Estimated life expectancy gains among adults with HIV with Antiretroviral Therapy in Latin America and the Caribbean: a multisite retrospective cohort study

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Abstract

BACKGROUND: Sparse data exist on life expectancy gains among persons living with HIV (PWH) in low- and middle-income settings where antiretroviral therapy (ART) is increasingly available. We calculated life expectancy trends among PWH initiating ART within the Caribbean, Central and South America network for HIV epidemiology (CCASAnet).

METHODS: PWH initiating ART and ≥ 20 years old between 2003–2017 from CCASAnet sites in Argentina, Brazil, Chile, Haiti, Honduras, Mexico, and Peru contributed person-time until the date of death, last contact, database closure, or December 2017. We used the Chiang method of abridged life tables to estimate life expectancy at age 20 for three eras (2003–2008, 2009–2012, and 2013–2017) overall and by demographic and clinical characteristics at ART initiation. We used Poisson regression models to weight mortality rates to account for informative censoring.

FINDINGS: Among 30,688 PWH, 17,491 (57%) were from Haiti and 13,197 (43%) were from all other sites. There were 1,470 deaths among PWH in Haiti and 1,167 deaths at other sites. Crude and weighted mortality rates decreased among all age groups over calendar eras. From 2003–2008 to 2013–2017, overall life expectancy for PWH at age 20 years increased from 13·9 (95% confidence interval [CI]: 12·5–15·2]) to 61·2 years (95%CI: 59·0–63·4) at Haiti and from 31·0 (95% CI: 29·3–32·8) to 69·5 years (95% CI: 67·2–71·8) at all other sites, approaching life expectancies of the general population (69·9 years in Haiti and 78·0 years at all other sites). However, disparities in life expectancy by sex/sexual HIV transmission risk factor, CD4 cell count, education, and tuberculosis at or prior to ART persisted across calendar eras.

INTERPRETATION: Life expectancy among PWH on ART has significantly improved in Latin America. Persistent disparities in life expectancy by demographic and clinical factors at ART initiation highlight vulnerable populations in the region.

FUNDING: US National Institutes of Health

Keywords

life expectancy; Latin America; HIV; ART; sex

Introduction

As combination antiretroviral therapy (ART) has become increasingly available, life expectancy has significantly improved for people with HIV (PWH), particularly in the U.S. and Canada, though disparities remain based on education, income level, and access to healthcare.[1] Studies from high-income settings have shown life expectancies among PWH increasing from approximately two-thirds that of the general population in 2005 to now approaching that of the general population.[1–3] However, sparse data exist on life expectancy in low- and middle-income settings where ART is increasingly available.

With improvements in infant and childhood mortality globally, life expectancy at birth in Latin America and the Caribbean has increased substantially in the general population, from 58·9 years in 1965–70 to 73·5 years in 2005–2010.[4] In contrast, recent trends in life expectancy in adulthood are more complex. Compared to high-income countries, low- and middle-income countries in Latin America have seen fewer gains in life expectancy at older

ages.[5] In the region, leading causes of premature mortality remain a mix of non-communicable diseases (namely heart disease and stroke) as well as violence, injury, and respiratory infections.[6] Additionally, examination of life expectancy gains in Latin America have shown significant disparities even within its largest cities, highlighting the impact of social inequalities on longevity in the region.[7] Little is known about life expectancy for those living with HIV in the region, and no large studies addressing the topic have yet been conducted. ART first became available in Latin America in the 1990s, but significantly expanded during the 2000s.[4] It is important to know the current life expectancies of PWH to anticipate healthcare needs in the region and to identify persistent disparities and areas for improvement.

In this study, we therefore sought to evaluate gains in life expectancy from 2003–2017 among adult PWH started on ART in Latin America and the Caribbean using data from the Caribbean, Central and South America network for HIV epidemiology (CCASAnet). We hypothesized that, with greater access to HIV care and ART, life expectancy among PWH in Latin America and the Caribbean would begin to approach that of the general population in the region.

Methods

Data Sources and Study Design

The study population included PWH who started ART at CCASAnet sites in Argentina, Brazil Chile, Haiti, Honduras, Mexico, and Peru. PWH included in this study were seen clinical sites at Instituto Nacional de Infectologia Evandro Chagas in Rio de Janeiro, Brazil; Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia in Lima, Peru; Centro Medico Huesped in Buenos Aires, Argentina; Fundación Arriarán in Santiago, Chile;Le Groupe Haitien d'Etude du Sarcome de Kaposi et des Infections Opportunistes (GHESKIO) in Port-au-Prince, Haiti; Instituto Hondureño de Seguridad Social and Hospital Escuela in Tegucigalpa, Honduras; and Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán in Mexico City, Mexico. Data from contributing sites were collected and sent to the CCASAnet data coordinating center at Vanderbilt University Medical Center per CCASAnet standardized protocols (more information available at www.ccasanet.org)where statistical analyses were performed. Institutional ethics review boards from all sites and Vanderbilt approved the project, waiving the requirement for individual patient informed consent.

