.

	Combination ART start year					
Variable	**1996–99**	**2000–04**	**2005–09**	**2010–14**	**2015-**	**All years**
Total	**34913 (16.9%)**	**32944 (15.9%)**	**43441 (21%)**	**58145 (28.1%)**	**37448 (18.1%)**	**206891 (100%)**
Male	25852 (74.1%)	22239 (67.5%)	30642 (70.5%)	45548 (78.3%)	29700 (79.3%)	153981 (74.4%)
Female	9061 (26%)	10705 (32.5%)	12799 (29.5%)	12597 (21.7%)	7748 (20.7%)	52910 (25.6%)
Ethnicity						
White	26601 (76.2%)	17877 (54.3%)	22450 (51.7%)	32832 (56.5%)	22086 (59.0%)	121846 (58.9%)
Black	3291 (9.4%)	6499 (19.7%)	8338 (19.2%)	8960 (15.4%)	6078 (16.2%)	33166 (16.0%)
Hispanic	443 (1.3%)	628 (1.9%)	1134 (2.6%)	1930 (3.3%)	1610 (4.3%)	5745 (2.8%)
Asian	1411 (4.0%)	1275 (3.9%)	1522 (3.5%)	2093 (3.6%)	1594 (4.3%)	7895 (3.8%)
Other/unknown	3167 (9.1%)	6665 (20.2%)	9997 (23.0%)	12330 (21.2%)	6080 (16.2%)	38239 (18.5%)
Prior AIDS	10653 (30.5%)	9424 (28.6%)	9308 (21.4%)	7327 (12.6%)	4710 (12.6%)	41422 (20%)
Tested HCV RNA positive	3788 (10.8%)	2429 (7.4%)	2226 (5.1%)	2112 (3.6%)	971 (2.6%)	11526 (5.6%)
HIV acquisition route						
Men having sex with men	14057 (40.3%)	11246 (34.1%)	18208 (41.9%)	31486 (54.2%)	20093 (53.7%)	95090 (46%)
Injecting drug use	7043 (20.2%)	4344 (13.2%)	3249 (7.5%)	3136 (5.4%)	1691 (4.5%)	19463 (9.4%)
Heterosexual sex	11407 (32.7%)	15063 (45.7%)	19140 (44.1%)	19834 (34.1%)	12598 (33.6%)	78042 (37.7%)
Other/unknown *	2406 (6.9%)	2291 (7%)	2844 (6.5%)	3689 (6.3%)	3066 (8.2%)	14296 (6.9%)
Follow-up start age (years)						
16–29	0 (0%)	105 (0.3%)	1123 (2.6%)	6931 (11.9%)	6398 (17.1%)	14557 (7%)
30–39	1077 (3.1%)	3602 (10.9%)	9581 (22.1%)	17449 (30%)	10808 (28.9%)	49158 (23.8%)
40–49	10517 (30.1%)	12466 (37.8%)	16219 (37.3%)	17990 (30.9%)	10200 (27.2%)	67392 (32.6%)
50–59	15611 (44.7%)	11351 (34.5%)	11543 (26.6%)	11150 (19.2%)	7067 (18.9%)	56722 (27.4%)
60–69	5644 (16.2%)	3970 (12.1%)	3804 (8.8%)	3666 (6.3%)	2334 (6.2%)	19418 (9.4%)
≥70	2064 (5.9%)	1450 (4.4%)	1171 (2.7%)	959 (1.6%)	641 (1.7%)	6285 (3%)

