Life expectancy of people with HIV on antiretroviral therapy in Spain

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Objective: To estimate life expectancy of people with HIV (PWH) and describe causes of death.

Design: Antiretroviral therapy (ART)-naive adults from the CoRIS cohort starting ART in 2004–2019.

Methods: We calculated life expectancy at age 40 for men and women according to their ART initiation period, and stratified by transmission category, $CD4^+$ cell count and AIDS diagnosis. We estimated life expectancy in 10-year age bands using life tables constructed from mortality rates, estimated through Poisson models.

Results: Life expectancy increased from 65.8 [95% confidence interval (CI) 65.0–66.6] in 2004–2008 to 72.9 (72.2–73.7) in 2014–2019 in men [general population comparators (GPC): 79.1 and 81.2 years, respectively] and from 65.8 (65.0–66.6) to 72.5 (71.8–73.3) in women (GPC: 84.9 and 86.4, respectively). Non-AIDS-related deaths accounted for 68% of deaths among men and 78% among women. Life expectancy was longer when starting ART with higher $CD4^+$ cell counts and without AIDS. For men acquiring HIV through sex with men, starting ART in 2014–2019 without AIDS, life expectancy was 75.0 (74.2–75.7) with $CD4^+$ cell count less than 200 cells/μl, rising to 78.1 (77.5–78.8) with $CD4^+$ cell count at least 350 cells/μl. Corresponding figures were 70.1 (69.4–70.9) and 76.0 (75.3–76.7) for men acquiring HIV heterosexually (HTX) and 61.5 (60.7–62.3) and 69.0 (68.2–69.8) for those acquiring HIV through injection drug use (IDU). For women starting ART from 2014 without AIDS, life expectancy increased from 71.7 (71.0–72.4) to 77.3 (76.7–77.9) among HTX and from 63.7 (62.9–64.5) to 70.7 (70.0–71.5) among IDU.

Conclusion: Our findings confirm the progressive improvement of life expectancy in PWH in Spain over the last decades, supporting the insurability of PWH on suppressive ART in our current setting and time.

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*The list of CoRIS members can be found in the Appendix 1 of the Supplemental Digital Content 1, http://links.lww.com/QAD/D32.

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Introduction

The life expectancy of people with HIV infection (PWH) on suppressive antiretroviral therapy (ART) has increased over the last decades and has been described to progressively approach that of the general population of the same age and sex [1,2]. However, a gap in life expectancy persists [3,4] and has unfortunately jeopardized the full enjoyment of the rights of PWH. One of the most important rights is access to housing and meeting mortgage eligibility criteria.

On 27 November 2018, the Ministry of Health of Spain presented and championed the Social Pact for Non-Discrimination and Equal Treatment Associated with HIV [5], whose objective is to eliminate the stigma and discrimination associated with HIV, guaranteeing equal treatment and equal opportunities, nondiscrimination and the full exercise of the fundamental rights of PWH. One of the rights the community of people with HIV has traditionally demanded is real and equitable access to noncompulsory private insurance to fulfil mortgage eligibility. ART for PWH is fully reimbursed in Spain, but PWH may wish to have a private insurance for other health issues. In spite of the reforms of the Insurance Contract Law in 2018 [6] to guarantee access to nonmandatory private insurance, especially health, life, and death insurance for PWH, there are challenges for its full implementation [7]. The Ministry of Health of Spain approached the Spanish Union of Insurance and Reinsurance Entities to produce a document with the most updated scientific evidence based on contemporary data on the life expectancy of PWH in Spain on which decisions about insurance can be made. No data on life expectancy of PWH was available in Spain. We present here the life expectancy, or equivalently the age at death, of PWH who started ART in Spain in 2004–2019, and describe causes of death.

Methods

Study population

CoRIS is an open, prospective, multicenter cohort of adults with confirmed HIV infection, naive to ART at study entry, recruited from 1 January 2004 in 47 clinical centers from 14 of 17 autonomous regions in Spain, and followed up until 30 November 2019, these being the administrative censoring date for these analyses. Summarily, CoRIS collects a minimum dataset that encompasses baseline and follow-up sociodemographic, immunological, and clinical data, including data on antiretroviral medications. Data are highly standardized and submitted to periodic quality control procedures. Participants are followed up periodically in accordance with routine clinical practice [8].

For this study, we included antiretroviral-naive individuals from CoRIS who started ART aged at least 20 years between 1 January 2004 and 30 November 2019.

Deaths and causes of death

Deaths were ascertained through cohort reporting, classified using revised CoDe in CoRIS and grouped as: AIDS-related death, non-AIDS-related malignancies (NADM), liver disease [including hepatitis C virus (HCV) and hepatitis B virus (HBV)-related liver cancers], non-AIDS infections, cardiovascular disease, lung disease, suicide, accidental/violent death, and other/unknown. Revised CoDe is a simplified version of CoDe coding system that has been proposed by the Antiretroviral Therapy Cohort Collaboration (ART-CC) [9], which has been previously applied to CoRIS [10].

Statistical analyses

Descriptive analysis of sociodemographic and clinical characteristics at ART initiation was carried out using frequency tables for categorical variables and median and interquartile range (IQR) for continuous variables.