We included PWH 16 years of age who starting ART and contributed person-time after the age of 20 years between January 1, 2003 and December 31, 2017. This analysis focused on clinical and demographic characteristics of PWH at the time of ART initiation. We excluded patients who started ART before cohort entry, those who never started ART, and those who received antiretroviral medications other than highly-active combination regimens prior to ART start. We excluded patients who started ART before age 16 years and person-time before age 20 years for those who started after age 16 years. All patients contributed person-time from date of ART initiation until death (if before December 31, 2017) or the first occurrence date of database closure at their respective site, the last documented contact with clinic if last contact was more than one year before database closure, or December 31, 2017.

All person-time during the observation period was included, regardless of documented virologic suppression or ART treatment interruptions. Our primary outcome of interest was death due to any cause for calculation of life expectancy at age 20 years. Ascertainment of death varies across CCASAnet sites. As clinical care sites, death data was obtained from medical records and supplemented from national and local registries when available.[8]

Statistical Approach

We used the Chiang method of abridged life tables to calculate life expectancy at age 20 years by creation of age-period-cohort tables and calculation of 95% confidence intervals of life expectancy at age 20 years.[9] Person-times of observation were stratified by age (20–34 years, 35–44 years, 45–54 years, and 55 years) over three calendar eras: 2003–2008, 2009–2012, and 2013–2017. Age and calendar eras were determined for balance of person-time across the study period. Individuals could contribute person-time to multiple age groups and calendar eras over time. For creation of stable life tables, we required a minimum of 100 person-years per age-period stratum and thus excluded person-time before age 20 and before 2003 as numbers were few. Given differences between clinical sites by methods of data collection and population characteristics, mortality rates per age group were calculated using inverse-probability-weighted Poisson regression to account for informative censoring. Inverse probability weights were generated based on the probability of loss to follow-up for each individual and were calculated using a multivariable logistic regression model for loss to follow-up including covariates of site, age at ART initiation, sex, year of ART initiation, education, CD4 cell count at ART initiation, history of AIDS at ART initiation, and HIV transmission risk factor.

We created life tables for key demographic and clinical characteristics determined *a priori*. We stratified all analyses by receipt of care at the Haiti site vs. at other sites except Haiti as recent life expectancy for the general population of Haiti is estimated as significantly lower than that of other Latin American countries represented in CCASAnet.[10,11] These countries, including Mexico, Honduras, Peru, Argentina, Chile, and Brazil will now to referred to as "Other sites". Additionally, GHESKIO in Haiti differs from other sites within CCASAnet with regards to scope of clinical care (e.g., it is the only site to offer HIV testing and counseling as well as clinical care) and historical availability of ART and clinical laboratory monitoring. Brazil was the first middle-income country to provide universal ART for PWH in 1996, and third to offer ART regardless of CD4 cell count in 2013 (though the WHO only recommended this beginning in 2015).[12] In contrast, other countries in Latin America only began their universal ART programs around 2000.[13,14] Recent life expectancy estimates for the general population were obtained from World Health Organization data and plotted for comparison, using a weighted average age for the general population among the sites other that Haiti for their relative proportion.[11] We constructed stratified abridged life tables for PWH receiving care in Haiti and at other sites combined over calendar eras by sex, HIV transmission risk factor (for PWH other than those in Haiti, where the epidemic is generalized and data on transmission risk factors was incomplete), CD4 cell count at ART initiation (closest value +/− 6 months), highest level of education, and history of tuberculosis before or within seven days after ART initiation. We also evaluated overall life expectancy trends over the calendar era for each contributing country with sufficient person-time of

observation and recorded deaths for adequate estimation in Supplemental Figure 1 (Appendix, page 1).

Statistical analyses were performed using Stata 12.1 (Stata Corporation, College Station, Texas, USA). All *p*-values were two-sided. Figures were created using Prism GraphPad version 8.

Role of the Funding Source

This study was supported by the U.S. National Institutes of Health. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

The study population included 42,519 PWH starting ART who contributed 146,958·4 person-years of follow-up between January 1, 2003 and December 31, 2017. We excluded 4,154 patients who never started ART, and 4,044 patients were removed for starting ART before cohort entry. An additional 1,222 patients were excluded for receiving antiretroviral therapy other than combination ART prior to ART, and 1,819 patients were removed for starting ART at age <16 years.

Table 1 displays overall demographic and clinical characteristics of all 30,688 included patients at ART initiation, stratified by receipt of care in Haiti vs. at any other site. After Haiti, patients from Peru, Brazil, and Chile contributed the most person-years. Compared to Haiti, patients from sites other than Haiti were more likely to be male, have higher education (when reported), and started ART in earlier calendar years. The overwhelming majority of patients at all other sites and from Haiti initiated ART with a non-nucleoside reverse transcriptase inhibitor included in the regimen, and a high proportion started ART at CD4 cell counts <200 cells per μL. Approximately 11% and 12% of patients at all other sites and from Haiti had a history of tuberculosis at any time before or at ART initiation, respectively. During the study period, there were 2,637 total deaths for an overall mortality rate of 17·9 deaths per 1,000 person-years. As individual patients could contribute person-time across multiple calendar eras, 2013–2017 contained the most person-years (26,177 vs. 16,178 in 2009–2012 and 8,707 in 2003–2008). The number of deaths were largely consistent across calendar eras at all other sites (328, 405, and 434 for 2003–2008, 2009–2012, and 2013–2017, respectively) and Haiti (517, 422, and 531 for 2003–2008, 2009–2012, and 2013–2017, respectively). The distribution of demographic and clinical characteristics of ART initiators were stable across all time periods (Supplemental Tables 4a and 4b, Appendix pages 7–10).

