Projection of age of individuals living with HIV and time since ART initiation in 2030: estimates for France

Lise Marty, Yakhara Diawara, Antoine Rachas, Sophie Grabar, Dominique Costagliola, Virginie Supervie

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY Open Access

Projection of age of individuals living with HIV and time since ART initiation in 2030: estimates for France

Journal:	*Journal of the International AIDS Society*
Manuscript ID	JIAS-2022-01-0047.R2
Wiley - Manuscript type:	Research Article
Date Submitted by the Author:	n/a
Complete List of Authors:	Marty, Lise; Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique Diawara, Yakhara; Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique Rachas, Antoine; Direction de la Stratégie, des Etudes et des Statistiques, CNAM GRABAR, Sophie; Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, AP-HP, Hôpital St Antoine Costagliola, Dominique; Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique Supervie, Virginie; Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique
Main Discipline:	Epidemiology
Please add secondary discipline if applicable:	
Additional Keywords:	aging, demographic profile, time since treatment initiation, Life expectancy
Keywords:	HIV epidemiology, Modeling
Abstract:	Introduction: Thanks to antiretroviral treatment (ART), people living with HIV (PLHIV) are living longer and ageing. However, ageing involves increased risks of co-morbidities, which also depend on when PLHIV individuals started ART. To tackle the HIV age-related upcoming challenges, knowledge of current and future age structure of HIV population is needed. Here, we forecast the demographic profile of the adult population diagnosed with HIV (aPDHIV) in France until 2030, accounting for the impact of ART initiation period on mortality. Methods: We used national data from the French Hospital Database on HIV (ANRS CO4-FHDH) and a sample of the National Health Data System to, first, characterize the aPDHIV in 2018 and estimate their mortality rates according to age, sex, and ART initiation period. Second, we used national HIV surveillance data to define three scenarios for the numbers of newly diagnosed HIV cases over 2019-2030: 30% decrease in HIV cases (S1), status quo situation (S2), and epidemic elimination (S3). We then combined these data using a matrix model, to project the age structure of aPDHIV, and time since ART initiation.

	Results: In 2018, there was an estimated 161,125 aPDHIV (33% women), of which 55% were aged 50 or older (50+), 22% aged 60+ and 8% aged 70+. In 2030, the aPDHIV would grow to 195,246 for S1, 207,972 for S2 and 167,221 for S3. Whatever the scenario, in 2030, estimated median time since ART initiation would increase and age distribution would shift towards older ages: with 65 to 72% aPDHIV aged 50+, 42-48% 60+ and 17-19% 70+. This corresponds to ~83,400 aPDHIV (28% women) aged 60+, among which ~69% started ART more than 20 years ago (i.e. before 2010) and ~39% >=30 years ago (i.e. before 2000), and to ~33,100 aPDHIV (27% women) aged 70+, among which ~72% started ART >=20 years ago and ~43% >=30 years ago. Conclusions: By 2030, in France, close to 20% of the aPDHIV will be aged 70+, of which >40% would have started ART more than 30 years ago. These estimates are essential to adapt co-morbidities screening and anticipate resource provision in the aged care sector.

Projection of age of individuals living with HIV and time since ART initiation in 2030: estimates for France

Lise Marty[1§], Yakhara Diawara[1], Antoine Rachas[2], Sophie Grabar[3], Dominique Costagliola[4], Virginie Supervie[1]

[1] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, F75012, Paris, France

[2] Direction de la Stratégie, des Etudes et des Statistiques, CNAM, F-75000 Paris, France

[3] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, AP-HP, Hôpital St Antoine, F75012, Paris, France

[4] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, F75013, Paris, France

[§]Corresponding author: Lise Marty 27 rue de Chaligny Paris, F75012, France

Phone number: +33(0)185347257 Lise.marty@iplesp.upmc.fr

E-mail addresses of authors:

LM: lise.marty@iplesp.upmc.fr

YD: yakharadiawara@yahoo.com

AR: antoine.rachas@assurance-maladie.fr

SG: sophie.grabar@iplesp.upmc.fr

DC: dominique.costagliola@iplesp.upmc.fr

VS: virginie.supervie@inserm.fr

Keywords : HIV ; ageing ; demographic profile ; time since treatment initiation ; modelling.