We calculated observed mortality rates per 1000 persons-year of follow-up, overall and according to sociodemographic and clinical characteristics at start of ART, as the number of observed deaths divided by the total person-years of follow-up, multiplied by 1000. Follow-up of individuals began on the date of ART initiation and ended on the date of death, date of last visit, or the administrative censoring date, whichever occurred earlier. We used Poisson regression models to estimate crude and adjusted mortality rate ratios (MRRs). Potential risk factors considered were: sex at birth (men, women), age (20–29, 30–39, 40–49, 50–59, 60–69, 70–79, $\geq$80 years), mode of HIV acquisition [MSM, heterosexual sex (HTX), injecting drug use (IDU), other/unknown], educational level (no/primary education, secondary education, university, other/unknown), region of origin (Spain, rest of Europe, sub-Saharan Africa, Latin America, other/unknown), $CD4^+$ cell count (cells/μl) ($<$200, 200–349, $\geq$350, unknown), viral load (copies/ml) ($<$10 000, 10 000–100 000, $>$100 000, unknown) and prior AIDS diagnosis (no, yes) at ART initiation, and period of ART initiation (2004–2008, 2009–2013, 2014–2019).

We calculated the expected remaining years of life for men and women starting ART at age 40 years, according to the period of ART initiation, and then obtained the estimated age at death from this. Subsequently, we calculated the estimated age at death further stratifying by transmission category, $CD4^+$ cell count and prior AIDS diagnosis at start of ART. These three variables were the ones that showed the strongest association with mortality in Poisson multivariable analyses. For comparison with previous literature [11], we used the same methods to calculate the estimated age at death for PWH starting ART at age 20 years.

In brief, within each population group, mortality rates for PWH in 10-year age bands (20–29, 30–39, 40–49, 50–59, 60–69, 70–79, ≥80 years) were calculated from coefficients produced by Poisson regression models and then entered into a life table to produce the estimates for the expected remaining years of life for each age group. In the age groups where the mortality rate estimates among PWH was less than among the general population, the general population rate was instead used. Furthermore, as the number of deaths and persons-years of follow-up in the oldest age group (≥80 years) was limited, the estimated mortality rate in this group was corrected as follows. First, we calculated the ratio of the mortality rates between PWH and the general population for each of the age groups above 20 and then took the average of the rate ratios to produce an overall rate ratio. Only the ratios from age groups where the mortality rates among PWH were higher than among the general population were included in the overall rate ratio calculation. The general population mortality rate in the oldest age group was multiplied by this rate ratio to obtain the corrected estimated mortality rate used in the calculations of the expected remaining years of life.

Mortality rates and remaining years of life at age 40 years of the Spanish general population were obtained from the Spanish National Institute of Statistics [12]. The calculated age of death of people from the general population aged 40 years in 2006, 2011, and 2016 were used for comparison with that of PWH starting ART in 2004–2008, 2009–2013, and 2014–2019, respectively.

Statistical analysis was performed in Stata (version 17.0; Stata Corporation, College Station, Texas, USA) and R [13].

Ethical statement

This study has been approved by the Ethics Committee of the Instituto de Salud Carlos III (CEI PI 75_2021). All individuals included in the CoRIS cohort have signed an informed consent form approved by the Ethics Committee of the Hospital General Universitario Gregorio Marañón.

Results

Among the 16 759 participants included in CoRIS between 1 January 2004 and 30 November 2019, the 14 194 who started ART aged at least 20 years were included in the study. Of them, 84.7% were men, and the most frequent mode of HIV acquisition was MSM (60.0%). Median age at starting ART was 37 (IQR: 30–44) years, 41.3% started ART with $CD4^+$ cell count at least 350 cells/μl and 13% had a previous AIDS diagnosis.

Participants' characteristics, according to the period of ART initiation, are shown in Table 1. PWH who started ART in the period 2014–2019, in relation to those who did so in the period 2004–2008, were more frequently men (88.2 versus 77.3%), who acquired HIV through MSM (67.5 versus 40.6%), who had started ART with a higher $CD4^+$ cell count (401 versus 206 cells/μl), and had not been diagnosed with AIDS (91 versus 75.6%).

Number of deaths, mortality rates, and mortality rate ratios (95% confidence interval)

During 73 733.9 person-years of follow-up, we observed 593 deaths, resulting in a mortality rate of 8.0 (95% CI 4.4–8.7) per 1000 person-years.

Table 2 displays the number of deaths, mortality rates, and estimated mortality rate ratios, according to socio-demographic and clinical characteristics at ART initiation. In the fully adjusted multivariable Poisson regression model, PWH who started ART more recently had lower mortality rates compared with those who started ART in 2004–2008 (MRR: 0.83; 95% CI: 0.69–1.00 for 2009–2013 and 0.79; 0.62–1.01 for 2014–2019). Women showed a 18% lower mortality rate than men (MRR: 0.82; 95% CI 0.65–1.02). The mortality rate increased with increasing age. Compared with men who acquired HIV infection through sex with men, those who did so through heterosexual sex and injecting drug use had a mortality rate a 67% (MRR: 1.67; 95% CI: 1.33–2.11) and three times higher (MRR: 3.68; 95% CI: 2.87–4.71), respectively. Having secondary or university studies reduced the mortality rate by 22% (MRR: 0.78; 95% CI: 0.63–0.96) compared with having primary studies or less. Compared with people who started ART with less than 200 cells/μl $CD4^+$ cell counts, those who started with 200–349 cells/μl (MRR: 0.76; 95% CI: 0.61–0.94), or at least 350 cells/μl (MRR: 0.46; 95% CI: 0.34–0.60) showed lower mortality rates. Starting ART with a prior AIDS diagnosis doubled the mortality rate (MRR: 2.13; 95% CI: 1.77–2.57).

