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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Summary

Background The life expectancy of people with HIV taking antiretroviral therapy (ART) has increased substantially over the past 25 years. Most previous studies of life expectancy were based on data from the first few years after starting ART, when mortality is highest. However, many people with HIV have been successfully treated with ART for many years, and up-to-date prognosis data are needed. We aimed to estimate life expectancy in adults with HIV on ART for at least 1 year in Europe and North America from 2015 onwards.

Methods We used data for people with HIV taking ART from the Antiretroviral Therapy Cohort Collaboration and the UK Collaborative HIV Cohort Study. Included participants started ART between 1996 and 2014 and had been on ART for at least 1 year by 2015, or started ART between 2015 and 2019 and survived for at least 1 year; all participants were aged at least 16 years at ART initiation. We used Poisson models to estimate the associations between mortality and demographic and clinical characteristics, including CD4 cell count at the start of follow-up. We also estimated the remaining years of life left for people with HIV aged 40 years who were taking ART, and stratified these estimates by variables associated with mortality. These estimates were compared with estimates for years of life remaining in a corresponding multi-country general population.

Findings Among 206 891 people with HIV included, 5780 deaths were recorded since 2015. We estimated that women with HIV at age 40 years had 35·8 years (95% CI 35·2–36·4) of life left if they started ART before 2015, and 39·0 years (38·5–39·5) left if they started ART after 2015. For men with HIV, the corresponding estimates were 34·5 years (33·8–35·2) and 37·0 (36·5–37·6). Women with CD4 counts of fewer than 49 cells per µL at the start of follow-up had an estimated 19·4 years (18·2–20·5) of life left at age 40 years if they started ART before 2015 and 24·9 years (23·9–25·9) left if they started ART after 2015. The corresponding estimates for men were 18·2 years (17·1–19·4) and 23·7 years (22·7–24·8). Women with CD4 counts of at least 500 cells per µL at the start of follow-up had an estimated 40·2 years (39·7–40·6) of life left at age 40 years if they started ART before 2015 and 42·0 years (41·7–42·3) left if they started ART after 2015. The corresponding estimates for men were 38·0 years (37·5–38·5) and 39·2 years (38·7–39·7).

Interpretation For people with HIV on ART and with high CD4 cell counts who survived to 2015 or started ART after 2015, life expectancy was only a few years lower than that in the general population, irrespective of when ART was started. However, for people with low CD4 counts at the start of follow-up, life-expectancy estimates were substantially lower, emphasising the continuing importance of early diagnosis and sustained treatment of HIV.

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Introduction

The life expectancy of people with HIV starting antiretroviral therapy (ART) has increased over the past 25 years.[1,2] During this period, the efficacy and side-effect profiles of ART regimens have steadily improved, as have time to virological suppression and comorbidity care.[3] Analyses of life expectancy have mainly been based on mortality during the first few years after starting ART,[4] which might not correspond to mortality after several years on ART. People who have been on ART for many years want to know if HIV infection has a long-term effect on health and life expectancy despite successful treatment.

Consistent with updated treatment guidelines, and as recommended by WHO, people with HIV are increasingly starting ART earlier and at higher CD4 cell counts than they used to.[5] Prolonged time from infection to initiation of effective treatment is associated with reduced CD4 cell counts at ART initiation and worse outcomes for several years after starting ART.[6] Time from diagnosis to initiation of ART, nadir CD4 cell count, peak CD8 cell count, and the speed of recovery of these cell counts after starting treatment could all influence subsequent morbidity and mortality.

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Research in context

Evidence before this study

We searched PubMed with the terms "life expectancy" and "HIV" for European or North American studies published in English up to March 30, 2022, in which life expectancy was estimated in people with HIV. Several studies showed that the life expectancy of people with HIV starting antiretroviral therapy (ART) has increased over the past 25 years. This improvement in life expectancy corresponded with increased and earlier access to ART and improved side-effect profiles of ART regimens. These studies all used follow-up data from the first few years after starting ART. In a meta-analysis, the estimated age at death was 63·3 years for patients who started ART with any CD4 cell count. In our previous analysis, in which we used follow-up data from the second and third years of ART use for patients who began ART between 1996 and 2013, the estimated age at death was 76·0 years for women aged 20 years and 73·1 years for men aged 20 years. In analyses by the Kaiser Permanente California cohort, the UK Collaborative HIV Cohort Study, the Swiss HIV Cohort Study, and collaborations of North American cohorts based on follow-up data from 1 year after ART initiation or among people with HIV starting ART with high CD4 cell counts, estimated ages at death for 20-year-olds varied from 69 to 83 years. These studies showed that some subgroups of people with HIV who were taking ART had life expectancy similar to that of the general population.

Added value of this study

Our study, which included follow-up data from 2015 (when treatment guidelines began to recommend ART for all patients irrespective of CD4 cell count) for over 200 000 people with HIV from 20 cohorts in North America and Europe who had started ART up to 20 years previously, showed that mortality was most strongly associated with age and current CD4 cell count. Various aspects of HIV history, such as previous low CD4 cell count or exposure to ART regimens no longer recommended due to side-effects, were also associated with mortality after 2015. At age 40 years, women had an estimated 35·8 years (95% CI 35·2–36·4) of life left if they started ART before 2015 and 39·0 years (38·5–39·5) left if they started ART after 2015, compared with 45·8 years in the general population. The corresponding figures for men were 34·5 years (33·8–35·2), 37·0 years (36·5–37·6), and 40·7 years.

Implications of all the available evidence

Estimated life expectancy for people with HIV on long-term ART with high CD4 cell counts is only a few years lower than that in the general population, irrespective of when ART was started. People who started ART after 2015 are estimated to have slightly higher life expectancy than those who started ART before 2015. Previous low CD4 cell counts and exposure to old ART regimens with poor side-effect profiles have less influence on prognosis than current CD4 cell counts and age. Our results suggest the continuing importance of early and sustained ART.