Word count:

Text: 3713/3500;

Abstract 350/350;

Abstract

Introduction: Thanks to antiretroviral treatment (ART), people living with HIV (PLHIV) are living longer and ageing. However, ageing involves increased risks of co-morbidities, which also depend on when PLHIV individuals started ART. To tackle the HIV age-related upcoming challenges, knowledge of current and future age structure of HIV population is needed. Here, we forecast the demographic profile of the adult population diagnosed with HIV (aPDHIV) in France until 2030, accounting for the impact of ART initiation period on mortality.

Methods: We used national data from the French Hospital Database on HIV (ANRS CO4-FHDH) and a sample of the National Health Data System to, first, characterize the aPDHIV in 2018 and estimate their mortality rates according to age, sex, and ART initiation period. Second, we used national HIV surveillance data to define three scenarios for the numbers of newly diagnosed HIV cases over 2019-2030: 30% decrease in HIV cases (S1), status quo situation (S2), and epidemic elimination (S3). We then combined these data using a matrix model, to project the age structure of aPDHIV, and time since ART initiation.

Results: In 2018, there was an estimated 161,125 aPDHIV (33% women), of which 55% were aged 50 or older (50+), 22% aged 60+ and 8% aged 70+. In 2030, the aPDHIV would grow to 195,246 for S1, 207,972 for S2 and 167,221 for S3. Whatever the scenario, in 2030, estimated median time since ART initiation would increase and age distribution would shift towards older ages: with 65 to 72% aPDHIV aged 50+, 42-48% 60+ and 17-19% 70+. This corresponds to ~83,400 aPDHIV (28% women) aged 60+, among which ~69% started ART more than 20 years ago (i.e. before 2010) and ~39% >=30 years ago (i.e. before 2000), and to ~33,100 aPDHIV (27% women) aged 70+, among which ~72% started ART >=20 years ago and ~43% >=30 years ago.

Conclusions: By 2030, in France, close to 20% of the aPDHIV will be aged 70+, of which >40% would have started ART more than 30 years ago. These estimates are essential to adapt co-morbidities screening and anticipate resource provision in the aged care sector.

Introduction

Since the beginning of the HIV epidemic, great progress has been made to improve the health of people living with HIV (PLHIV). The introduction of combination antiretroviral therapy (cART) in 1996 has led to rapid decrease in mortality [1]. With increased cART efficacy and tolerability over time, life expectancy (LE) within 3 years of cART initiation further increased, and continued to increase even in the late cART era [2]. Currently the LE of treated PLHIV approaches that of the general population [3,4].

Consequently, HIV populations are ageing. According to UNAIDS estimates, in high-income countries, one-third of PLHIV were aged 50 or more in 2013 [5]. Ageing will involve new care challenges. First, age is associated with chronic conditions like non-AIDS defining cancers, cardiovascular, renal, liver, bone, and neurological diseases, and HIV infection further increases the risk of these conditions [6]. Increased burden of polypharmacy and risk of drug-drug interactions with cART could therefore represent an upcoming issue in HIV care [7,8]. Second, ageing PLHIV will possibly need access to assisted living facility for elderly people. Resource provision in the aged care sector will thus need to be addressed in the coming years, including specific HIV care training for medical staff.

To anticipate for needs and resources, it is essential to foresee the number and age of PLHIV. Beyond age-related chronic morbidities, the period at which PLHIV started ART is also key, as it reflects the type of ART regimen to which individuals had been exposed, the level of immune dysfunction reached before ART initiation, which varied according to ART guidelines, and indirectly the lifetime duration with HIV. At any age, comorbidity and mortality risks are higher for individuals ageing with a longer duration of HIV infection than for individuals who seroconverted at an older age [9]. The period of ART initiation is thus likely to influence mortality risk, but also comorbidity risk and the potential

occurrence of side-effects of long-term treatment.

So far, none of the studies that projected the number and age structure of PLHIV accounted for the issue of the ART initiation period [10–16]. In this study, we propose to fill this gap, and project the demographic profile of the adult population living with diagnosed HIV (aPLdHIV) in France until 2030. For this purpose, we estimated mortality rates according to ART initiation period, and considered several scenarios for the numbers of new HIV cases that will be diagnosed by 2030. We also used mortality rate estimates to provide updated estimates of LE for PLHIV currently on ART, by sex and ART initiation period, and compared these estimates to those for the French general population.