Estimated age at death for men and women starting antiretroviral therapy at age 40 years and causes of death

The estimated MRRs from the Poisson model that was used for the life expectancy calculations for men and women starting ART at 40 years according to period of

Table 1. Sociodemographic and clinical characteristics at antiretroviral therapy initiation according to the period of antiretroviral therapy initiation.

	2004–2008 *N* = 2864	2009–2013 *N* = 4659	2014–2019 *N* = 6671	Total *N* = 14 194
Sex [*N* (%)]				
Male	2213 (77.3)	3925 (84.2)	5884 (88.2)	12 022 (84.7)
Female	651 (22.7)	734 (15.8)	787 (11.8)	2172 (15.3)
Age, years [*N* (%)]				
Median (IQR)	37.9 (31.6–44.7)	36.7 (30.5–44.0)	36.2 (29.6–44.5)	36.7 (30.2–44.4)
20–29	553 (19.3)	1086 (23.3)	1765 (26.5)	3404 (24.0)
30–39	1120 (39.1)	1847 (39.6)	2370 (35.5)	5337 (37.6)
40–49	808 (28.2)	1148 (24.6)	1646 (24.7)	3602 (25.4)
50–59	284 (9.9)	416 (8.9)	689 (10.3)	1389 (9.8)
60–69	81 (2.8)	131 (2.8)	154 (2.3)	366 (2.6)
70–79	17 (0.6)	31 (0.7)	40 (0.6)	88 (0.6)
≥80	1 (0.0)	0 (0.0)	7 (0.1)	8 (0.1)
Mode of HIV acquisition [*N* (%)]				
MSM	1164 (40.6)	2853 (61.2)	4505 (67.5)	8522 (60.0)
Heterosexual sex	1149 (40.1)	1338 (28.7)	1644 (24.6)	4131 (29.1)
Injecting drug use	456 (15.9)	317 (6.8)	197 (2.9)	970 (6.8)
Other/unknown	95 (3.3)	151 (3.2)	325 (4.9)	571 (4.0)
Educational level [*N* (%)]				
No/primary education	476 (16.6)	611 (13.1)	1646 (24.7)	4230 (29.8)
Secondary/university	1444 (50.4)	2177 (46.7)	3594 (53.9)	7372 (51.9)
Other/unknown	455 (15.9)	1199 (25.7)	1431 (21.4)	2592 (18.3)
Country of origin [*N* (%)]				
Spain	1716 (59.9)	2814 (60.4)	3929 (58.9)	8459 (59.6)
Rest of Europe	415 (14.5)	778 (16.7)	746 (11.2)	1939 (13.7)
Sub-Saharan Africa	198 (6.9)	181 (3.9)	263 (3.9)	642 (4.5)
Latin America	480 (16.8)	822 (17.6)	1540 (23.1)	2842 (20.0)
Other/unknown	55 (1.9)	64 (1.4)	193 (2.9)	312 (2.2)
$CD4^+$ cell count, cells/μl [*N* (%)]				
Median (IQR)	206 (90, 299)	310 (193, 421)	401 (234–574)	316 (179–468)
<200	1300 (45.4)	1154 (24.8)	1308 (19.6)	3762 (26.5)
200–349	997 (34.8)	1508 (32.4)	1294 (19.4)	3799 (26.8)
≥350	414 (14.5)	1772 (38.0)	3672 (55.0)	5858 (41.3)
Unknown	153 (5.3)	225 (4.8)	397 (5.9)	775 (5.5)
Viral load (copies/ml) [*N* (%)]				
<10 000	364 (12.7)	676 (14.5)	1244 (18.6)	2284 (16.1)
10 000–100 000	1023 (35.7)	1960 (42.1)	2695 (40.4)	5796 (40.8)
>100 000	1316 (45.9)	1750 (37.6)	2364 (35.4)	5312 (37.4)
Unknown	161 (5.6)	273 (5.9)	368 (5.5)	802 (5.6)
AIDS diagnosis [*N* (%)]				
No	2166 (75.6)	4107 (88.2)	6072 (91.0)	12 345 (87.0)
Yes	698 (24.4)	552 (11.8)	599 (9.0)	1849 (13.0)

IQR, interquartile range.