Demographic and clinical characteristics of patients by lost to follow-up status are shown in Supplemental Table 1 (Appendix, page 2).There were 10,328 individuals lost to follow-up from all sites. Overall, the total proportion of patients lost to follow-up during the study period was highest in Haiti (7,154/17,491, 40·9% of all patients) and Chile (1,676/2,584, 64·9%). The number of patients lost to follow-up were highest in the 2013–2017 time

period: 2,565/11,855 (21·6%) for all other sites except Haiti and 4,924/14,322 (34·4%) for Haiti. Though statistically differing due to the large sample size, patients lost to follow-up were clinically similar to those retained with respect to age, sex, HIV transmission risk factor, CD4 cell count, HIV RNA, history of tuberculosis, and calendar year at ART initiation.

The overall weighted mortality rates by age and calendar era are shown in Figure 1. For all other sites except Haiti (A) and Haiti (B), the overall weighted mortality decreased significantly from 2003–2008 to 2013–2017. Older patients in both groups had the highest mortality rates in all calendar eras. The unadjusted and weighted mortality rates by other key patient characteristics for patients from Haiti and from other sites are shown in Supplemental Tables 2 and 3 (Appendix, pages 4–6). As expected, weighted mortality rates were highest in those 55 years of age, males, those with low CD4 cell count at ART initiation, history of tuberculosis, and those with less education. Compared to the unadjusted calculations, mortality rates were generally higher at sites other than Haiti after being weighted by the likelihood of loss to follow-up. In contrast, unadjusted and weighted mortality rates were fairly similar across all patient characteristics among patients in Haiti, suggesting those patients lost to follow-up were similar to those retained.

Figure 2 demonstrates significant gains in life expectancy at 20 years at Haiti and at other sites during the study period. Estimated life expectancy for individual sites over the calendar eras are shown in Supplemental Figure 1 (Appendix, page 1). By the last era (2013–2017), overall life expectancy at age 20 in both groups was within ten years of that of the general population for 2018 (69·5 vs. 78·0 years in other sites and 61·2 vs. 69·9 years in Haiti). Figure 3 shows life expectancy changes over time by sex/sexual HIV transmission risk factor for other sites (A) and by sex for Haiti (B). For all sites except Haiti, differences in sex/ sexual HIV transmission risk factors were consistent across all calendar eras, with higher life expectancy among women and MSM compared to heterosexual males and those with other or unknown risk factors. In Haiti, women had higher life expectancy and had a smaller difference in life expectancy compared to that in the general population by the final era (65·3 vs 71·7 years for women and 56·0 vs. 68·1 years for men in Haiti).

Figure 4 displays key differences in life expectancy based on CD4 cell count (A), history of tuberculosis (B), and education level (C) at initiation of ART. Life expectancy has significantly improved among all groups of PWH in Haiti and at all sites except Haiti, with higher life expectancy across all eras among those with a higher CD4 cell count at ART initiation, no tuberculosis, and higher education levels. The differences in life expectancy by CD4+ cell count, prior tuberculosis, and education appear to have remained stable or increased over time in the region.

Discussion

With decreasing mortality rates over time, we observed that among CCASAnet sites in Latin America and Caribbean, life expectancy of PWH on ART significantly improved from 2003 to 2017 and now approaches that of the general population in these areas. However, differences in life expectancy based on sex, HIV transmission risk factor, CD4 cell count at

ART initiation, history of tuberculosis, and education remain and may be increasing in some instances, highlighting vulnerable populations in these regions and areas for future intervention.

Using mortality rates weighted to account for informative censoring, our study reveals significant improvements in life expectancy at age 20 among PWH in CCASAnet initiating ART, now approaching that of the general population in the region. This improvement correlates with the increased availability of ART in these countries. Treatment guidelines during this time also changed significantly, with the WHO ending CD4 cell count-based treatment decisions and inaugurating the treat-all era in 2015. Indeed, the greatest gains in life expectancy in our study occurred in the most recent calendar era, 2013–2017. Additionally, the improvements in life expectancy during this time period occurred concurrent with improvements in life expectancy at birth in the region. Latin America and the Caribbean is an economically heterogenous region with high-, middle-, and low-income countries; however, all have seen improvements in general population life expectancy from birth as well as shifting morbidity from infectious to non-infectious etiologies.[6,15]