Methods

Data Sources

Three data sources were used. First, the permanent beneficiary sample (Échantillon Généraliste des Bénéficiaires, EGB) is a representative cohort of the population covered by the main health insurance schemes, which monitors beneficiaries' health care consumption and long-term illness status. It is a sample of 1/97th of the insured individuals in France [17]. Second, the French Hospital Database on HIV (ANRS CO4-FHDH) is a nationwide open hospital cohort created, in 1989, to enroll adult PLHIV receiving medical care, in currently 182 hospitals located throughout France [18]. The FHDH is representative of PLHIV receiving care in France [18]. Data, including demographic characteristics, biological markers, and ART regimen, are collected prospectively, at each outpatient visit or hospital admission, using standardized forms. By 2019, FHDH included data on ~210,000 individuals aged ≥18 years, including ~106,000 with at least one follow-up visit in 2019. Third, routine national surveillance on individuals newly diagnosed with HIV is managed by Santé publique France [19].

Projecting the demographic profile of aPLdHIV

To determine the demographic profile of aPLdHIV (i.e. age, sex and ART initiation period) by 2030, we first needed data, estimates or assumptions on three parameters: (i) the demographic profile of aPLdHIV in 2018, (ii) the number and age distribution of newly diagnosed HIV cases over 2019-2030, and (iii) the mortality rates of aPLdHIV in 2018 and of new cases diagnosed beyond 2018. Only adults (i.e. aged ≥18 years) were included in the analysis. Specifically, we considered 14 age groups: 18-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, ≥80.

Demographic profile of aPLdHIV in 2018

To estimate the number and age distribution of aPLdHIV in 2018, we used data from EGB and an algorithm initially developed by the general health scheme fund to study chronic diseases (including HIV) in terms of numbers, prevalence rates, etc. [20]. For HIV, the algorithm relies on long-term illness status, dispensations of HIV-specific drugs and biological exams, as well as HIV diagnosis during hospital stays (see details in the supplemental material, section A). We first used the algorithm to determine the numbers of beneficiaries, by sex and age group, managed for HIV at least once over 2014-2018 and still alive in 2018. We then extrapolated these numbers to the whole population of France, by dividing them by the EGB representativeness (i.e. 1/97) and the proportion of the population covered by the health insurance schemes included in the EGB (i.e. 95.6% of the whole population). Then we used data from EGB and FHDH to determine for each individual his/her date of ART initiation (supplemental material, section B). We considered five ART initiation periods: 1985-1996, 1997-2005, 2006-2010, 2011-2016 and ≥2017; the choice of the periods was mainly based on the amount of available data and changes in ART eligibility criteria (supplemental material, section B). Individuals who had not started ART by 2018 were assumed to initiate ART in 2019, as median time between care entry and ART initiation was less than 1 month (FHDH data).

New HIV cases over 2019-2030

To set the annual numbers of newly diagnosed HIV cases over 2019-2030, we projected the mean annual number of newly diagnosed cases over 2015-2018 according to three scenarios: a 30% decrease scenario (scenario 1, reference scenario), i.e. a linear decrease with 30% fewer cases in 2030 compared to 2015-2018, a status quo scenario (scenario 2, pessimistic scenario), with a steady annual number of cases over 2019-2030, and an

epidemic elimination scenario (scenario 3, optimistic scenario), with a linear decrease in the number of cases until zero case in 2030 (supplemental material, section C, figure S1). Scenario 1 was set as the reference as it is a broad extrapolation of the temporal trend in newly diagnosed HIV cases observed over 2012-2018. Age distribution of newly diagnosed cases over 2019-2030 was obtained by extrapolating that of cases newly diagnosed over 2010-2018 (supplemental material, section C, Figure S2). We assumed that newly diagnosed individuals would initiate ART within their diagnosis year.

Mortality rates in 2018 and beyond

To estimate mortality rates for aPLdHIV still alive in 2018, according to ART initiation period, we used data on aPLdHIV enrolled in the FHDH who had at least one follow-up visit between January 1, 2017 and December 31, 2019 and a known date of ART initiation. Person-years were calculated for each sex and ART initiation period separately. They were accumulated from January 1, 2017 or cohort enrolment, until death, loss to follow-up (LTFU, defined as no clinical visit for 18 months, in line with French HIV guidelines [21], supplemental material section D), or December 31, 2019, whichever came first. For LTFU patients, follow-up stopped 6 months after the last visit. Patients with a clinical visit within the 6-month period before December 31, 2019 were censored on December 31, 2019.

As the number of deaths is underreported in the FHDH [22], it was adjusted using data from the health insurance schemes on beneficiaries living with HIV (supplemental material, section E).

We then used a Poisson model, with age reached in 2018 by aPLdHIV and ART initiation period as covariates, to estimate mortality rates by sex and age group, stratified by ART initiation period.