	Combination ART start year					
Variable	**1996–99**	**2000–04**	**2005–09**	**2010–14**	**2015-**	**All years**
Median age [IQR]	53 [48–58]	50 [44–56]	46 [40–53]	42 [34–50]	41 [33–51]	47 [39–54]
Follow-up start CD4 count (cells/μL)						
0–49	162 (0.5%)	144 (0.4%)	181 (0.4%)	188 (0.3%)	1555 (4.2%)	2230 (1.1%)
50–99	219 (0.6%)	204 (0.6%)	208 (0.5%)	302 (0.5%)	1128 (3%)	2061 (1%)
100–199	876 (2.5%)	816 (2.5%)	858 (2%)	1548 (2.7%)	2572 (6.9%)	6670 (3.2%)
200–349	2718 (7.8%)	2551 (7.7%)	3455 (8%)	5031 (8.7%)	5688 (15.2%)	19443 (9.4%)
350–499	4922 (14.1%)	4982 (15.1%)	6980 (16.1%)	8851 (15.2%)	7260 (19.4%)	32995 (15.9%)
≥500	21427 (61.4%)	19671 (59.7%)	25922 (59.7%)	35358 (60.8%)	15413 (41.2%)	117791 (56.9%)
Missing	4589 (13.1%)	4576 (13.9%)	5837 (13.4%)	6867 (11.8%)	3832 (10.2%)	25701 (12.4%)
Median CD4 count [IQR]	646 [462–870]	634 [457–840]	617 [457–808]	610 [443–803]	551 [430–731]	623 [452–824]
Median nadir CD4 pre-ART (cells/μL) [IQR]	209 [91–336]	200 [90–300]	225 [125–306]	316 [200–432]	345 [185–510]	260 [138–387]
Nadir CD4 pre-ART missing	5576 (16%)	5425 (16.5%)	6152 (14.2%)	6940 (11.9%)	3576 (9.5%)	27669 (13.4%)
Median nadir CD4 post-ART to 2015 [IQR]	200 [96–320]	220 [118–335]	283 [170–397]	428 [288–584]	469 [290–676]	315 [175–486]
Nadir CD4 post-ART to 2015 missing	671 (1.9%)	702 (2.1%)	1193 (2.7%)	3790 (6.5%)	3931 (10.5%)	10287 (5%)
Median CD4 1-year post-ART [IQR]	381 [233–571]	370 [240–532]	422 [290–570]	565 [400–750]	624 [420–845]	480 [310–680]
CD4 1-year post ART missing	6444 (18.5%)	5665 (17.2%)	6383 (14.7%)	4142 (7.1%)	2146 (5.7%)	24780 (12%)
Follow-up start Viral load (copies/mL)						
<50	27744 (79.5%)	24231 (73.6%)	31583 (72.7%)	44615 (76.7%)	10981 (29.3%)	139154 (67.3%)
≥50	3334 (9.6%)	4838 (14.7%)	6990 (16.1%)	8184 (14.1%)	19962 (53.3%)	43308 (20.9%)
Missing	3835 (11%)	3875 (11.8%)	4868 (11.2%)	5346 (9.2%)	6505 (17.4%)	24429 (11.8%)
Viral load 1-year post ART (copies/mL)						
<50	14590 (41.8%)	16018 (48.6%)	24971 (57.6%)	43358 (74.6%)	30453 (81.3%)	129390 (62.5%)
≥50	13906 (39.8%)	11268 (34.2%)	11757 (27.1%)	9432 (16.2%)	4564 (12.2%)	50927 (24.6%)
Missing	6417 (18.4%)	5658 (17.2%)	6713 (15.5%)	5355 (9.2%)	2431 (6.5%)	26574 (12.8%)
Follow-up start CD8 count (cells/μL)						
0–399	1773 (5.1%)	1884 (5.7%)	2450 (5.6%)	2782 (4.8%)	2095 (5.6%)	10984 (5.3%)
400–799	9007 (25.8%)	9268 (28.1%)	12524 (28.8%)	15995 (27.5%)	9025 (24.1%)	55819 (27%)