ART initiation is shown in Table 1 of the Supplemental Digital Content 2, http://links.lww.com/QAD/D33 (model 1). Overall, the estimated age at death for men aged 40 years starting ART in 2004–2008 was 65.8 (95% CI: 65.0–66.6) years, 13.3 years less than in men of the general population, increasing up to 72.9 (95% CI: 72.2–73.7) years in those starting ART in 2014–2019, reducing the difference with men of the general population up to 8.3 years. In women aged 40 years starting ART in 2004–2008, the estimated age at death was 65.8 (95% CI: 65.0–66.6) years, 19.1 years less than in women of the general population, and increased up to 72.5 (95% CI: 71.8–73.3) years in those who started ART in 2014–2019, with a difference of 13.9 years with women of the general population (Table 2, Supplemental Digital Content 3, http://links.lww.com/QAD/D34).

Non-AIDS-related deaths accounted for 68% ($n = 331$) and 78% ($n = 83$) of deaths in men and women, respectively. The most frequent non-AIDS-related deaths were those due to NADM (29% in men and 25% in women), liver disease (15 and 14%), and non-AIDS infections (13 and 12%). Among NADM deaths, those from lung cancer accounted for 40 and 30% of deaths in men and women, respectively. AIDS-related deaths were mainly seen in men and women who started ART with a previous AIDS diagnosis and with $CD4^+$ cell count less than 200 cells/μl.

Estimates of the age at death for men and women starting ART at 40 years according to period of ART initiation, transmission category, prior AIDS diagnosis, and $CD4^+$ count at ART initiation are shown in Table 3 and in Figs. 1 and 2. The estimated MRRs from the Poisson

Table 2. Number of deaths, mortality rates, and estimated mortality rate ratios, according to sociodemographic and clinical characteristics at antiretroviral therapy initiation.

	Number deaths	Mortality rate (per 1000 PY) (95% CI)	MRR (95% CI)	
			Crude	Adjusted
Period of ART initiation				
2004–2008	305	11.9 (10.6–13.3)	1.00	1.00
2009–2013	195	6.3 (5.4–7.2)	0.53 (0.44–0.63)	0.83 (0.69–1.00)
2014–2019	93	5.5 (4.4–6.6)	0.46 (0.36–0.57)	0.79 (0.62–1.01)
Sex				
Male	487	8.0 (7.3–8.7)	1.00	1.00
Female	106	8.2 (6.8–9.9)	1.03 (0.83–1.27)	0.82 (0.65–1.02)
Age (years)				
20–29	36	2.2 (1.6–3.1)	1.00	1.00
30–39	139	4.9 (4.1–5.8)	2.18 (1.51–3.15)	1.63 (1.14–2.40)
40–49	210	10.6 (9.3–12.1)	4.73 (3.32–6.74)	2.65 (1.86–3.86)
50–59	128	18.4 (15.5–21.9)	8.22 (5.68–11.90)	4.76 (3.29–7.04)
60–69	51	25.4 (19.3–33.5)	11.36 (7.42–17.41)	6.36 (4.10–9.96)
70–79	27	62.9 (43.2–91.8)	28.11 (17.06–46.29)	15.55 (9.18–26.04)
≥80	2	87.8 (22–351.2)	39.23 (9.45–162.92)	18.93 (3.02–64.38)
Mode of HIV acquisition				
MSM	159	3.8 (3.3–4.5)	1.00	1.00
Heterosexual sex	230	9.7 (8.5–11.1)	2.53 (2.06–3.09)	1.67 (1.33–2.11)
Injecting drug use	154	24.5 (20.9–28.7)	6.36 (5.10–7.94)	3.68 (2.87–4.71)
Other/unknown	50	20.1 (15.3–26.6)	5.23 (3.81–7.19)	2.92 (2.07–4.05)
Educational level				
No/compulsory education	295	12.3 (11–13.8)	1.00	1.00
Upper secondary/university	161	4.2 (3.6–5)	0.45 (0.37–0.55)	0.78 (0.63–0.96)
Other/unknown	137	11.6 (9.8–13.7)	0.86 (0.68–1.09)	1.15 (0.90–1.47)
Region of origin				
Spain	428	9.43 (8.54–10.33)	1.00	1.00
Rest of Europe	84	7.53 (5.92–9.15)	0.80 (0.63–1.00)	1.10 (0.86–1.39)
Sub–Saharan Africa	19	6.02 (3.31–8.73)	0.64 (0.39–0.98)	0.74 (0.45–1.16)
Latin America	53	4.17 (3.05–5.30)	0.44 (0.33–0.58)	0.78 (0.57–1.04)
Other/Unknown	9	6.64 (2.30–10.97)	0.70 (0.34–1.28)	0.74 (0.35–1.36)
$CD4^+$ cell count (cells/μl)				
<200	344	15.0 (13.5–16.6)	1.00	1.00
200–349	138	6.2 (5.2–7.3)	0.41 (0.34–0.50)	0.76 (0.61–0.94)
≥350	75	3 (2.4–3.8)	0.20 (0.16–0.26)	0.46 (0.34–0.60)
Unknown	36	10.1 (7.3–14.0)	0.68 (0.48–0.95)	1.10 (0.66–1.76)
viral load (copies/ml)				
<10 000	72	6.8 (5.4–8.6)	1.00	1.00
10 000–100 000	214	7.0 (6.1–8.0)	1.02 (0.78–1.33)	1.05 (0.80–1.39)
>100 000	272	9.6 (8.5–10.8)	1.40 (1.08–1.82)	0.95 (0.73–1.25)
Unknown	35	8.6 (6.2–12.0)	1.26 (0.84–1.89)	0.63 (0.36–1.07)
AIDS diagnosis				
No	346	5.5 (5.0–6.1)	1.00	1.00
Yes	247	22.2 (19.6–25.1)	4.01 (3.40–4.72)	2.13 (1.77–2.57)