Early ART regimens included less-effective drugs than are now available,[3] and previous treatment with mono-nucleoside or dual-nucleoside reverse transcriptase inhibitors could have induced drug resistance, limiting future treatment options.[7] Use of drugs with severe metabolic side-effects (eg, stavudine,[8] zidovudine[9]) could also have had long-term effects.

In this study, we aimed to provide estimates of life expectancy for people with HIV in the current ART era, particularly those on long-term therapy. We used HIV cohort follow-up data from 2015 onwards to estimate life expectancy of adults with HIV in Europe and North America who started ART during the early years of ART, and in those who started ART from 2015 onwards. We also examined the association between markers of delayed or unsuccessful treatment and subsequent mortality.

Methods

Data sources and participants

This study was a retrospective analysis of data from the Antiretroviral Therapy Cohort Collaboration, which combines data from various European and North American cohorts of people with HIV,[10] and data from the UK Collaborative HIV Cohort Study (UK CHIC).[11] Overall, 20 cohorts were included in our study (appendix p 1). Our study included people with HIV who were aged 16 years or older when starting combination ART. They had to have either started combination ART between 1996 and 2014 and were still taking it in 2015, having survived for at least a year since treatment initiation, or started combination ART between 2015 and 2019 and subsequently survived for at least a year. We chose 2015 as the cutoff because it was the year when treatment guidelines changed to recommend ART for all people with HIV irrespective of CD4 cell count. Our definition of combination ART (henceforth referred to as ART) included different numbers and varieties of drugs, but excluded mono-nucleoside reverse transcriptase inhibitor (NRTI) or dual-NRTI regimens.

Ethics committees or institutional review boards approved the 20 individual cohorts, which each used standardised data collection methods and regularly followed up participants who consented to be included. No specific additional ethics approval was required for this study.

Procedures

In each cohort, information about mortality was gathered through linkage with vital statistics agencies and hospitals, physician reports, and active clinical follow-up of participants. Data were extracted from each cohort and sent to the Antiretroviral Therapy Cohort

Collaboration data centre in Bristol to be cleaned and combined.

For people with HIV who started combination ART before 2015, follow-up started on either Jan 1, 2015 or 1 year after ART initiation (for those who started ART during 2014)—whichever was later. For people with HIV who started combination ART between 2015 and 2019, follow-up began 1 year after treatment initiation. Follow-up ended at the earliest of death, loss-to-follow-up, or administrative censoring.

The variables included in analyses (decided a priori through consultation with HIV clinicians and representatives of groups of people with HIV) were combination ART start year (1996–99, 2000–04, 2005–09, 2010–14, and 2015–19), demographics (including age, birth sex, and mode of HIV acquisition), characteristics measured at start of follow-up (including AIDS status, hepatitis C virus RNA status, CD4 and CD8 cell counts, and viral load), and characteristics measured before start of follow-up (including exposure to ART drugs with increased side-effects [specifically zidovudine, stavudine, zalcitabine, didanosine, indinavir, or mono-NRTI or dual-NRTI regimens], viral load 1 year after initiation of ART, and CD4 and CD8 cell counts before ART initiation, between ART initiation and 2015, and 1 year after ART initiation). Some variables were sometimes unavailable for individual people with HIV or cohorts. Frequencies of missing data were tabulated. Data for 20 people with HIV who were reported to have died but whose dates of death were unknown were excluded from our analyses.

Statistical analysis

Poisson regression models were used to estimate mortality rate ratios after the start of follow-up for each variable. Our first analysis was adjusted for cohort and age. A second analysis was adjusted for cohort, age, ART start year group, sex, route of HIV acquisition, and characteristics measured at the start of follow-up. A third analysis was adjusted for cohort, age, ART start year group, sex, route of HIV acquisition, characteristics measured at the start of follow-up, and characteristics measured in the years before follow-up. 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 years was estimated for various sex-stratified population groups, with the expected age at death then calculated. Briefly, for each ART start year group, mortality rates were calculated in 5-year age bands (up to 80–84 years; the subsequent group was ≥85 years) 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 which data are commonly available from the cohorts and from people with HIV and their clinicians. The methods for estimating life expectancy are described in more detail in the appendix (p 2). The same methods were used to estimate life expectancy from age 20 years, for comparison with previous literature.

There were few patients in the oldest age group (ie, ≥85 years), so follow-up time was limited and deaths few. Therefore, we calculated the ratio of the mortality rates comparing people with HIV and the general population in each of the age groups from 20 years up, and then the average of these rate ratios. We subsequently calculated an estimated rate ratio for people with HIV compared with the general population, with separate estimates for those who started ART before 2015 and those who started ART in or after 2015. There were low numbers of events in some age groups, so only the ratios from age groups in which mortality among people with HIV was higher than that in the general population were included in the overall rate ratio calculation. To account for the lack of statistical power in the oldest age group of people with HIV, we multiplied this rate ratio by the general population mortality rate in the oldest age group (≥85 years). In the age groups in which mortality estimates among people with HIV were lower than those among the general population, the general population rate was used instead (appendix p 2).