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	Combination ART start year					
Variable	**1996–99**	**2000–04**	**2005–09**	**2010–14**	**2015-**	**All years**
800–1199	6873 (19.7%)	6303 (19.1%)	8642 (19.9%)	11975 (20.6%)	7447 (19.9%)	41240 (19.9%)
≥1200	4519 (12.9%)	3712 (11.3%)	4635 (10.7%)	6948 (11.9%)	6010 (16%)	25824 (12.5%)
Missing	12741 (36.5%)	11777 (35.7%)	15190 (35%)	20445 (35.2%)	12871 (34.4%)	73024 (35.3%)
Median CD8 count [IQR]	812 [588–1116]	776 [563–1060]	771 [564–1044]	806 [589–1095]	1127 [809–1514]	794 [578–1082]
Median peak CD8 pre-ART (cells/μL) [IQR]	1152 [790–1615]	1060 [690–1526]	1128 [752–1637]	1150 [794–1622]	1100 [755–1561]	1123 [761–1600]
Peak CD8 pre-ART missing	16510 (47.3%)	16699 (50.7%)	17264 (39.7%)	20032 (34.5%)	12079 (32.3%)	82584 (39.9%)
Median peak CD8 post-ART to 2015 [IQR]	1544 [1143–2043]	1345 [991–1814]	1229 [909–1666]	1046 [766–1428]	1127 [809–1514]	1250 [905–1718]
Peak CD8 post-ART to 2015 missing	8280 (23.7%)	7433 (22.6%)	10086 (23.2%)	19177 (33%)	36626 (97.8%)	81602 (39.4%)
Median CD8 1-year post-ART [IQR]	900 [635–1236]	856 [610–1186]	839 [600–1150]	820 [597–1115]	820 [595–1117]	840 [604–1151]
CD8 1-year post ART missing	15663 (44.9%)	14116 (42.8%)	15204 (35%)	19869 (34.2%)	11834 (31.6%)	76686 (37.1%)
Exposure to ART drugs with more side effects	33342 (95.5%)	27481 (83.4%)	13652 (31.4%)	5402 (9.3%)	1723 (4.6%)	81600 (39.4%)
Median duration on these drugs (days) [IQR]	4720 [3315–6272]	2153 [984–3556]	0 [0–370]	0 [0–0]	0 [0–0]	0 [0–2476]
Zidovudine (AZT) exposure	30475 (87.3%)	23783 (72.2%)	12319 (28.4%)	5080 (8.7%)	1593 (4.3%)	73250 (35.4%)
Stavudine (D4T) exposure	23766 (68.1%)	8226 (25%)	1342 (3.1%)	493 (0.8%)	233 (0.6%)	34060 (16.5%)
Zalcitabine (DDC) exposure	7632 (21.9%)	889 (2.7%)	279 (0.6%)	142 (0.2%)	67 (0.2%)	9009 (4.4%)
Didanosine (DDI) exposure	20468 (58.6%)	9171 (27.8%)	2317 (5.3%)	641 (1.1%)	281 (0.8%)	32878 (15.9%)
Indinavir (IDV) exposure	17070 (48.9%)	2797 (8.5%)	657 (1.5%)	335 (0.6%)	155 (0.4%)	21014 (10.2%)
Mono/dual-NRTI exposure	13017 (37.3%)	5188 (15.7%)	3962 (9.1%)	2978 (5.1%)	584 (1.6%)	25729 (12.4%)
Mono/dual-NRTI duration (days) [IQR]	553 [194–1228]	418 [119–1189]	417 [104–1143]	280 [77–792]	365 [82–1045]	469 [141–1156]

HCV: Hepatitis C virus. RNA: Ribonucleic acid. ART: Antiretroviral therapy. γ Characteristics for those in the pre-2014 combination ART start groups are time-updated for 2015, whilst those starting in or after 2015 are taken from a year after combination ART start. NRTI: Nucleoside reverse transcriptase inhibitors. IQR: Interquartile range.

* Mode of HIV acquisition was not recorded for the US Veterans' Affairs Cohort, which had a higher prevalence of comorbidities and substance use than other cohorts.

Table 2:

Estimated mortality rate ratios (with 95% CIs) among PWH treated with ART, using follow-up from 2015 onwards*.