Although we observed significant increases in life expectancy, disparities remain between life expectancy of PWH and the general population in Latin America and the Caribbean. This may be due to persistent effects of social determinants of health (including socioeconomic status, housing instability, and stigma) and of prevalent late presentation to HIV care. While we have observed improvements in mortality over time in our cohort, nearly half of all PWH included started ART with CD4 cell counts <200 cells per μL, a trend that was stable across all calendar eras.[16] A recent CCASAnet analysis of more than 9,000 adult PWH found that 86%, 71%, and 58% of all deaths in the first one, five, and ten years following enrollment might have been prevented had patients enrolled in care and initiated ART before progression to advanced disease (<200 cells per μL).[17] Late presentation and initiation of treatment leads to increased morbidity from infections such as tuberculosis and other opportunistic infections and has been associated with increased risk of non-communicable diseases later in life, which could account for persistent disparities in life expectancy in more recent calendar years as described elsewhere.[18–21] Our findings of increased life expectancy with CD4 cell counts >200 cells per μL at ART start also supports early diagnosis and treatment with ART, as recommended for all PWH as soon as possible.[22]

There also remained significant gaps in life expectancy by demographic and clinical characteristics at ART initiation which appeared to be increasing by sex/HIV transmission risk factors, history of tuberculosis, and education. These results are consistent with persistent disparities in life expectancy gains in studies of PWH in high-income settings as well.[1,23] Within our region, recent CCASAnet studies have shown differences in mortality by both sex/sexual transmission risk factors and tuberculosis.[24,25] A recent study from our region showed differences in mortality risk by sexual modes of HIV transmission regardless of early retention in care.[24] Consistent with those results, this study also showed differences in life expectancy among MSM and heterosexual men, underscoring heterogeneity of outcomes among men with HIV in the region. Lastly, this study highlights the ongoing importance of tuberculosis in our region. In a recent CCASAnet study, tuberculosis was independently associated with increased mortality rates even after adjusting for CD4 cell

count, age, and sex.[25] In PWH, the most important risk factor for tuberculosis has been a low CD4 cell count at ART start, supporting the importance of early interventions; this finding was reinforced in this study, with low CD4 count and history of tuberculosis at ART start both leading to decreased life expectancy.[26]

Our study is strengthened by use of the largest multi-cohort study of PWH in Latin America and the Caribbean, CCASAnet. However, there remain some important limitations to consider. While the high data quality of standards within CCASAnet make missed capture of mortality among retained PWH unlikely, our study is limited by high number of patients lost to follow-up. We attempted to account for this potential source of selection bias by weighting mortality rates by adjusted probabilities of being lost to follow-up. Indeed, our weighted mortality rates were slightly higher compared to unweighted estimates. However, without tracing or linkage to well-maintained national death registries (which are not available at CCASAnet sites in Argentina, Haiti, and Honduras), we do not know the true mortality after loss to follow-up among those PWH who were lost to follow-up in those settings. As mortality rates among those lost to follow-up may be higher than among those retained, if our inverse probability weighting models were misspecified or lacked important predictors, it is possible our results have been biased toward an underestimation of mortality (and overestimation of life expectancy) among those groups with higher rates of loss to follow-up (including PWH in Haiti, males, PWH with lower education, and those with missing HIV transmission risk data). A second limitation of our study is the lack of adjustment for confounders of the age- or treatment era-mortality relationships in our life expectancy estimates. We used the Chiang method for calculation of abridged life tables and stratified by key patient characteristics. However, this method does not allow for calculation of life expectancy for a given characteristic independent of other known factors. For example, differences in life expectancy by sexual HIV transmission risk factor and tuberculosis status may also be reflective of known disparities in CD4+ cell count at ART initiation between these groups, and differences by income and education may also be reflective of disparities in sex. Third, with the exception of GHESKIO in Haiti, which provides HIV testing, most CCASAnet clinical sites are referral clinics located at tertiary medical centers in major urban centers. Thus, mortality estimates from our sites may not be reflective of trends in rural or less populous settings. Similarly, as only one country from Central America and only one site from a Social Health Insurance subsystem is represented in the CCASAnet clinical sites, these estimates may not fully reflect the experiences of all PWH initiating ART this region. Fourth, very few PWH age greater than 60 years were included in these cohorts, and for this reason life expectancy is likely overestimated. Additionally, as our study was looking at life expectancy gains in those started on ART for the first time following cohort entry, we excluded those who never started ART, those who started ART before cohort entry, and those who received antiretroviral medications other than highly-active combination regimens prior to ART start to limit biases due to lack of ART therapy, initiation at lower CD4 cell counts based upon prior treatment guidelines, and survivorship bias. Thus, our estimates only reflect estimated life expectancy gains among treatment-naïve individuals starting therapy but are not reflective of all PWH in care. Finally, we were limited by lack of complete information of other key demographic and social

characteristics that could contributed disparities in estimated life expectancy in the region, including ethnicity and race, stigma, and poverty.