Standardised estimates of remaining years of life at ages 40 years and 20 years were derived by weighting the life-expectancy estimates in each population group by the proportion of the sample in that group starting ART between 2015 and 2019. These derivations were done by sex, and were also stratified by CD4 cell count at the start of follow-up. General population mortality rates and life expectancies were taken for 2015. Sex-specific rates were calculated for each country and then weighted to correspond to the countries of residence of the people with HIV in our dataset. Analyses were done in Stata (version 16.1).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

206 891 people with HIV were included in our study. 5780 deaths were recorded during 619 356 person-years of follow-up after 2015. People with HIV who started ART in later calendar years tended to be younger and to have lower CD4 cell counts and higher viral loads at the start of follow-up compared with those who started ART in earlier calendar years (table 1). A smaller proportion of people starting ART in later calendar years had received an AIDS diagnosis, been exposed to ART drugs with increased side-effects, or been treated with mono-NRTI or dual-NRTI regimens than of those starting ART in

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See **Online** for appendix

For **general population mortality rates and life expectancies** see https://www.mortality.org

	Started ART 1996–99 (n=34 913)	Started ART 2000–04 (n=32 944)	Started ART 2005–09 (n=43 441)	Started ART 2010–14 (n=58 145)	Started ART 2015–19 (n=37 448)
Sex					
Male	25 852 (74·0%)	22 239 (67·5%)	30 642 (70·5%)	45 548 (78·3%)	29 700 (79·3%)
Female	9061 (26·0%)	10 705 (32·5%)	12 799 (29·5%)	12 597 (21·7%)	7748 (20·7%)
Ethnicity					
White	26 601 (76·2%)	17 877 (54·3%)	22 450 (51·7%)	32 832 (56·5%)	22 086 (59·0%)
Black	3291 (9·4%)	6499 (19·7%)	8338 (19·2%)	8960 (15·4%)	6078 (16·2%)
Hispanic	443 (1·3%)	628 (1·9%)	1134 (2·6%)	1930 (3·3%)	1610 (4·3%)
Asian	1411 (4·0%)	1275 (3·9%)	1522 (3·5%)	2093 (3·6%)	1594 (4·3%)
Other or unknown	3167 (9·1%)	6665 (20·2%)	9997 (23·0%)	12 330 (21·2%)	6080 (16·2%)
AIDS before start of follow-up	10 653 (30·5%)	9424 (28·6%)	9308 (21·4%)	7327 (12·6%)	4710 (12·6%)
Tested positive for hepatitis C virus RNA	3788 (10·8%)	2429 (7·4%)	2226 (5·1%)	2112 (3·6%)	971 (2·6%)
HIV acquisition route					
Men having sex with men	14 057 (40·3%)	11 246 (34·1%)	18 208 (41·9%)	31 486 (54·2%)	20 093 (53·7%)
Injecting drug use	7043 (20·2%)	4344 (13·2%)	3249 (7·5%)	3136 (5·4%)	1691 (4·5%)
Heterosexual sex	11 407 (32·7%)	15 063 (45·7%)	19 140 (44·1%)	19 834 (34·1%)	12 598 (33·6%)
Other or unknown*	2406 (6·9%)	2291 (7·0%)	2844 (6·5%)	3689 (6·3%)	3066 (8·2%)
Age at start of follow-up, years					
16–29	0 (0)	105 (0·3%)	1123 (2·6%)	6931 (11·9%)	6398 (17·1%)
30–39	1077 (3·1%)	3602 (10·9%)	9581 (22·1%)	17 449 (30·0%)	10 808 (28·9%)
40–49	10 517 (30·1%)	12 466 (37·8%)	16 219 (37·3%)	17 990 (30·9%)	10 200 (27·2%)
50–59	15 611 (44·7%)	11 351 (34·5%)	11 543 (26·6%)	11 150 (19·2%)	7067 (18·9%)
60–69	5644 (16·2%)	3970 (12·1%)	3804 (8·8%)	3666 (6·3%)	2334 (6·2%)
≥70	2064 (5·9%)	1450 (4·4%)	1171 (2·7%)	959 (1·6%)	641 (1·7%)
Median	53 (48–58)	50 (44–56)	46 (40–53)	42 (34–50)	41 (33–51)
CD4 cells per μL at start of follow-up					
0–49	162 (0·5%)	144 (0·4%)	181 (0·4%)	188 (0·3%)	1555 (4·2%)
50–99	219 (0·6%)	204 (0·6%)	208 (0·5%)	302 (0·5%)	1128 (3·0%)
100–199	876 (2·5%)	816 (2·5%)	858 (2·0%)	1548 (2·7%)	2572 (6·9%)
200–349	2718 (7·8%)	2551 (7·7%)	3455 (8·0%)	5031 (8·7%)	5688 (15·2%)
350–499	4922 (14·1%)	4982 (15·1%)	6980 (16·1%)	8851 (15·2%)	7260 (19·4%)
≥500	21 427 (61·4%)	19 671 (59·7%)	25 922 (59·7%)	35 358 (60·8%)	15 413 (41·2%)
Missing	4589 (13·1%)	4576 (13·9%)	5837 (13·4%)	6867 (11·8%)	3832 (10·2%)
Median	646 (462–870)	634 (457–840)	617 (457–808)	610 (443–803)	551 (430–731)
Nadir CD4 cells per μL					
Pre-ART median	209 (91–336)	200 (90–300)	225 (125–306)	316 (200–432)	345 (185–510)
Pre-ART count missing	5576 (16·0%)	5425 (16·5%)	6152 (14·2%)	6940 (11·9%)	3576 (9·5%)
Post-ART to 2015 median	200 (96–320)	220 (118–335)	283 (170–397)	428 (288–584)	469 (290–676)
Post-ART to 2015 count missing	671 (1·9%)	702 (2·1%)	1193 (2·7%)	3790 (6·5%)	3931 (10·5%)
CD4 cells per μL 1 year post ART					
Median	381 (233–571)	370 (240–532)	422 (290–570)	565 (400–750)	624 (420–845)
Count missing	6444 (18·5%)	5665 (17·2%)	6383 (14·7%)	4142 (7·1%)	2146 (5·7%)
Viral load at start of follow-up, copies per mL					
<50	27 744 (79·5%)	24 231 (73·6%)	31 583 (72·7%)	44 615 (76·7%)	10 981 (29·3%)
≥50	3334 (9·5%)	4838 (14·7%)	6990 (16·1%)	8184 (14·1%)	19 962 (53·3%)
Missing	3835 (11·0%)	3875 (11·8%)	4868 (11·2%)	5346 (9·2%)	6505 (17·4%)
Viral load 1 year post ART, copies per mL					
<50	14 590 (41·8%)	16 018 (48·6%)	24 971 (57·5%)	43 358 (74·6%)	30 453 (81·3%)
≥50	13 906 (39·8%)	11 268 (34·2%)	11 757 (27·1%)	9432 (16·2%)	4564 (12·2%)
Missing	6417 (18·4%)	5658 (17·2%)	6713 (15·5%)	5355 (9·2%)	2431 (6·5%)