		Mortality rate ratio (95% confidence intervals)		
Variable		**Adjusted for age and cohort**	**Additionally adjusted for ART start year group, sex, HIV acquisition route, and characteristics at start of follow-up**	**Additionally adjusted for characteristics measured before start of follow-up**
Combination ART start year group	1996–1999	1	1	1
	2000–2004	0.82 (0.76–0.88)	0.86 (0.80–0.93)	0.91 (0.84–0.98)
	2005–2009	0.64 (0.59–0.69)	0.74 (0.69–0.80)	0.88 (0.81–0.97)
	2010–2014	0.51 (0.47–0.56)	0.65 (0.60–0.71)	0.88 (0.79–0.99)
	2015–2019	0.58 (0.52–0.66)	0.47 (0.41–0.53)	0.70 (0.58–0.84)
Age (years)	16–29	0.67 (0.54–0.83)	0.79 (0.63–0.98)	0.80 (0.65–0.99)
	30–39	1	1	1
	40–49	1.53 (1.38–1.69)	1.26 (1.14–1.40)	1.26 (1.14–1.39)
	50–59	2.47 (2.24–2.72)	1.76 (1.59–1.94)	1.75 (1.58–1.94)
	60–69	3.93 (3.53–4.37)	3.18 (2.85–3.55)	3.19 (2.86–3.56)
	≥70	9.08 (8.11–10.16)	7.60 (6.76–8.54)	7.66 (6.81–8.61)
Sex	Male	1	1	1
	Female	0.85 (0.80–0.91)	0.79 (0.73–0.85)	0.77 (0.72–0.83)
HIV acquisition-route	MSM	1	1	1
	IDU	3.93 (3.65–4.24)	2.59 (2.38–2.82)	2.48 (2.28–2.71)
	Heterosexual	1.22 (1.15–1.31)	1.25 (1.16–1.34)	1.24 (1.16–1.34)
	Other/unknown	1.53 (1.38–1.70)	1.35 (1.21–1.50)	1.35 (1.22–1.51)
CD4 count (cells/μL) at follow-up start	0–49	7.78 (6.62–9.13)	5.54 (4.65–6.61)	4.72 (3.88–5.74)
	50–99	6.43 (5.47–7.55)	4.82 (4.07–5.69)	3.91 (3.26–4.69)
	100–199	4.32 (3.90–4.79)	3.35 (3.01–3.74)	2.86 (2.54–3.23)
	200–349	2.50 (2.30–2.71)	2.15 (1.97–2.32)	1.92 (1.75–2.10)
	350–499	1.48 (1.37–1.60)	1.40 (1.29–1.51)	1.31 (1.21–1.43)
	≥500	1	1	1
	Missing	2.83 (2.63–3.05)	2.04 (1.81–2.29)	2.34 (2.06–2.66)
Viral load (copies/mL) at follow-up start	<50	1	1	1
	≥50	1.74 (1.61–1.87)	1.36 (1.26–1.47)	1.31 (1.21–1.42)
	Missing	2.52 (2.35–2.71)	1.98 (1.79–2.20)	1.89 (1.70–2.11)
AIDS at follow-up start	No	1	1	1
	Yes	2.10 (1.99–2.22)	1.64 (1.55–1.73)	1.60 (1.51–1.70)

		Mortality rate ratio (95% confidence intervals)		
Variable		**Adjusted for age and cohort**	**Additionally adjusted for ART start year group, sex, HIV acquisition route, and characteristics at start of follow-up**	**Additionally adjusted for characteristics measured before start of follow-up**
CD8 count (cells/μL) at follow-up start	0–399	1	1	1
	400–799	0.56 (0.50–0.62)	0.78 (0.70–0.88)	0.78 (0.69–0.88)
	800–1199	0.58 (0.52–0.65)	0.83 (0.74–0.94)	0.80 (0.70–0.91)
	≥1200	0.77 (0.69–0.87)	1.06 (0.94–1.20)	0.96 (0.83–1.11)
	Missing	0.85 (0.76–0.95)	0.65 (0.57–0.73)	0.58 (0.50–0.68)
HCV RNA status at follow-up start	Negative	1	1	1
	Positive	1.97 (1.76–2.20)	1.40 (1.25–1.56)	1.38 (1.23–1.54)
	Missing	0.69 (0.63–0.75)	0.88 (0.80–0.97)	0.90 (0.82–0.99)
Exposure to ART drugs with more side-effects pre-follow-up start	No	1		1
	Yes	1.71 (1.61–1.82)		1.18 (1.08–1.29)
	Not available ¥	1.00 (0.83–1.20)		1.04 (0.85–1.27)
Mono/dual-NRTI regimen exposure pre-follow-up start	No	1		1
	Yes	1.39 (1.30–1.48)		1.03 (0.96–1.11)
Pre-ART start CD4 count (cells/μL) nadir	0–49	1.98 (1.74–2.25)		0.83 (0.96–1.31)
	50–99	1.88 (1.64–2.16)		0.92 (0.79–1.07)
	100–199	1.68 (1.48–1.90)		1.00 (0.87–1.15)
	200–349	1.28 (1.13–1.45)		1.05 (0.92–1.19)
	350–499	1.04 (0.91–1.20)		0.98 (0.85–1.13)
	≥500	1		1
	Missing	1.47 (1.29–1.68)		0.96 (0.83–1.12)
Pre-ART start CD8 count (cells/μL) peak	0–399	1		1
	400–799	0.85 (0.73–1.00)		1.12 (0.96–1.31)
	800–1199	0.84 (0.73–0.98)		1.21 (1.03–1.41)
	≥1200	0.87 (0.75–1.00)		1.28 (1.09–1.49)
	Missing	0.90 (0.78–1.03)		1.11 (0.94–1.30)
Nadir CD4 count (cells/μL) between ART start and 2015	0–49	4.34 (3.89–4.84)		1.45 (1.24–1.69)
	50–99	3.56 (3.17–3.99)		1.55 (1.34–1.80)
	100–199	2.59 (2.34–2.88)		1.39 (1.21–1.58)
	200–349	1.74 (1.57–1.93)		1.21 (1.07–1.36)
	350–499	1.28 (1.15–1.44)		1.11 (0.98–1.25)
	≥500	1		1
	Missing	1.44 (1.21–1.71)		0.62 (0.51–0.76)
Peak CD8 count (cells/μL) between ART start and 2015	0–399	1		1