It was not possible to estimate mortality rate for individuals who started ART from 2017 due to lack of follow-up data after ART initiation. Then for these individuals and for newly diagnosed cases over 2019-2030, mortality rates were assumed, conservatively, to be the same as those for individuals who started ART during 2011-2016. Likewise, due to data scarcity, mortality rate for individuals aged 18-19 years were assumed to be the same as those for individuals aged 20-24 years.

Projection matrix model and projection of age and time since ART initiation

We used a matrix population model to project the size of aPLdHIV until 2030, using estimates for aPLdHIV in 2018, scenarios on newly diagnosed cases over 2019-2030, and estimates of mortality rates (supplemental material, section F). Distributions of time since ART initiation were also projected, together with age distributions, stratified by ART initiation period, using the same matrix model.

Life Expectancy

Using estimated mortality rates and life table method [23], we estimated LE for PLHIV on ART, by sex, age and ART initiation period. LE at a given age is defined as the expected number of years of life remaining for those surviving to that age (supplemental material, section H). LE for the general population at age 20, 40 and 60 years in 2018 were obtained from the Human Mortality Database (https://www.mortality.org).

Ethical statement

The ANRS CO4-FHDH project was approved by CNIL (French data protection authority) on November 27, 1991, Journal Officiel, January 17, 1992. To conform to new regulations, the ANRS CO4-FHDH was then approved by the CEREES (Expertise Committee for

Research, Studies and Evaluations in the field of Health) on July 20, 2018 and as a hospital datawarehouse by CNIL on February 19, 2021. The cohort received authorization to conduct research projects on the datawarehouse by CNIL on March 30, 2021. All ANRS CO4-FHDH participants signed informed consent forms mentioning use of data for research purposes. INSERM has a regulatory permanent access to EGB data, according to Article R1431-13 of the French Public Health Code, as modified by the Decree 2021-848 of June 22, 2021. All data were deidentified, thus informed consent was not necessary.

Results

Demographic characteristics (age, sex, country of birth) of participants to the three data sources are provided in Table 1.

Mortality rates and life expectancies

We used data on 104,042 adults (35% women), enrolled in the FHDH, who initiated ART before 2017 and had at least one follow-up visit between January 1, 2017 and December 31, 2019 to estimate mortality rates (supplemental material, figure S3), as well as LE, which are presented in Table 2 together with LE for the general population. For instance, LE for individuals aged 40 in 2018 who started ART over 2011-2016 was 39.2 years for men and 40.2 years for women. In comparison, it was respectively 40.9 and 46.3 years for the general population. In general, whatever the age group, LE was higher for individuals who initiated ART over 2011-2016, i.e. the most recent period, compared to those who initiated ART earlier. Whatever the period and age group, women had higher LE than men, however this difference tended to decrease over time, from 7 to 10% for women who started ART over 1985-1996 to 3 to 4% for women who started ART over 2011-2016. In addition, for individuals who initiated ART over 2011-2016, i.e. those with the highest LE, the gap in LE compared to the general population was higher for women than for men, whatever the age group, ranging from 3.8 to 6.8 years for women and from 0.4 to 2.4 for men.

Demographic profile of aPLdHIV in 2030

In 2018, an estimated 161,125 adults (33% women) were living with diagnosed HIV. Assuming a 30% decrease in the annual number of newly diagnosed cases over 2019-2030 (scenario 1), and using the population matrix model together with mortality rate

estimates, we estimated that 195,246 adults (33% women) would be living with diagnosed HIV in 2030, i.e. an increase of 21% of the epidemic size. It was 207,972 assuming a steady number of newly diagnosed cases until 2030 (scenario 2) and 167,221 under the epidemic elimination scenario (scenario 3).

For all scenarios, we found that age distribution of aPLdHIV would shift towards older ages in 2030 (Figure 1). For scenario 1, the proportion of individuals aged ≥50 increased between 2018 and 2030, from 61% to 68% for men, and from 44% to 63% for women. The proportion of individuals aged ≥60 doubled, from 24% to 47% for men, and from 17% to 36% for women, like the proportion of individuals aged ≥70, from 8% to 18% for men, 7% to 14% for women. These proportions were slightly lower for scenario 2 (Figure 1, C-D) and slightly higher for scenario 3 (Figure 1, E-F). Whatever the scenario, we estimated that, in 2030, there would be ~83,400 individuals (~28% women) aged ≥60 and ~33,100 individuals aged ≥70 (~27% women); in comparison, in 2018, it was respectively 35,715 (~25% women) and 12,582 (~27% women).