(Table 1 continues on next page)

	Started ART 1996–99 (n=34 913)	Started ART 2000–04 (n=32 944)	Started ART 2005–09 (n=43 441)	Started ART 2010–14 (n=58 145)	Started ART 2015–19 (n=37 448)
(Continued from previous page)					
CD8 cells per µL at start of follow-up					
0–399	1773 (5·1%)	1884 (5·7%)	2450 (5·6%)	2782 (4·8%)	2095 (5·6%)
400–799	9007 (25·8%)	9268 (28·1%)	12 524 (28·8%)	15 995 (27·5%)	9025 (24·1%)
800–1199	6873 (19·7%)	6303 (19·1%)	8642 (19·9%)	11 975 (20·6%)	7447 (19·9%)
≥1200	4519 (12·9%)	3712 (11·3%)	4635 (10·7%)	6948 (11·9%)	6010 (16·0%)
Missing	12 741 (36·5%)	11 777 (35·7%)	15 190 (35·0%)	20 445 (35·2%)	12 871 (34·4%)
Median	812 (588–1116)	776 (563–1060)	771 (564–1044)	806 (589–1095)	1127 (809–1514)
Peak CD8 cells per µL					
Pre-ART median	1152 (790–1615)	1060 (690–1526)	1128 (752–1637)	1150 (794–1622)	1100 (755–1561)
Pre-ART count missing	16 510 (47·3%)	16 699 (50·7%)	17 264 (39·7%)	20 032 (34·5%)	12 079 (32·3%)
Post-ART to 2015 median	1544 (1143–2043)	1345 (991–1814)	1229 (909–1666)	1046 (766–1428)	1127 (809–1514)
Post-ART to 2015 count missing	8280 (23·7%)	7433 (22·6%)	10 086 (23·2%)	19 177 (33·0%)	36 626 (97·8%)
CD8 cells per µL 1 year post ART					
Median	900 (635–1236)	856 (610–1186)	839 (600–1150)	820 (597–1115)	820 (595–1117)
Count missing	15 663 (44·9%)	14 116 (42·8%)	15 204 (35%)	19 869 (34·2%)	11 834 (31·6%)
Exposure to ART drugs with increased side-effects					
Any	33 342 (95·5%)	27 481 (83·4%)	13 652 (31·4%)	5402 (9·3%)	1723 (4·6%)
Treatment duration, days	4720 (3315–6272)	2153 (984–3556)	0 (0–370)	0 (0–0)	0 (0–0)
Zidovudine	30 475 (87·3%)	23 783 (72·2%)	12 319 (28·4%)	5080 (8·7%)	1593 (4·3%)
Stavudine	23 766 (68·1%)	8226 (25·0%)	1342 (3·1%)	493 (0·8%)	233 (0·6%)
Zalcitabine	7632 (21·9%)	889 (2·7%)	279 (0·6%)	142 (0·2%)	67 (0·2%)
Didanosine	20 468 (58·6%)	9171 (27·8%)	2317 (5·3%)	641 (1·1%)	281 (0·8%)
Indinavir	17 070 (48·9%)	2797 (8·5%)	657 (1·5%)	335 (0·6%)	155 (0·4%)
Mono-NRTIs or dual-NRTIs	13 017 (37·3%)	5188 (15·7%)	3962 (9·1%)	2978 (5·1%)	584 (1·6%)
Duration of exposure to mono-NRTIs or dual-NRTIs, days	553 (194–1228)	418 (119–1189)	417 (104–1143)	280 (77–792)	365 (82–1045)

Data are n (%) or median (IQR). Characteristics for those in the pre-2014 ART start groups are time-updated for 2015, whereas those for people starting ART in or after 2015 are taken from 1 year after ART initiation. ART=antiretroviral therapy. NRTI=nucleoside reverse transcriptase inhibitor. *Mode of HIV acquisition was not recorded for the US Veterans' Affairs Cohort, in which the prevalence of comorbidities and substance use was higher than that in other cohorts.

Table 1: **Characteristics of people with HIV, by ART start year**

earlier years. 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.

Table 2 shows mortality analyses adjusted for age and cohort. Compared with people who started ART in 1996–99, those who started ART more recently had lower mortality; mortality rate ratios for people who started ART in 2010–14 (0·51 [95% CI 0·47–0·56]) were similar to those for people who started ART in 2015–19 (0·58 [0·52–0·66]). In the analysis additionally adjusted for sex, HIV acquisition route, and characteristics at the start of follow-up, mortality was lower in women than in men, and men who acquired HIV via sexual contact with men had lower mortality rates than those who acquired HIV via other routes (particularly injecting drug use; table 2). For most variables, associations with mortality were somewhat lessened after additional adjustment for characteristics at the start of follow-up, but overall patterns were similar to those in the analyses adjusted for age and cohort only (table 2). However, in the additionally adjusted analyses the association with mortality became stronger for people starting ART in 2015–19 (0·47 [0·41–0·53]) compared with those starting in 1996–99 (0·58 [0·52–0·66]). Compared with CD4 counts of 500 cells per µL or more at the start of follow-up, lower CD4 counts were strongly associated with increased mortality (table 2). High viral load (≥50 copies per mL), a diagnosis of AIDS, and chronic hepatitis C virus infection at the start of follow-up were all associated with increased mortality both in analyses adjusted for age and cohort only and in those additionally adjusted for sex, HIV acquisition route, and characteristics at follow-up initiation (table 2). However, the association between mortality and CD8 cell counts was weaker in the additionally adjusted analyses (table 2).