		Mortality rate ratio (95% confidence intervals)		
Variable		**Adjusted for age and cohort**	**Additionally adjusted for ART start year group, sex, HIV acquisition route, and characteristics at start of follow-up**	**Additionally adjusted for characteristics measured before start of follow-up**
	400–799	0.63 (0.49–0.81)		0.86 (0.66–1.11)
	800–1199	0.58 (0.45–0.74)		0.79 (0.61–1.03)
	≥1200	0.79 (0.63–1.00)		0.94 (0.72–1.22)
	Missing	0.64 (0.50–0.82)		0.90 (0.68–1.18)
CD4 count (cells/μL) 1-year after ART start	0–49	5.03 (4.24–5.97)		1.40 (1.14–1.71)
	50–99	3.26 (2.84–3.75)		1.06 (0.90–1.26)
	100–199	2.34 (2.14–2.56)		0.97 (0.86–1.09)
	200–349	1.81 (1.67–1.95)		0.99 (0.90–1.09)
	350–499	1.33 (1.22–1.44)		0.97 (0.89–1.06)
	≥500	1		1
	Missing	1.71 (1.56–1.87)		1.04 (0.90–1.21)
CD8 count (cells/μL) 1-year after ART start	0–399	1		1
	400–799	0.74 (0.66–0.84)		0.93 (0.81–1.06)
	800–1199	0.73 (0.65–0.83)		0.86 (0.74–1.00)
	≥1200	0.83 (0.73–0.95)		0.87 (0.74–1.02)
	Missing	0.85 (0.75–0.96)		0.99 (0.85–1.15)
Viral load (copies/mL) 1-year after ART start	<50	1		1
	≥50	1.65 (1.55–1.75)		1.13 (1.06–1.20)
	Missing	1.43 (1.32–1.55)		1.00 (0.87–1.13)

*Follow-up starts on or after 01/01/2015.

ΨData on historic exposure to these ART drugs was not requested from UK-CHIC.

MSM: Men who have sex with men. IDU: Injecting drug use. HCV: Hepatitis C virus. NRTI: Nucleoside reverse transcriptase inhibitors

Table 3:

Estimates of remaining years of life expectancy for females at exact age 40, stratified by HIV mode of acquisition, ART start year, and viral load (VL) suppression (<50 cells/ml), prior AIDS, and CD4 count (cells/μL) at follow-up start (2015 onwards).