In conclusion, this study described significant improvements in life expectancy at age 20 for PWH on ART in Latin American/Caribbean countries from 2003–2017, consistent with findings seen in analyses of higher income countries.[1,2,27] Increased life expectancy among those who start ART with CD4 cell counts >200 cells per μL supports early HIV screening and initiation of ART. With ongoing efforts, life expectancies in low- and middle-income countries should continue to increase and more closely approach those of the general population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Panel

Evidence before:

Large cohort studies from Europe, United States, and Canada (including the Antiretroviral Therapy Cohort Collaboration and the North American AIDS Cohort Collaboration on Research and Design) have shown significant increases in life expectancy and decreases in mortality for persons living with HIV (PWH) who initiate ART. Studies of life expectancy among PWH in low- and middle-income countries have been limited to single-country analyses (namely from South Africa and Brazil). We searched PubMed from inception to October 19, 2020m for publications in English using the search terms "life expectancy," "Latin America," "HIV," "ART," and "sex." We found no multisite nor large studies describing life expectancy changes among PWH initiated on ART in Latin America.

Added value:

This is the largest study to examine life expectancy changes in PWH initiating ART in Latin America and the Caribbean over time. It shows that significant increases in life expectancy from 2003–2017, now within ten years of those in the general populations of these countries. Disparities in life expectancy among PWH remain, however, including differences by sex/sexual HIV transmission risk factors, education, a history of tuberculosis, and CD4+ cell count at time of ART initiation.

Implications:

Since the beginning of the treat-all era, this study shows significant improvement in life expectancy among PWH in the diverse region of Latin America, showing that ART can narrow the gap in life expectancy for PWH in regions outside high-income settings.
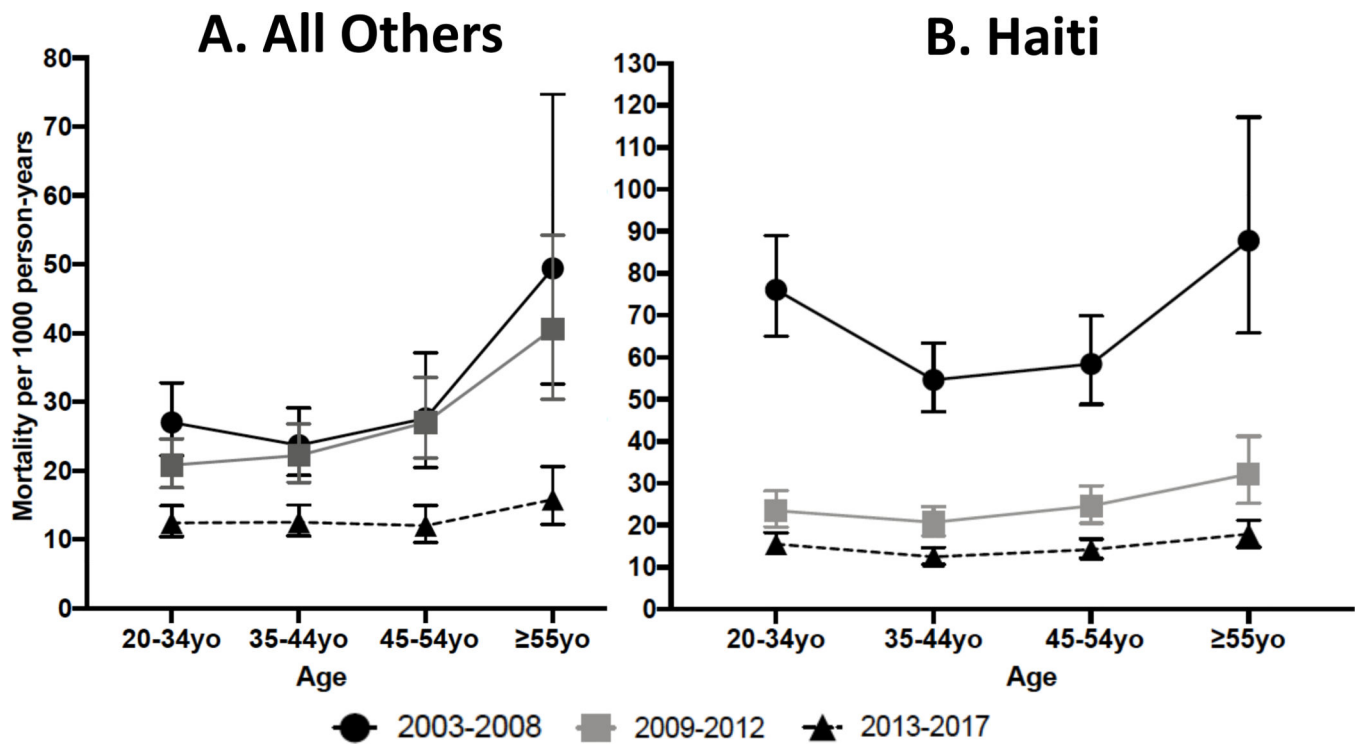
Figure 1.
Weighted, age-specific mortality rates of adults initiated on ART at all CCASAnet sites
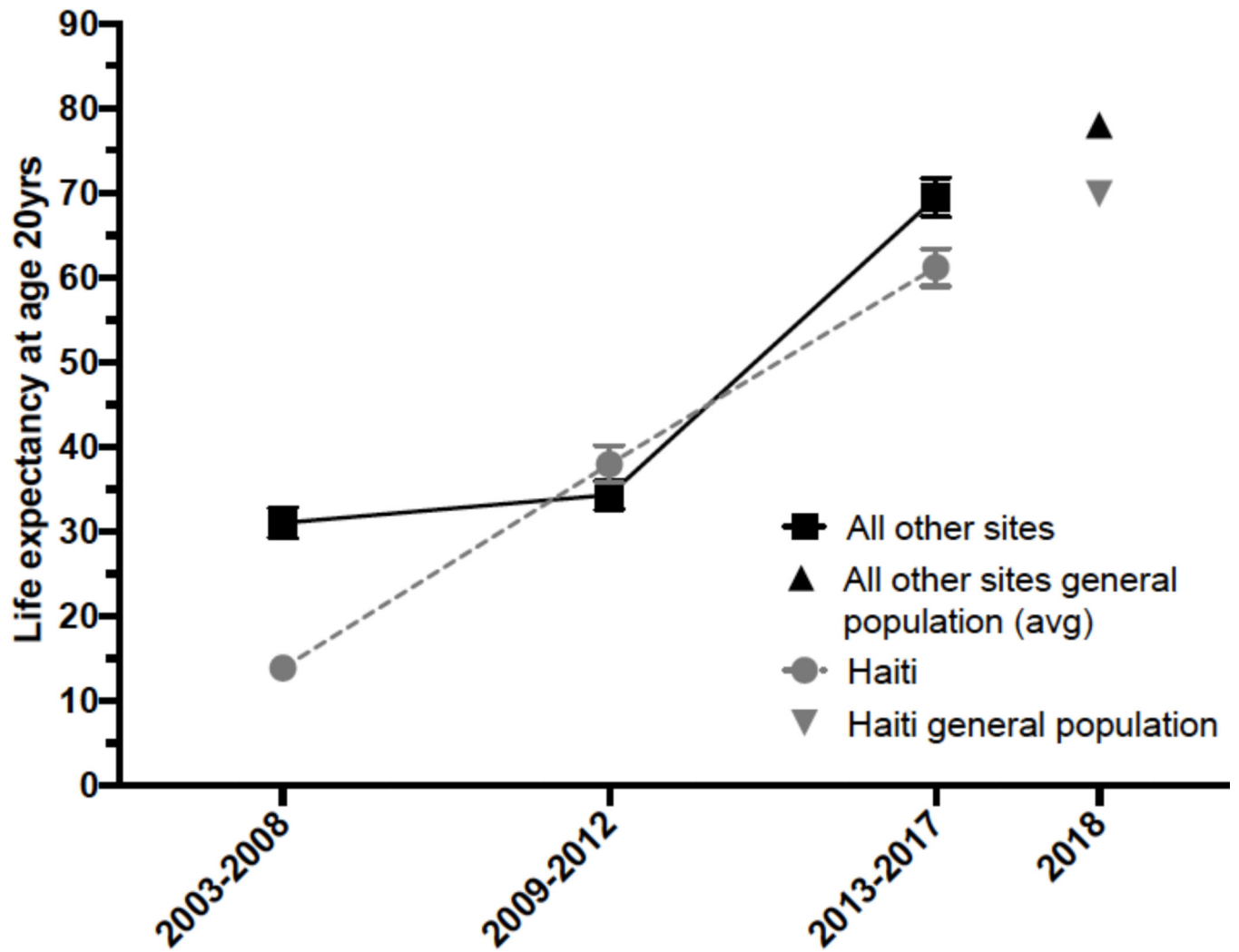except for Haiti (A) and Haiti (B) over calendar eras.