After additional adjustment for characteristics measured before the start of follow-up, mortality rate ratios for

	Adjusted for age and cohort	Adjusted for ART start year group, age, cohort, sex, HIV acquisition route, and characteristics at start of follow-up	Adjusted for ART start year group, age, cohort, sex, HIV acquisition route, and characteristics before and at start of follow-up
ART start year			
1996–99	1 (ref)	1 (ref)	1 (ref)
2000–04	0·82 (0·76–0·88)	0·86 (0·80–0·93)	0·91 (0·84–0·98)
2005–09	0·64 (0·59–0·69)	0·74 (0·69–0·80)	0·88 (0·81–0·97)
2010–14	0·51 (0·47–0·56)	0·65 (0·60–0·71)	0·88 (0·79–0·99)
2015–19	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 (ref)	1 (ref)	1 (ref)
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 (ref)	1 (ref)	1 (ref)
Female	0·85 (0·80–0·91)	0·79 (0·73–0·85)	0·77 (0·72–0·83)
HIV acquisition route			
Men having sex with men	1 (ref)	1 (ref)	1 (ref)
Injecting drug use	3·93 (3·65–4·24)	2·59 (2·38–2·82)	2·48 (2·28–2·71)
Heterosexual sex	1·22 (1·15–1·31)	1·25 (1·16–1·34)	1·24 (1·16–1·34)
Other or unknown	1·53 (1·38–1·70)	1·35 (1·21–1·50)	1·35 (1·22–1·51)
CD4 cells per µL at start of follow-up			
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 (ref)	1 (ref)	1 (ref)
Missing	2·83 (2·63–3·05)	2·04 (1·81–2·29)	2·34 (2·06–2·66)
Viral load at start of follow-up, copies per mL			
<50	1 (ref)	1 (ref)	1 (ref)
≥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 start of follow-up			
No	1 (ref)	1 (ref)	1 (ref)
Yes	2·10 (1·99–2·22)	1·64 (1·55–1·73)	1·60 (1·51–1·70)
CD8 cells per µL at start of follow-up			
0–399	1 (ref)	1 (ref)	1 (ref)
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)
Hepatitis C virus RNA status at start of follow-up			
Negative	1 (ref)	1 (ref)	1 (ref)
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)

(Table 2 continues on next page)

demographics and ART start date remained similar to those in the other analyses (table 2). However, the mortality rate ratios for those starting ART after 2000 were more similar in this analysis to those for people starting ART between 1996 and 1999 (table 2). Exposure to ART drugs with increased side-effects and mono-NRTI or dual-NRTI

	Adjusted for age and cohort	Adjusted for ART start year group, age, cohort, sex, HIV acquisition route, and characteristics at start of follow-up	Adjusted for ART start year group, age, cohort, sex, HIV acquisition route, and characteristics before and at start of follow-up
(Continued from previous page)			
Previous exposure to ART drugs with increased side-effects at start of follow-up			
No	1 (ref)	..	1 (ref)
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)
Previous exposure to mono-NRTI or dual-NRTI regimens before follow-up			
No	1 (ref)	..	1 (ref)
Yes	1·39 (1·30–1·48)	..	1·03 (0·96–1·11)
CD4 cell nadir per µL before ART			
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 (ref)	..	1 (ref)
Missing	1·47 (1·29–1·68)	..	0·96 (0·83–1·12)
Peak CD8 cell count per µL before ART			
0–399	1 (ref)	..	1 (ref)
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)
CD4 cell nadir per µL between ART initiation 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 (ref)	..	1 (ref)
Missing	1·44 (1·21–1·71)	..	0·62 (0·51–0·76)
Peak CD8 cell count per µL between ART initiation and 2015			
0–399	1 (ref)	..	1 (ref)
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 cells per µL 1 year after ART initiation			
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 (ref)	..	1 (ref)
Missing	1·71 (1·56–1·87)	..	1·04 (0·90–1·21)
CD8 cells per µL 1 year after ART initiation			
0–399	1 (ref)	..	1 (ref)
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)

(Table 2 continues on next page)

	Adjusted for age and cohort	Adjusted for ART start year group, age, cohort, sex, HIV acquisition route, and characteristics at start of follow-up	Adjusted for ART start year group, age, cohort, sex, HIV acquisition route, and characteristics before and at start of follow-up
(Continued from previous page)			
Viral load 1 year after ART initiation, copies per mL			
<50	1 (ref)	..	1 (ref)
≥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)

Data in parentheses are 95% CIs. Follow-up began on or after Jan 1, 2015. ART=antiretroviral therapy. NRTI=nucleoside reverse transcriptase inhibitor. *Information about previous exposure to these ART drugs was not requested in the UK Collaborative HIV Cohort.