ART, antiretroviral therapy.

model containing these variables that was used for the life expectancy calculations is shown in Table 1 of the Supplemental Digital Content 2, http://links.lww.com/QAD/D33 (model 2). Overall, both men and women who started ART in more recent periods had higher estimated life expectancy than those who started in 2004–2008. Furthermore, life expectancy was also higher in those starting ART with higher $CD4^+$ counts and without a previous AIDS diagnosis.

In men who acquired HIV infection through sex with men, aged 40 years starting ART in 2014–2019 with no prior AIDS diagnosis, and with a $CD4^+$ cell count less than 200 cells/μl, the estimated age at death was 75 (95% CI: 74.2–75.7) years, rising to 78.1 (95% CI: 77.5–78.8) years in those with $CD4^+$ cell count at least 350 cells/μl at start of ART. Corresponding figures for men who acquired HIV infection through heterosexual contact and those who did so through injection drug use were 70.1 (69.4–70.9) years and 76.0 (75.3–76.7) years, and 61.5 (60.7–62.3) years and 69.0 (68.2–69.8) years, respectively.

For women who acquired HIV through heterosexual contact, starting ART in 2014–2019 at age 40 years with no prior AIDS, the estimated age at death increased from 71.7 (71.0–72.4) years to 77.3 (76.7–77.9) years in those with $CD4^+$ cell counts less than 200 and at least 350 cells/μl, respectively, at start of ART. Corresponding figures for women who acquired HIV through injection drug use were 63.7 (62.9–64.5) years and 70.7 (70.0–71.5) years, respectively.

Table 3. Estimated age at death (95% confidence interval) for men and women aged 40 years at starting antiretroviral therapy, stratified by period of antiretroviral therapy initiation, mode of HIV acquisition, prior AIDS, and CD4$^+$ cell count (cells/μl) at antiretroviral therapy initiation.

Men				
Period of ART initiation: 2004–2008				
		<200	200–349	≥350
MSM	No prior AIDS	73.6 (72.8–74.4)	75.3 (74.6–76.1)	77.5 (76.8–78.2)
	Prior AIDS	66.3 (65.5–67.1)	69.0 (68.2–69.8)	73.7 (72.9–74.5)
Heterosexual sex	No prior AIDS	68.3 (67.5–69.1)	70.9 (70.1–71.7)	75.0 (74.3–75.7)
	Prior AIDS	60.7 (59.9–61.5)	63.5 (62.6–64.3)	68.4 (67.6–69.2)
Injecting drug use	No prior AIDS	59.4 (58.6–60.1)	62.1 (61.3–62.9)	67.1 (66.3–67.9)
	Prior AIDS	52.4 (51.8–53.1)	54.8 (54.1–55.5)	59.5 (58.7–60.2)
Period of ART initiation: 2009–2013				
		<200	200–349	≥350
MSM	No prior AIDS	75.0 (74.3–75.7)	76.2 (75.5–76.9)	78.0 (77.4–78.7)
	Prior AIDS	68.1 (67.3–68.9)	70.7 (69.9–71.4)	75.1 (74.3–75.8)
Heterosexual sex	No prior AIDS	70.0 (69.2–70.8)	72.5 (71.7–73.2)	75.9 (75.2–76.6)
	Prior AIDS	62.7 (61.9–63.5)	65.4 (64.6–66.2)	70.1 (69.3–70.9)
Injecting drug use	No prior AIDS	61.3 (60.5–62.1)	64.0 (63.2–64.8)	68.9 (68.1–69.7)
	Prior AIDS	54.1 (53.4–54.8)	56.6 (55.8–57.3)	61.4 (60.6–62.2)
Period of ART initiation: 2014–2019				
		<200	200–349	≥350
MSM	No prior AIDS	75.0 (74.2–75.7)	76.3 (75.6–77.0)	78.1 (77.5–78.8)
	Prior AIDS	68.3 (67.5–69.1)	70.8 (70.0–71.5)	75.1 (74.3–75.8)
Heterosexual sex	No prior AIDS	70.1 (69.4–70.9)	72.5 (71.8–73.3)	76.0 (75.3–76.7)
	Prior AIDS	62.9 (62.1–63.7)	65.6 (64.8–66.4)	70.2 (69.5–71.0)
Injecting drug use	No prior AIDS	61.5 (60.7–62.3)	64.2 (63.4–65.0)	69.0 (68.2–69.8)
	Prior AIDS	54.3 (53.6–55.0)	56.8 (56.0–57.5)	61.6 (60.8–62.4)
Women				
Period of ART initiation: 2004–2008				
		<200	200–349	≥350
Heterosexual sex	No prior AIDS	70.0 (69.2–70.8)	72.3 (71.5–73.0)	76.1 (75.4–76.7)
	Prior AIDS	62.9 (62.1–63.7)	65.5 (64.7–66.3)	70.1 (69.3–70.9)
Injecting drug use	No prior AIDS	61.6 (60.8–62.4)	64.2 (63.4–65.0)	68.9 (68.1–69.7)
	Prior AIDS	54.3 (53.6–55.0)	56.8 (56.1–57.6)	61.7 (60.9–62.5)
Period of ART initiation: 2009–2013				
		<200	200–349	≥350
Heterosexual sex	No prior AIDS	71.6 (70.8–72.3)	73.7 (73.0–74.4)	77.3 (76.7–77.9)
	Prior AIDS	64.8 (64.0–65.6)	67.4 (66.6–68.1)	71.7 (70.9–72.4)
Injecting drug use	No prior AIDS	63.5 (62.7–64.3)	66.1 (65.3–66.9)	70.6 (69.8–71.3)
	Prior AIDS	56.1 (55.4–56.8)	58.6 (57.9–59.4)	63.6 (62.8–64.4)
Period of ART initiation: 2014–2019				
		<200	200–349	≥350
Heterosexual sex	No prior AIDS	71.7 (71.0–72.4)	73.8 (73.1–74.5)	77.3 (76.7–77.9)
	Prior AIDS	65.0 (64.2–65.8)	67.5 (66.8–68.3)	71.8 (71.1–72.5)
Injecting drug use	No prior AIDS	63.7 (62.9–64.5)	66.3 (65.5–67.1)	70.7 (70.0–71.5)
	Prior AIDS	56.3 (55.6–57.0)	58.9 (58.1–59.6)	63.8 (63.0–64.6)