Projected time since ART initiation

Proportions of individuals who started ART more than 20 or 30 years ago will increase over 2018-2030 (Figure 2), especially for older age groups. For brevity, we only present results for scenario 1, results for other scenarios are described in the supplemental material, section I. Proportions of individuals with ≥20 years of ART exposure will increase from 27% to 42% for men, and from 21% to 44% for women. In particular, for individuals aged ≥60, these proportions will increase from 43% to 68% for men, and from 33% to 67% for women. Proportions of individuals with ≥30 years of ART exposure will increase from <1% to 21% for men, and from <1% to 18% for women. In particular, for individuals aged ≥60, these proportions will increase from 1% to 39% for men, and from

<1% to 37% for women. In consequence, median time since ART initiation will increase, especially for older age groups. For individuals aged ≥60, it will increase from 18.4 (IQR 10.4-22.4) to 25.9 years (17.6-33.4) for men, and from 15.2 (7.9-21.4) to 25.8 years (16.8-33.1) for women, while for individuals aged <60, it will only increase from 9.8 (4.8-19.0) to 12.0 years (6.5-17.8) for men, and from 11.0 (5.2-17.7) to 14.5 years (7.5-21.8) for women.

Of note, we estimated that, in 2030, 83,659 individuals (34% women) would have started ART ≥20 years ago and 38,492 individuals (30% women) would have started ART ≥30 years ago - versus respectively 40,667 and 573 in 2018 (Figure 2). Among men who started ART ≥20 years ago, 77% would be aged ≥60, 33% ≥70, 8% ≥80. It was respectively 54%, 21% and 4% for women. Among men who started ART ≥30 years, 89% would be aged ≥60, 40% ≥70, 8% ≥80. It was respectively 75%, 29% and 6% for women.

Discussion

We projected that by 2030, the HIV epidemic in France would be growing, most likely by more than 20%, and ageing, with a doubling of the proportion of individuals aged ≥60 and ≥70. More than two-third of aPLdHIV would be aged ≥50, ~50% aged ≥60, and ~20% aged ≥70. Interestingly, whatever the scenario considered for the epidemic dynamics over 2019-2030, we estimated that ~83,000 individuals will be aged ≥60 in 2030, including ~33,000 aged ≥70. Our results are in line with studies forecasting the age structure of HIV population in other high-income countries [10,11,13,14,16]. It was estimated that the proportion of PLHIV on ART aged ≥50 would be 73% in 2030 in the Netherlands [13] and 54% in the United States (US) [16], and ~75% in 2035 in the US and in Italy [14]. Bretaña et al. [10] performed projections for Australia, considering three scenarios for the future number of newly diagnosed cases over 2018-2027. They highlighted that, whatever the scenario, the age distribution of PLHIV would have its highest peak in the 55-59 age group in 2027, which aligns with our findings of highest peak in the 60-64 age group for men, 50-54 for women.

In addition, our study predicts that in 2030, in France, there will be more than 38,000 individuals who would have started ART more than 30 years ago (i.e. before 2000), with most of them being aged ≥60 (85%, ~33,000), 37% aged ≥70 (~14,000) and 8% aged ≥80 (~3,000). These individuals were thus exposed to the first generation of nucleoside reverse transcriptase inhibitors (AZT, D4T) and protease inhibitors, which have been associated with body morphology changes and cardiovascular diseases [24,25]. In addition, ART duration and time living with diagnosed HIV infection have been associated with increased risk of multimorbidity [7,9], but also with psychological morbidity and lower quality of life [26,27], which should be considered as part as integrated HIV care.

To the best of our knowledge, our study is the first to project time spent since ART initiation for an HIV population. However, previous studies emphasized other important aspects for the projected demographic profile of HIV populations, which we were unable to take into account. First, a study investigating the capacity of current cART to offer long-term HIV control found that median time until exhaustion of treatment options was 45.5 years (IQR 34.0–61.0 years) [28]. Furthermore, some studies showed important heterogeneity in the projections of PLHIV according to race/ethnicity, with older projected population of white PLHIV compared to Black and Hispanic minorities [11,29]. Other studies [13,14] focused on the burden and prevalence of age-related co-morbidities: Smit et al. [13] predicted that in 2030, 84% of PLHIV in the Netherlands will have at least one age-related non-communicable disease, with 28% having three or more, mainly due to cardiovascular disease. This could generate complications due to drug-drug interactions for 40% of patients with the currently recommended first-line HIV regimen. Finally, a study for Australia [15] highlighted that the number of PLHIV in non-metropolitan areas, where PLHIV median age is higher, are expected to increase at a greater rate than that in the major cities.