Table 2: **Estimated mortality rate ratios in people with HIV on ART**

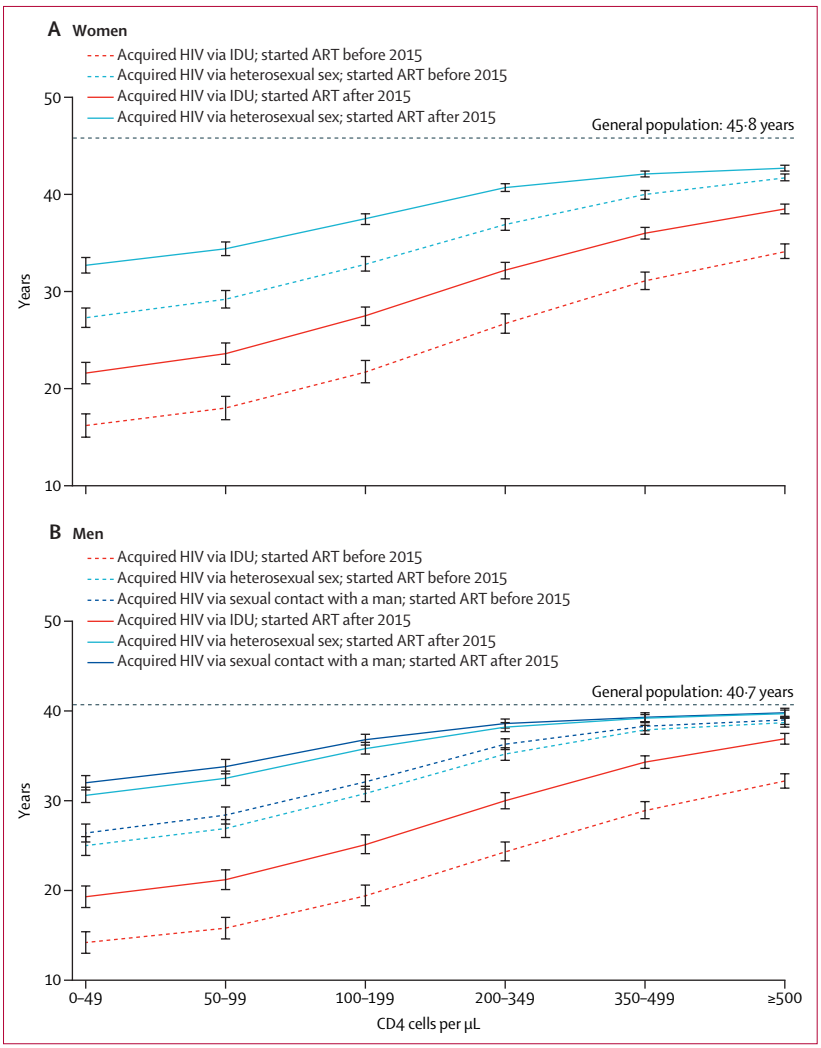

Figure: **Estimated years of life left at age 40 years for women (A) and men (B) with HIV on ART who had suppressed viral loads and did not have AIDS at the start of follow-up**
Data are stratified by CD4 cell count, HIV acquisition route, and ART start year. Error bars show 95% CIs. ART=antiretroviral therapy. IDU=injecting drug use.

regimens, pre-ART peak CD8 cell count, low CD4 cell nadir between ART initiation and 2015, and increased viral load 1 year after ART initiation were all associated with increased mortality after adjustment (table 2). However, mortality associations were generally weaker for characteristics measured before the start of follow-up than for those measured at the start of follow-up (table 2).

For the life-expectancy analyses, we split participants into those who started ART before 2015 and those who started ART after 2015 because of the small differences between adjusted mortality rate ratios for the pre-2015 groups. The other variables included in these analyses were HIV acquisition category and viral load, AIDS status, and CD4 cell count at the start of follow-up. The appendix (p 4) includes estimated mortality rate ratios from the Poisson model including the variables that were used for the life-expectancy calculations.

At age 40 years, women who started ART before 2015 had a standardised estimated 35·8 years (95% CI 35·2–36·4) of life left, whereas those who started ART in 2015–19 had an estimated 39·0 years (38·5–39·5) of life left (figure A; table 3). For women who started ART before 2015 and had CD4 counts between 0 and 49 cells per µL at the start of follow-up, remaining life expectancy at age 40 years was 19·4 years (18·2–20·5). Remaining life expectancy increased with increasing CD4 cell counts up to 40·2 years (39·7–40·6) for those with CD4 counts of 500 or more cells per µL at the start of follow-up (table 3). Among women who started ART after 2015, expected years of life left at age 40 years increased from 24·9 years (23·9–25·9) for those with CD4 counts of 0–49 cells per µL at the start of follow-up, to 42·0 years (41·7–42·3) for those starting follow-up with 500 or more cells per µL at the start of follow-up (table 4). The expected remaining years of life at age 40 years for women in the comparator general population was 45·8 years.

At age 40 years, men who started ART before 2015 had an estimated 34·5 years (33·8–35·2) of life left, and those who started ART in 2015–19 had an estimated 37·0 years (36·5–37·6) of life left (figure B; table 4). For men who began ART before 2015 and had CD4 counts of 49 or fewer cells per µL at the start of follow-up, the estimated remaining years of life at age 40 years was 18·2 years (17·1–19·4). The estimated amount of life left increased with increasing CD4 cell count category to 38·0 years

	0–49 CD4 cells per µL	50–99 CD4 cells per µL	100–199 CD4 cells per µL	200–349 CD4 cells per µL	350–499 CD4 cells per µL	≥500 CD4 cells per µL
ART started 1996–2014						
HIV acquired via injecting drug use						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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)
HIV acquired via heterosexual sex						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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	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 started 2015–19						
HIV acquired via injecting drug use						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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)
HIV acquired via heterosexual sex						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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	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)

Estimates are stratified by HIV acquisition route, ART start year, viral load suppression (<50 copies per mL), AIDS, and CD4 cell count at the start of follow-up (2015 onwards). Overall, women who started ART before 2015 had an estimated 35·8 years (95% CI 35·2–36·4) of life left, whereas those who started ART after 2015 had an estimated 39·0 years (38·5–39·5) left. ART=antiretroviral therapy.