ART, antiretroviral therapy.

Estimates of the age at death for men and women starting ART at age 20 are shown in Table 3 of the Supplemental Digital Content 4, http://links.lww.com/QAD/D35. Furthermore, estimates of the age at death for men and women starting ART at age 40 years with mode of acquisition stratified in MSM/HTX and IDU are shown in Table 4 of the Supplemental Digital Content 5, http://links.lww.com/QAD/D36.

Discussion

We have shown that the life expectancy of PWH in Spain has increased in recent years and that the gap of the age at death of both men and women with HIV compared with the general population decreased considerably in 2014–2019 compared with 2004–2008. Age at death in the later period was 72.9 (72.2–73.7) years in men and 72.5 (71.8–73.3) years in women. A gap of 8.3 and 13.9 years in men and women, respectively, compared with the general population persists but does not preclude the insurability of PWH on suppressive ART in our current setting and time. The life expectancy of PWH who started ART with elevated CD4$^+$ cell counts, and without a previous AIDS diagnosis is close to that of the general population, especially among MSM. The most frequent causes of death nowadays are deaths because of non-AIDS-defining cancers, the most common being lung cancer, death from liver causes, and from non-AIDS infections.

These are the most accurate estimates of the life-expectancy in PWH to date in Spain. Life expectancy has increased over the last decades, mainly because of the increasing use of ART. After year 2014, the Spanish