Figure 2.
Overall life expectancy at age 20 years for adults initiated on ART at all CCASAnet sites except for Haiti and Haiti across calendar eras. General population life expectancy of all other sites (weighted average) and Haiti from United Nations' data in 2018 shown by triangle symbols.
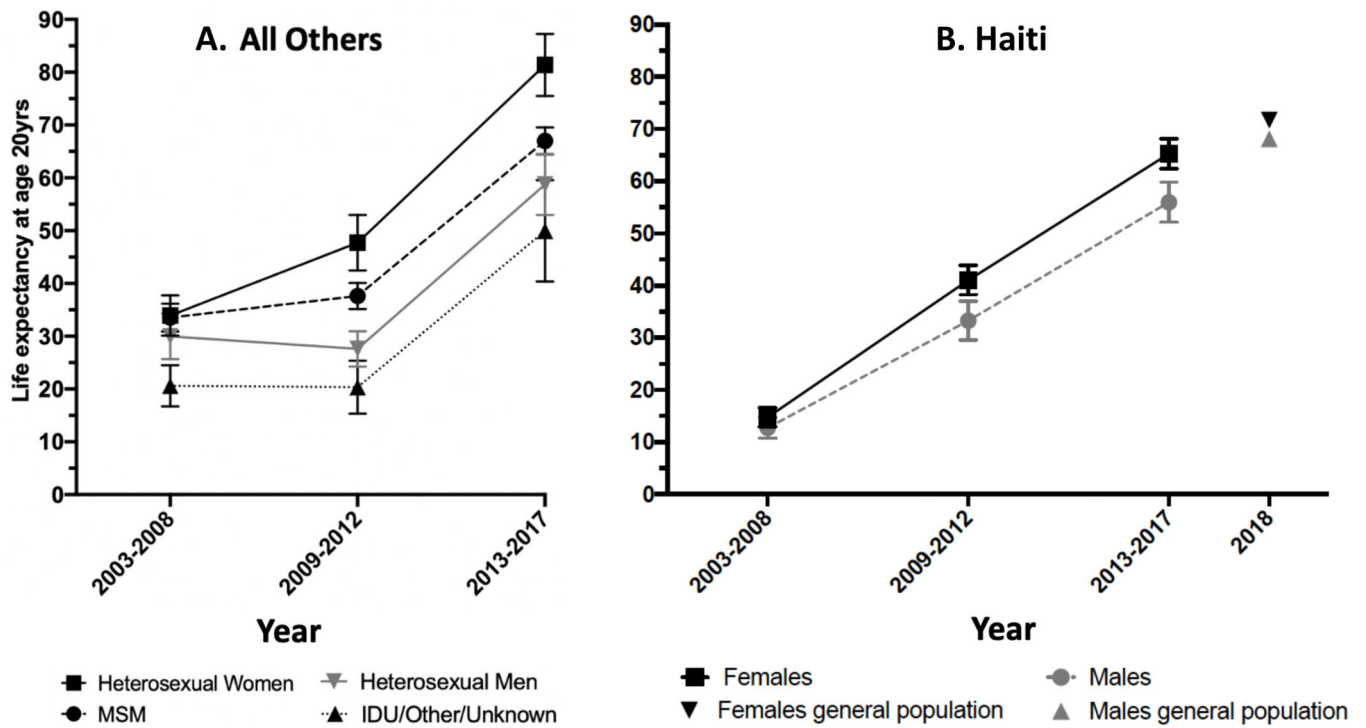
Figure 3.
Life expectancy at age 20 years for adults initiated on ART at all CCASAnet sites except for Haiti by sex/sexual HIV transmission risk factor (A) and at Haiti by sex (B) across calendar eras. General population life expectancy in Haiti by sex from United Nations' data in 2018 shown by triangle symbols. Abbreviations used: MSM – men who have sex with men; IDU – injection drug use

Figure 4.
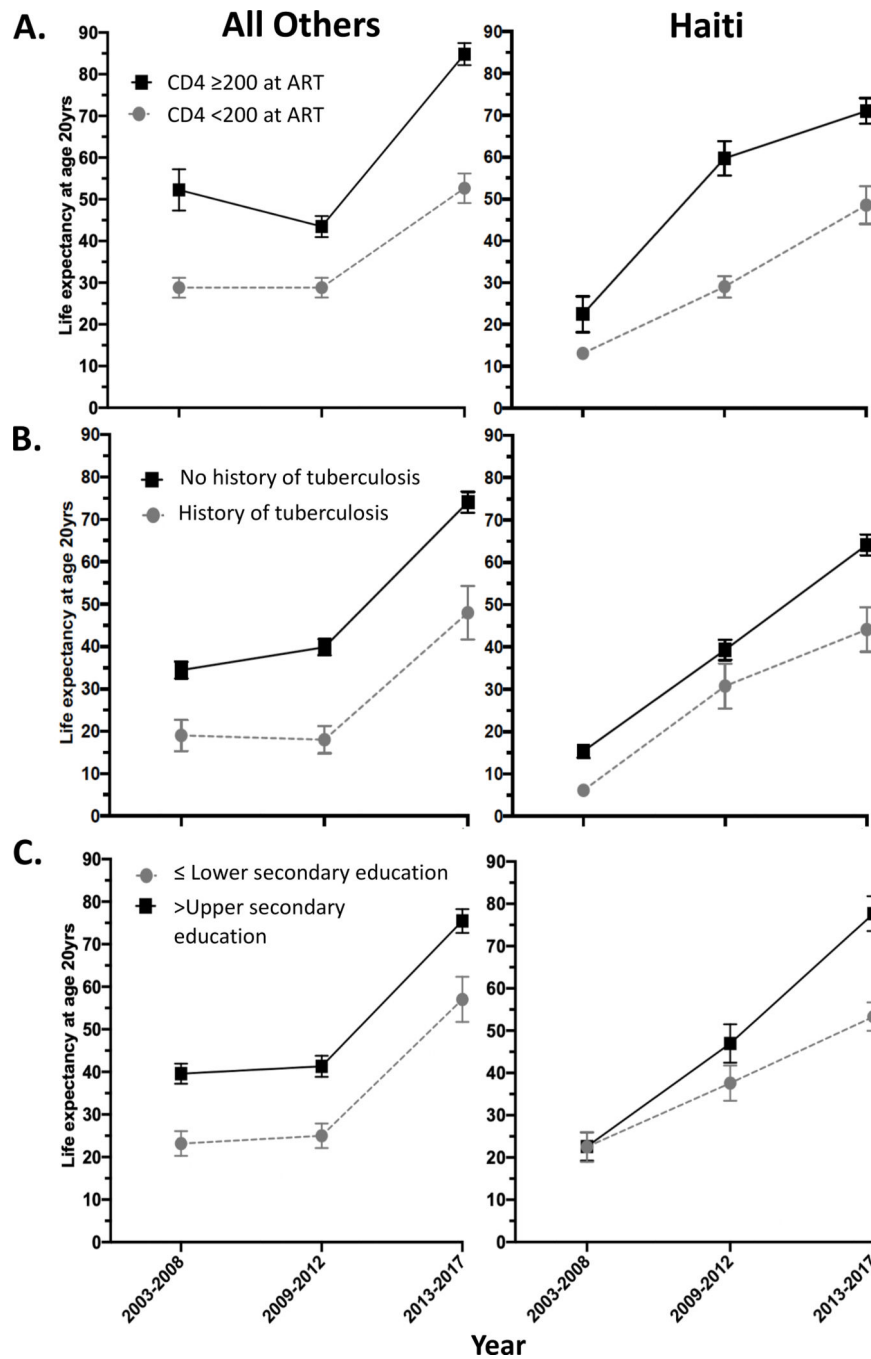Life expectancy at age 20 years for adults initiated on ART all CCASAnet sites except for Haiti (left column) and Haiti (right column) across calendar eras by CD4 cell count at ART initiation (A), history of tuberculosis at ART initiation (B), and education (C). Results exclude individuals with missing CD4 cell count (+/− 6 months) at ART initiation (n=5,134) and missing education (n=4720).