ART start: 1996–2014	**CD4 count:**	**0–49**	**50–99**	**100–199**	**200–349**	**350–499**	**≥500**
Acquisition route: Injecting drug use (IDU)	VL suppressed, no prior AIDS	16.2 (15.0, 17.4)	18.0 (16.8, 19.2)	21.7 (20.6, 22.9)	26.7 (25.7, 27.7)	31.1 (30.2, 32.0)	34.1 (33.4, 34.9)
	VL suppressed, prior AIDS	11.6 (10.4, 12.8)	13.1 (11.9, 14.3)	16.4 (15.2, 17.6)	21.0 (19.9, 22.2)	25.6 (24.6, 26.6)	29.0 (28.1, 29.9)
	VL unsuppressed, no prior AIDS	13.0 (11.8, 14.2)	14.6 (13.4, 15.8)	18.0 (16.9, 19.2)	22.8 (21.7, 24.0)	27.4 (26.4, 28.4)	30.7 (29.9, 31.6)
	VL unsuppressed, prior AIDS	9.0 (7.9, 10.1)	10.3 (9.1, 11.4)	13.1 (11.9, 14.3)	17.4 (16.2, 18.6)	21.8 (20.6, 22.9)	25.2 (24.1, 26.2)
Acquisition route: Heterosexual sex	VL suppressed, no prior AIDS	27.3 (26.3, 28.3)	29.2 (28.3, 30.1)	32.8 (32.1, 33.6)	36.9 (36.3, 37.5)	40.0 (39.5, 40.4)	41.7 (41.4, 42.1)
	VL suppressed, prior AIDS	21.7 (20.5, 22.8)	23.6 (22.5, 24.7)	27.5 (26.5, 28.5)	32.2 (31.4, 33.0)	36.0 (35.4, 36.7)	38.5 (38.0, 39.1)
	VL unsuppressed, no prior AIDS	23.5 (22.4, 24.6)	25.4 (24.4, 26.5)	29.3 (28.4, 30.2)	33.8 (33.0, 34.5)	37.4 (36.9, 38.0)	39.7 (39.3, 40.2)
	VL unsuppressed, prior AIDS	18.0 (16.8, 19.1)	19.8 (18.7, 21.0)	23.7 (22.6, 24.8)	28.6 (27.6, 29.5)	32.8 (32.1, 33.6)	35.7 (35.1, 36.4)
Standardised	**Overall: 35.8 (35.2, 36.4)**	**19.4 (18.2, 20.5)**	**23.2 (22.2, 24.3)**	**27.8 (26.8, 28.7)**	**33.6 (32.8, 34.3)**	**37.6 (37.0, 38.1)**	**40.2 (39.7, 40.6)**
ART start: 2015–19	**CD4 count:**	**0–49**	**50–99**	**100–199**	**200–349**	**350–499**	**≥500**
Acquisition route: Injecting drug use (IDU)	VL suppressed, no prior AIDS	21.6 (20.5, 22.7)	23.6 (22.5, 24.7)	27.5 (26.5, 28.4)	32.2 (31.3, 33.0)	36.0 (35.4, 36.6)	38.5 (38.0, 39.0)
	VL suppressed, prior AIDS	16.3 (15.1, 17.5)	18.0 (16.9, 19.2)	21.8 (20.7, 22.9)	26.7 (25.7, 27.7)	31.2 (30.3, 32.0)	34.2 (33.5, 34.9)
	VL unsuppressed, no prior AIDS	17.9 (16.7, 19.1)	19.8 (18.6, 20.9)	23.6 (22.5, 24.7)	28.5 (27.6, 29.5)	32.8 (32.0, 33.6)	35.7 (35.0, 36.3)
	VL unsuppressed, prior AIDS	13.0 (11.8, 14.2)	14.6 (13.4, 15.8)	18.1 (16.9, 19.3)	22.9 (21.8, 24.0)	27.5 (26.5, 28.5)	30.3 (29.4, 31.2)
Acquisition route: Heterosexual sex	VL suppressed, no prior AIDS	32.7 (31.9, 33.5)	34.4 (33.7, 35.1)	37.5 (36.9, 38.0)	40.7 (40.3, 41.1)	42.1 (41.8, 42.4)	42.7 (42.4, 43.0)
	VL suppressed, prior AIDS	27.4 (26.4, 28.4)	29.3 (28.4, 30.2)	32.9 (32.1, 33.6)	36.9 (36.3, 37.5)	40.0 (39.6, 40.4)	41.8 (41.4, 42.1)
	VL unsuppressed, no prior AIDS	29.2 (28.2, 30.1)	31.0 (30.2, 31.9)	34.4 (33.7, 35.1)	38.2 (37.7, 38.8)	40.9 (40.6, 41.3)	42.0 (41.7, 42.3)
	VL unsuppressed, prior AIDS	23.5 (22.4, 24.6)	25.5 (24.5, 26.5)	29.3 (28.4, 30.3)	33.8 (33.1, 34.6)	37.5 (36.9, 38.1)	39.8 (39.3, 40.2)
Standardised	**Overall: 39.0 (38.5, 39.5)**	**24.9 (23.9, 25.9)**	**28.9 (27.9, 29.8)**	**33.0 (32.2, 33.7)**	**38.0 (37.4, 38.5)**	**40.8 (40.4, 41.2)**	**42.0 (41.7, 42.3)**