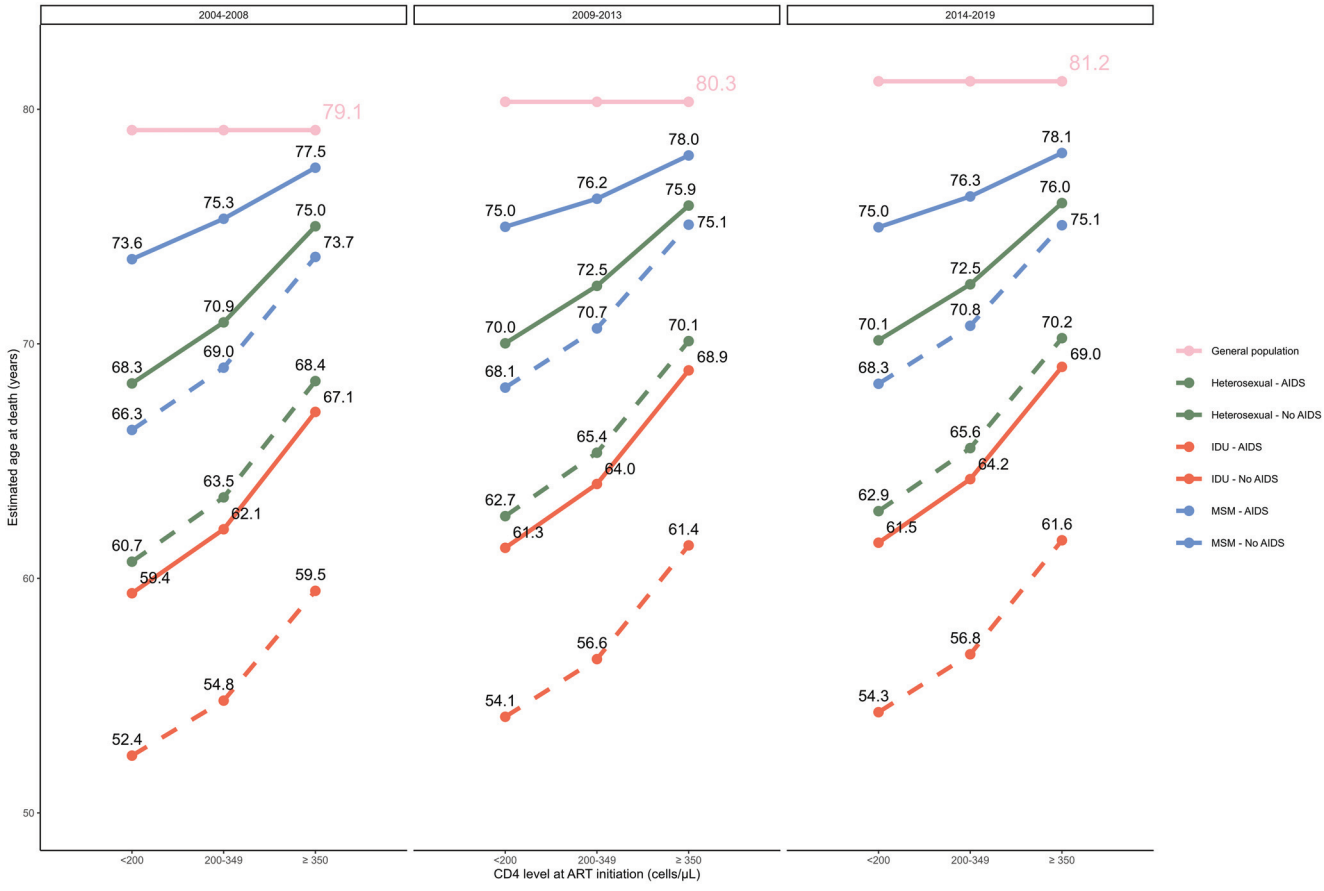

Fig. 1. Estimated age at death for men aged 40 years starting antiretroviral therapy in 2004–2008, 2009–2013, and 2014–2019, stratified by mode of HIV acquisition, prior AIDS, and CD4$^+$ cell count at antiretroviral therapy initiation. HTX, heterosexual sex; IDU, injecting drug use.

ART guidelines recommend the initiation of ART regardless of the CD4$^+$ cell count, which is now standard practice [14]. In addition, the progressive improvement in ART effectiveness, adverse effect profile, and simplicity of use may have further contributed in reducing mortality and increasing life expectancy [15]. For MSM, aged 40 years who started ART in 2014–2019 with no prior AIDS diagnoses, and a CD4$^+$ cell count over 350 cells/μl, life expectancy was 78.1 years, only 3.1 years lower than the overall life expectancy (81.2 years) in men of the general population in Spain. Our estimates are based on a large, representative, and well established cohort of PWH, CoRIS, and compared with data from the Spanish National Institute of Statistics. CoRIS was established in 2004, so these analyses apply largely to the people newly diagnosed with HIV in the last 20 years. The median age of people starting ART in this study was 37 years. Whereas the inclusion of PWH with HIV diagnoses prior to 2004 may lead to lower life expectancy estimates, for the purpose of assessing the insurability for a house mortgage in Spain, this is an adequate study population. Indeed, these estimates are likely to improve overtime as HIV diagnosis and treatment start at earlier stages.

Our findings are consistent with the published literature on the topic but are specific to the life expectancy patterns of Spain [16,17]. Spain has some of the highest life expectancies of the world, particularly for women, so these life expectancy gaps need to take this into account when comparing these figures with those from other settings [4]. Kaulich-Bartz *et al.* [18] published very encouraging data supporting the insurability of PWH in 2013 in the ART-CC. Our findings are built on those results and provide timelier and stronger evidence of the increasing life expectancy of PWH on suppressive ART. The lower mortality of PWH has been accompanied by a shift in the causes of death from AIDS-defining to non-AIDS-defining causes; in particular to non-AIDS-defining malignancies, with lung cancer on top. These findings are also in line with most publications from settings with large proportions of PWH on suppressive ART.

There is an inherent and inevitable limitation in this type of studies that use the general population as the comparison group to the group of PWH. Ideally PWH should be compared with people without HIV from a population with similar characteristics except for HIV but this is seldom feasible so they end up being compared with the