Table 1.

Demographic and clinical characteristics at the time of ART initiation among PWH from CCASAnet sites

	All Sites Except Haiti[a]	Haiti
	N=13,197	N=17,491
Country, n (%)		
Argentina	548 (4·2)	
Brazil	3,327 (25·2)	
Chile	2,584 (19·6)	
Honduras	1027 (7·8)	
Mexico	1,177 (8·9)	
Peru	4,534 (34·4)	
Age at ART initiation in years, median (IQR)	34·3 (28·0–42·3)	37·2 (30·1–45·4)
Sex, n (%)		
Female	3,086 (23·4)	10,250 (58·6)
Male	10,111 (76·6)	7,241 (41·4)
HIV Transmission Risk Factor, n (%)		
Heterosexual women	2,765 (21·0)	
Heterosexual men	3,067 (23·2)	
Men who have sex with men	6,296 (47·7)	
Injection drug use	55 (0·4)	
Other or unknown	1014 (7·7)	
Education, n (%)		
Lower Secondary and Below	2,895 (21·9)	7,739 (44·2)
Upper Secondary and Above	8,784 (66·5)	6,550 (37·5)
Other or missing	1,518 (11·5)	3,202 (18·3)
Year of ART initiation, median (IQR)	2011 (2007–2014)	2012 (2009–2014)
ART regimen, n (%)		
NNRTI + two NRTIs	10,584 (80·2)	16,402 (93·8)

	All Sites Except Haiti[a] N=13,197	Haiti N=17,491
PI + two NRTIs	2,096 (15·9)	969 (5·5)
Other	517 (3·9)	120 (0·7)
CD4 cell count (cells per μL) at ART initiation[b], n (%)		
<200	6,071 (46·0)	6,276 (35·9)
200	6,033 (45·7)	7,126 (40·7)
Missing	1,045 (7·9)	4,089 (23·4)
Log_{10} HIV RNA (copies per mL) at ART initiation[c], median (IQR)	4.9 (4·3–5·4)	4.2 (3·7–4·9)
History of tuberculosis[d], n (%)	1,429 (10·8)	2,141 (12·2)
Died during study period, n (%)	1,167 (8·8)	1,470 (8·4)
Lost to follow-up during study period[e], n (%)	3,174 (24·1)	7,154 (40·9)

[a] All others sites include from CCASAnet sites in Argentina, Brazil, Chile, Honduras, and Peru.

[b] CD4 cell count closest within 6 months before or after ART initiation date

[c] HIV RNA value closest within 6 months before or 30 days after ART initiation date

[d] Diagnosis of active pulmonary or extra-pulmonary tuberculosis any time before or within 7 days of ART

[e] Lost to follow-up defined as no clinic contact within 12 months of database closure and not known to have died.

Abbreviations used:

ART: antiretroviral therapy

IQR: interquartile range

NNRTI: non-nucleoside reverse transcriptase inhibitor

NRTI: nucleoside reverse transcriptase inhibitor

PI: protease inhibitor