Table 4:

Estimates of remaining years of life expectancy for males at exact age 40, stratified by HIV mode of acquisition, ART start year, and viral load (VL) suppression (<50 cells/ml), prior AIDS, and CD4 count (cells/μL) at follow-up start (2015 onwards).

ART start: 1996–2014	**CD4 count:**	**0–49**	**50–99**	**100–199**	**200–349**	**350–499**	**≥500**
Acquisition route: Men having sex with men (MSM)	VL suppressed, no prior AIDS	26.4 (25.4, 27.4)	28.4 (27.4, 29.3)	32.1 (31.3, 32.9)	36.3 (35.7, 36.9)	38.3 (37.8, 38.8)	39.0 (38.5, 39.4)
	VL suppressed, prior AIDS	20.7 (19.6, 21.9)	22.7 (21.6, 23.8)	26.6 (25.6, 27.6)	31.4 (30.6, 32.3)	35.5 (34.8, 36.2)	37.8 (37.2, 38.3)
	VL unsuppressed, no prior AIDS	22.5 (21.4, 23.7)	24.5 (23.4, 25.6)	28.4 (27.5, 29.4)	33.1 (32.4, 33.9)	36.8 (36.2, 37.4)	38.2 (37.7, 38.7)
	VL unsuppressed, prior AIDS	17.1 (15.9, 18.3)	18.9 (17.7, 20.1)	22.7 (21.6, 23.8)	27.7 (26.7, 28.7)	32.1 (31.3, 33.0)	35.2 (34.5, 35.9)
Acquisition route: Injecting drug use (IDU)	VL suppressed, no prior AIDS	14.2 (13.0, 15.4)	15.8 (14.6, 17.0)	19.4 (18.3, 20.6)	24.3 (23.3, 25.4)	28.9 (28.0, 29.9)	32.2 (31.4, 33.0)
	VL suppressed, prior AIDS	9.9 (8.8, 11.1)	11.3 (10.1, 12.5)	14.3 (13.1, 15.5)	18.7 (17.6, 19.9)	23.2 (22.1, 24.3)	26.7 (25.7, 27.7)
	VL unsuppressed, no prior AIDS	11.2 (10.0, 12.4)	12.7 (11.5, 13.8)	15.9 (14.7, 17.1)	20.5 (19.4, 21.7)	25.1 (24.0, 26.1)	28.5 (27.6, 29.5)
	VL unsuppressed, prior AIDS	7.6 (6.6, 8.6)	8.7 (7.6, 9.8)	11.3 (10.2, 12.5)	15.3 (14.1, 16.5)	19.4 (18.3, 20.6)	22.8 (21.7, 23.9)
Acquisition route: Heterosexual sex	VL suppressed, no prior AIDS	25.0 (23.9, 26.0)	26.9 (25.9, 27.9)	30.8 (29.9, 31.6)	35.2 (34.5, 35.9)	37.9 (37.4, 38.4)	38.7 (38.2, 39.2)
	VL suppressed, prior AIDS	19.3 (18.2, 20.5)	21.3 (20.1, 22.4)	25.2 (24.1, 26.2)	30.1 (29.2, 31.0)	34.3 (33.6, 35.1)	36.9 (36.3, 37.5)
	VL unsuppressed, no prior AIDS	21.1 (20.0, 22.3)	23.1 (22.0, 24.2)	27.0 (26.0, 28.0)	31.8 (31.0, 32.7)	35.8 (35.2, 36.5)	37.8 (37.2, 38.3)
	VL unsuppressed, prior AIDS	15.8 (14.6, 17.0)	17.6 (16.4, 18.8)	21.3 (20.2, 22.5)	26.3 (25.3, 27.3)	30.8 (29.9, 31.7)	34.0 (33.2, 34.7)