Table 3: **Estimated remaining years of life for women with HIV aged 40 years**

(37·5–38·5) for those who had 500 or more cells per µL at the start of follow-up. At age 40 years, men who started ART in or after 2015 with CD4 counts of fewer than 49 cells per µL at the start of follow-up had an estimated 23·7 years (22·7–24·8) of life left, whereas those who had 500 or more cells per µL at the start of follow-up had an estimated 39·2 years (38·7–39·7) of life left (table 4). In the comparator general population, men aged 40 years had an expected 40·7 years of life left. For both men and women, those who acquired HIV through injecting drug use and had AIDS when follow-up started had the lowest remaining life expectancies (tables 3, 4).

At age 20 years, women who started ART before 2015 had an estimated 52·3 years (51·7–52·9) of life left, whereas those who started ART in 2015–19 had 56·6 years (56·2–57·1) of life yet (appendix p 5). The corresponding estimates for men at age 20 years were 50·8 years (50·1–51·4) and 54·5 years (appendix p 6).

Discussion

From 2015, life expectancy among women with HIV who started ART before 2015 and had CD4 counts of at least 500 cells per µL at the start of follow-up was 5·6 years shorter, and life expectancy in those who started ART after 2015 3·8 years shorter, than that in the general population. The corresponding deficits in life expectancy in men were 2·7 years and 1·5 years, respectively. However, for people with low CD4 cell counts 1 year after starting ART, estimated life expectancy could be up to 30 years lower than that in the general population. Life expectancy was lowest among people who acquired HIV via injecting drug use and those who had AIDS at the start of follow-up. People who started ART in 2015–19 had slightly higher estimated life expectancy than those who started ART earlier. However, the differences between these groups were smaller when CD4 cell counts were high at the start of follow-up. Mortality rates were higher among people with HIV who were exposed to early ART drugs with more side-effects and who had other adverse characteristics before the start of follow-up. However, age and CD4 cell count at the start of follow-up were the factors most strongly associated with mortality from 2015 onwards.

We estimated that life expectancy at age 20 years was 72·3 years among women who started ART before 2015

	0–49 CD4 cells per µL	50–99 CD4 cells per µL	100–199 CD4 cells per µL	200–349 CD4 cells per µL	350–499 CD4 cells per µL	≥500 CD4 cells per µL
ART started 1996–2014						
HIV acquired via men having sex with men						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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)
HIV acquired via injecting drug use						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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)
HIV acquired via heterosexual sex						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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	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 started 2015–19						
HIV acquired via men having sex with men						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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)
HIV acquired via injecting drug use						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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)
HIV acquired via heterosexual sex						
Suppressed viral load, no 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)
Suppressed viral load, 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)
Unsuppressed viral load, no 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)
Unsuppressed viral load, 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	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)

Estimates are stratified by HIV acquisition route, ART start year, viral load suppression (<50 cells per mL), AIDS, and CD4 cell count at the start of follow-up (2015 onwards). Overall, men who started ART before 2015 had an estimated 34·5 years (95% CI 33·8–35·2) of life left, whereas those who started ART after 2015 had an estimated 37·0 years (36·5–37·6) left. ART=antiretroviral therapy.

Table 4: **Estimated remaining years of life for men with HIV aged 40 years**

and 76·6 years for women who started ART after 2015. The corresponding estimates for men were 70·8 and 74·5 years. In a meta-analysis[5] of life expectancies of people with HIV starting ART aged 20 years with any CD4 cell count in high-income countries, the estimated age at death was 63·3 years, substantially lower than our estimate. However, estimated life expectancies were similar to those we report here in studies[1,2,12–19] of people with HIV in North America and western Europe in which follow-up data after the first year of ART were used or in which participants started ART with high CD4 cell counts. These estimates varied by country, but were mostly between 70 and 77 years, with higher estimates generally in studies based on more recent follow-up, studies in which follow-up began longer after ART initiation, and studies in which only people starting ART with the highest CD4 cell counts were included.

In analyses by Kaiser Permanente California,[2,12] in which age of death was estimated for people with HIV aged 20 years who started ART with CD4 counts of at least 500 cells per µL, life expectancy was 74·5 years during 2008–11 and 77·4 years during 2011–16. Studies estimating life expectancy for people with HIV aged 20 years who had CD4 counts of at least 350 cells per µL

at ART initiation included a collaboration of Canadian cohorts[18] (life expectancy 70·8 years), a US collaboration[19] (74·6 years), a study[17] in British Columbia, Canada (73·1 years), and the Swiss HIV Cohort Study[15] (83·9 years). In UK CHIC,[20] estimated life expectancy was 73·4 years for people with HIV aged 20 years starting ART with CD4 counts of 200–350 cells per µL.

Studies estimating life expectancy from age 20 years that were based on follow-up that did not start immediately at ART initiation included a previous Antiretroviral Therapy Cohort Collaboration analysis[1] of follow-up data from the second and third years after starting ART between 1996 and 2013 (life expectancy was 76·0 years for women and 73·1 for men). UK CHIC[13] used follow-up data from 5 years after ART initiation for people who started ART in 2000–12 (life expectancy was 77 years in women and 72 years in men). The lowest estimated life expectancy from such a study was 68·7 years, which came from a Canadian study[17] based on follow-up data after 1 year on ART. In an Italian study,[16] it was estimated that a 25-year-old on ART who had immunologically recovered (ie, who had high CD4 cell counts at the censoring date) would live to age 75·6 years. In the Danish Cohort Study,[21] the estimated age at death was 73·9 years for people with HIV aged 25 years (including those not on ART) based on follow-up between 2010 and 2015. Differences in estimated remaining life expectancy between these studies and ours could be due to differences in duration of ART before the start of follow-up, calendar years of follow-up, the relative prevalence of different modes of HIV acquisition (particularly acquisition via injecting drug use), background mortality rates, and methods used.