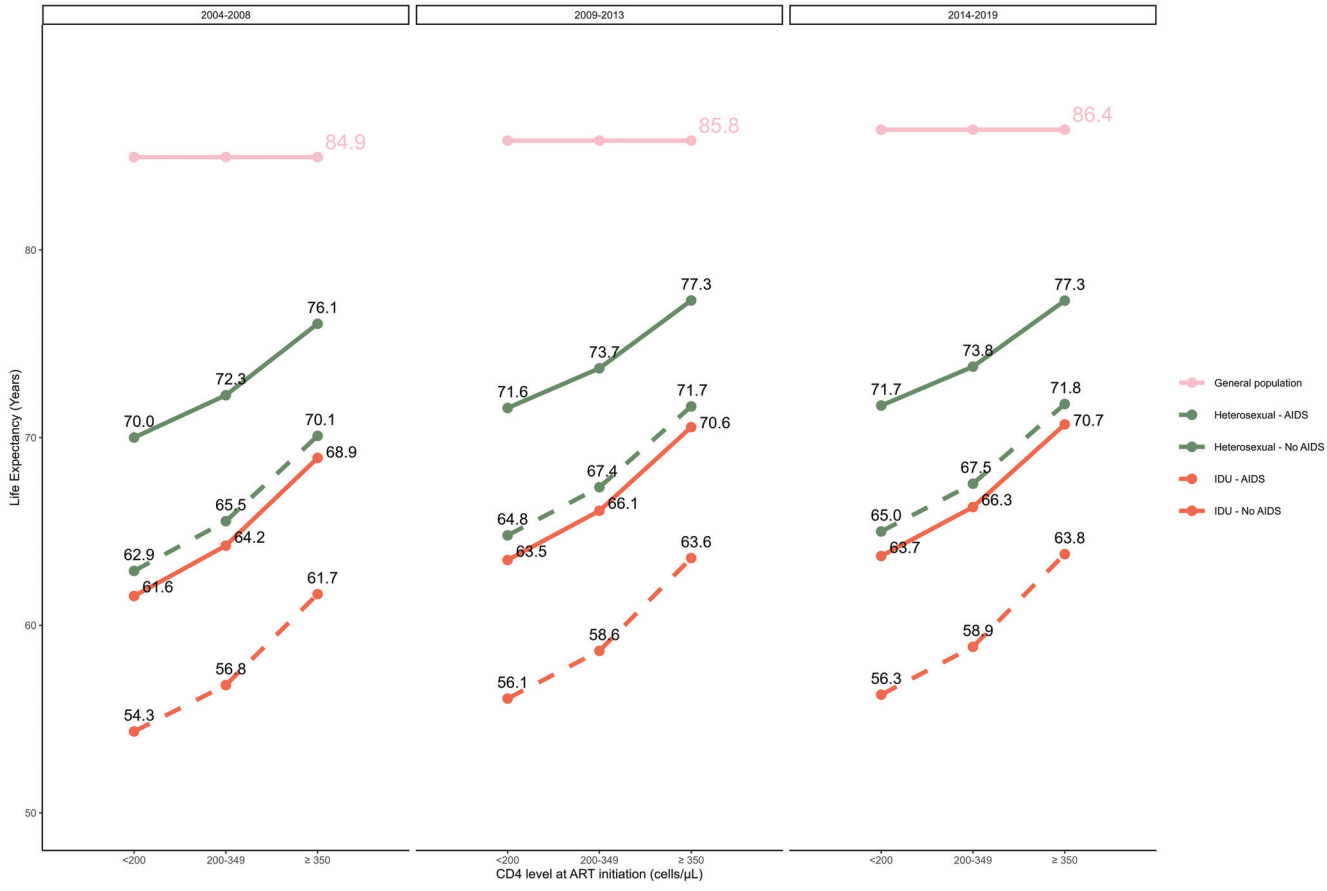

Fig. 2. Estimated age at death for women aged 40 years starting antiretroviral therapy in 2004–2008, 2009–2013, and 2014–2019, stratified by mode of HIV acquisition, prior AIDS, and CD4$^+$ cell count at antiretroviral therapy initiation. Solid pink lines represent life expectancy in women from the general population. HTX, heterosexual sex; IDU, injecting drug use.

general population. However, this is not necessarily a fair comparison as the proportion of smokers and the prevalence of other co-infections such as viral hepatitis is higher in PWH than in the general population.

In conclusion, these findings confirm the progressive improvement in the life expectancy of PWH in Spain over the last decades and support the insurability of PWH on suppressive ART in our current setting and time. These findings have a direct translation in policy and practice and will be used by the Ministry of Health of Spain and the Spanish Union of Insurance and Reinsurance Entities to draw best practices guidelines on the implementation of the Spanish legislation regarding the Insurance Contract Law in 2018 [6] in line with the Social Pact for Non-Discrimination and Equal Treatment Associated with HIV [5].

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Conflicts of interest

M.R. has received a research grant from Gilead Science outside the submitted work. J.M.-S. reports personal fees from ViiV Healthcare, Janssen Cilag, Gilead Sciences, and MSD, nonfinancial support from ViiV Healthcare, Jannsen Cilag, and Gilead Sciences, and research grants from Gilead Sciences, outside the submitted work. J.R.B. has carried out consulting work for Abbvie, Bristol-Myers Squibb, Gilead Sciences, Janssen, Merck, and ViiV Healthcare; has received compensation for lectures from Abbvie, Bristol-Myers Squibb, Gilead Sciences, Janssen, Merck, and ViiV Healthcare, as well as grants and payments for the development of educational presentations for Gilead Sciences, Bristol-Myers Squibb, and ViiV Healthcare. A.R. or his institution has received grants for research, educational, or advisory activities from Gilead Sciences, ViiV Healthcare, Janssen Cilag, Abbvie, and Merck Sharp&Dohm. M.d.L. has received fees from Gilead, MSD, Janssen, and ViiV for educational scientific reviews and funds for registration in scientific congresses from Gilead, Janssen and Viiv. All the other authors declare that they have no competing interests.

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