Standardised	**Overall: 34.5 (33.8, 35.2)**	**18.2 (17.1, 19.4)**	**21.3 (20.2, 22.4)**	**26.2 (25.2, 27.2)**	**32.1 (31.3, 32.9)**	**36.2 (35.6, 36.9)**	**38.0 (37.5, 38.5)**
ART start: 2015–19	**CD4 count:**	**0–49**	**50–99**	**100–199**	**200–349**	**350–499**	**≥500**
Acquisition route: Men having sex with men (MSM)	VL suppressed, no prior AIDS	32.0 (31.2, 32.8)	33.8 (33.0, 34.6)	36.8 (36.2, 37.4)	38.6 (38.1, 39.1)	39.3 (38.8, 39.8)	39.8 (39.3, 40.3)
	VL suppressed, prior AIDS	26.5 (25.4, 27.5)	28.4 (27.5, 29.4)	32.2 (31.3, 33.0)	36.3 (35.7, 37.0)	38.3 (37.8, 38.8)	39.0 (38.5, 39.5)
	VL unsuppressed, no prior AIDS	28.3 (27.3, 29.3)	30.2 (29.3, 31.1)	33.9 (33.1, 34.6)	37.5 (36.9, 38.1)	38.7 (38.2, 39.1)	39.2 (38.8, 39.7)
	VL unsuppressed, prior AIDS	22.6 (21.5, 23.7)	24.6 (23.5, 25.6)	28.5 (27.5, 29.4)	33.2 (32.4, 34.0)	36.8 (36.2, 37.4)	38.2 (37.7, 38.7)
Acquisition route: Injecting drug use (IDU)	VL suppressed, no prior AIDS	19.3 (18.1, 20.5)	21.2 (20.1, 22.3)	25.1 (24.1, 26.2)	30.0 (29.1, 30.9)	34.3 (33.6, 35.0)	36.9 (36.3, 37.5)
	VL suppressed, prior AIDS	14.2 (13.0, 15.4)	15.9 (14.7, 17.1)	19.5 (18.3, 20.7)	24.4 (23.3, 25.5)	29.0 (28.0, 29.9)	32.3 (31.4, 33.1)
	VL unsuppressed, no prior AIDS	15.8 (14.6, 17.0)	17.5 (16.3, 18.7)	21.3 (20.1, 22.4)	26.2 (25.2, 27.3)	30.7 (29.9, 31.6)	33.9 (33.2, 34.7)
	VL unsuppressed, prior AIDS	11.2 (10.1, 12.4)	12.7 (11.5, 13.9)	15.9 (14.7, 17.1)	20.6 (19.4, 21.7)	25.1 (24.1, 26.2)	28.6 (27.6, 29.5)
Acquisition route: Heterosexual sex	VL suppressed, no prior AIDS	30.6 (29.8, 31.5)	32.5 (31.7, 33.3)	35.8 (35.2, 36.5)	38.2 (37.7, 38.7)	39.2 (38.7, 39.6)	39.7 (39.2, 40.1)
	VL suppressed, prior AIDS	25.0 (24.0, 26.1)	27.0 (26.0, 28.0)	30.8 (30.0, 31.7)	35.3 (34.6, 36.0)	38.0 (37.4, 38.5)	38.7 (38.2, 39.2)

	VL unsuppressed, no prior AIDS	26.9 (25.9, 27.9)	28.8 (27.9, 29.8)	32.6 (31.7, 33.4)	36.6 (36.0, 37.2)	38.4 (37.9, 38.9)	39.1 (38.6, 39.5)
	VL unsuppressed, prior AIDS	21.2 (20.0, 22.3)	23.1 (22.0, 24.2)	27.1 (26.1, 28.1)	31.9 (31.0, 32.7)	35.9 (35.2, 36.5)	37.8 (37.3, 38.4)
Standardised	**Overall: 37.0 (36.5, 37.6)**	**23.7 (22.7, 24.8)**	**26.9 (25.9, 27.9)**	**31.7 (30.9, 32.5)**	**36.5 (35.9, 37.1)**	**38.4 (37.9, 38.9)**	**39.2 (38.7, 39.7)**