Our analysis was based on a large, detailed longitudinal dataset containing data for over 200 000 adults with HIV on ART across cohorts in Europe and North America. Our findings should therefore be generalisable to adults on ART in other high-income countries, although they might be less relevant in low-income and middle-income settings or settings where access to ART is restricted or costly. We were able to produce life-expectancy estimates for subgroups defined by sex, HIV acquisition route, viral suppression status, AIDS status, ART start year, and CD4 cell count. This study is, therefore, one of the most detailed analyses of life expectancy among people with AIDS treated in the modern ART era.

Our study had some limitations. Follow-up was short in the oldest age groups, and therefore there were few deaths. As a result, our life-expectancy estimates were dependent on assumptions about mortality rate ratios extrapolated from younger age groups. This limitation is common to all analyses of life expectancy among people with HIV. Under-ascertainment of deaths is also a possible limitation. However, over half of the included cohorts are linked with national death registries, several others are linked with local death registries, and several others use procedures to track patients who have been lost to follow-up.[14] We compared our findings with general population data, but characteristics of people with HIV included in our study will differ from those in the general population in terms of behaviours and demographics. Missing data were accounted for by including indicators for missing data in each variable in regression models. Although the proportions of missing data were small, adjustments for these variables are thus imperfect. Although we were able to estimate the number of years of life left, we could not estimate quality of life. A previous study[12] suggested that people with HIV have proportionally fewer remaining years of life without disability than general population comparator groups. Another limitation was the lack of available data for variables linked to socioeconomic status, such as education. Furthermore, our analysis did not include people with HIV who started ART as children or adolescents—groups at high risk of adverse events.

Although our analyses suggested that factors related to HIV history are less important than age and CD4 cell count, comorbidities during ART are an important predictor of mortality. Most deaths in people with HIV on ART in high-income countries are now due to non-AIDS causes such as cancer and cardiovascular disease.[22] These comorbidities are more common in people with HIV than in the HIV-negative population,[23] and their importance will increase as the population of people with HIV continues to age.[24] Communicable diseases such as hepatitis C virus infection are also more common among people with HIV (particularly among those who acquired HIV via injecting drug use) than among the HIV-negative population, although the prevalence of hepatitis C virus infection among people with HIV is decreasing as a result of the availability of curative treatment.[25,26] The prevalence of injecting drug use is decreasing in Europe[27] but not in North America.[28] Conditions such as cytomegalovirus infection, which is linked with ageing,[29] are also more common in people with HIV than in the HIV-negative population.[30] Therefore, treatment and prevention of comorbidities in people with HIV is important to ensure the quality of remaining years of life.[12,31] Adverse markers related to HIV history, such as very low CD4 cell counts before ART initiation and exposure to regimens that are no longer available because of their side-effect profiles or lower effectiveness, continue to predict mortality much later on. Exposure to ART regimens with poor side-effect profiles could have caused unplanned treatment interruptions, leading to increased long-term mortality. However, the associations between these adverse markers and mortality from 2015 onwards were modest after accounting for factors at the start of follow-up.

Our finding that life expectancy of people with HIV in North America and Europe who have been on ART is only somewhat lower than that in the general population will be reassuring for affected people. Our life-expectancy estimates will also be useful for clinicians and might

enable improved access to affordable life insurance policies for people with HIV.[32] Further research should focus on estimating the quality as well as the quantity of life left for people with HIV, with a particular focus on comorbidities that are more common in people with HIV.

Contributors

JACS and AT conceived and designed the study. AT combined, checked, and cleaned the datasets. CAS, GB, HC, Ad'AM, ME, MJG, SG, JLG, IJ, FCL, NO, JMR, CS, TRS, RT, GT, J-CW, FW, LW, RZ, MJS, and AJ—the individual cohort representatives—provided cohort data. AT did all statistical analyses. All authors contributed to the interpretation of the data. AT and JACS drafted the Article, which was critically revised for important intellectual content by all authors. AT and JACS accessed and verified the data, and had final responsibility for the decision to submit for publication.

Declaration of interests

CAS has received honoraria from Gilead, ViiV Healthcare, and Janssen-Cilag for participation on data safety and monitoring boards and advisory boards and for preparation of educational materials, and is the Vice Chair of the British HIV Association. GB has received consulting fees from MedIQ and payments and honoraria from the University of Kentucky and StateServ. GB's institution has received funding from Merck, Eli Lilly, Kaiser Permanente, and Amgen. HC has received research funding from ViiV, the US National Institutes of Health (NIH), and the US Agency for Healthcare Research and Quality, all paid to their institution, and sits on the NIH Office of AIDS Research Advisory Council. ME chairs the National Research Council of the Swiss National Science Foundation, which supports the Swiss HIV Cohort Study that contributed data to this analysis. MJG has received honoraria for membership of national HIV advisory boards and from Merck, Gilead, and ViiV. IJ has received teaching fees from ViiV, fees for evaluating scientific projects and participating in expert panels from Gilead, and fees for statistical analyses from Grupo de Estudio del SIDA. NO's institution has received funding from the Preben og Anne Simonsens Fond. CS has received honoraria from Gilead, ViiV Healthcare, and Janssen-Cilag for participation on scientific advisory boards and for delivering educational lectures. RT has received research funding from Gilead. GT has received research funding from Gilead, the EU, University College London, Novo Nordisk, and the Greek Government, all paid to her institution. FW has received consulting fees from ViiV Healthcare. All other authors declare no competing interests.

Data sharing

The data-sharing agreements between individual cohorts and the Antiretroviral Therapy Cohort Collaboration mean that the data collected for this study cannot be shared. Data are owned by the individual cohorts, and people wishing to access these data should contact the individual cohorts (appendix p 1).

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