We also found that LE of adults who started ART from 2011 onwards was either equal or approaching that of the general population: for instance, at age 60 in 2018 it was ~23 and ~24 years for respectively men and women living with diagnosed HIV versus respectively ~23 and ~28 years in the general population. Individuals who started ART in 2005 or earlier, and still alive in 2018, had lower LE, but the difference was only 2 to 4 years. This can have important implications for health-related insurance policies for PLHIV. Marcus et al. [30] reported an overall LE of 56.0 years at age 21 over 2014-2016, close to our estimates for individuals of age 20 in 2018, ranging from 51.4 to 57.4 years. Studies that

311 estimated LE for earlier periods of follow-up found, expectedly, lower LE than ours [3,31].
312 We also found that although women living with diagnosed HIV had higher LE than men,
313 the gap in LE compared to the general population was higher for women than for men,
314 which is in line with previous results [2,3]. Potential explanations for this higher gap
315 include later access to HIV care for women than for men. However, in France, time
316 between infection and care entry was estimated to be shorter for women than for men
317 [32,33]. Another explanation is that among women living with diagnosed HIV in France, a
318 vast majority was born abroad (63%, of which 77% in sub-Saharan African countries,
319 Table 1), while among men a vast majority was born in France (71%). Hence, differences
320 in socio-economic levels and access to health care system between born-abroad and born-
321 in-France individuals, but also stigma, and marginalization, probably play an important
322 role in the observed sex difference in LE gap between PLHIV and the general population
323 [34,35].
324
325 The main novelty of our approach is that it accounts for the impact of ART initiation
326 period on mortality rates to project the demographic profile of HIV population. In
327 addition, our projections for the population size aged ≥60 are robust to assumptions
328 regarding epidemic dynamics over 2019-2020. However, our study has also a number of
329 limitations. First, the projection method and LE estimates rely on the assumption that age-
330 specific mortality rates estimated over 2017-2019 will remain constant over 2019-2030.
331 On one hand, lower mortality beyond 2019 would lead to higher LE estimates and larger
332 HIV population in 2030. On the other hand, higher mortality among older age groups, due
333 to covid-19 during 2020-2021 for instance, could lead to a decrease in LE, total population
334 size and proportions of older PLHIV in 2030. Second, several limitations affect HIV care
335 data. Data on deaths in FHDH were not comprehensive, and were adjusted for under-

reporting, with potential inaccurate adjustments (supplemental material, section G for details). As health insurance schemes do not collect data on HIV exposure group, this factor could not be accounted for. Third, we could not include individuals aged <18 years for population size estimates. According to health insurance and HIV surveillance data, this could represent ~5200 individuals in 2030, comprising ~4000 individuals aged <18 years living with diagnosed HIV in 2018, plus ~100 individuals who could be newly diagnosed each year over 2019-2030. Fourth, our global LE estimates do not capture the comorbidity-free LE. This was estimated to remain much lower for PLHIV than for the general population (9.5 years difference in a US cohort of insured adults [30]). Finally, HIV becoming more prevalent among older adults, transmission risk of higher age groups might increase, if for instance older PLHIV are not adherent to their treatment. This may impact the age distribution of individuals becoming newly infected, with for instance more individuals seroconverting at an older age. As a consequence, interventions explicitly targeting older individuals may be needed, as older individuals were recently shown to be at increased risk of delayed presentation for HIV care [36].

CONCLUSIONS

By 2030, in France, close to 20% of the adult population living with diagnosed HIV will be aged ≥70 (i.e. ~33,000 individuals), of which >40% would have started ART more than 30 years. Ageing of HIV population has important implications for care, generating an increase in comorbidity prevalence and treatment complexity. Our findings can help to measure the burden of ageing, and anticipate health care needs, resource provision and screening guidelines in HIV care, in France but also in other high-income countries. Indeed, our estimates probably provide a broad picture of what is likely to occur in term

of HIV population ageing in other settings, with similar historical access to ART and free access to care.

Conflict of interest statement: VS reports lecture fees from ViiV (2019), Gilead (2019, 2020), and Janssen-Cilag (2020), outside the submitted work.

DC reports an HIV grant from Janssen (2019-2020), and personal fees from Gilead (2020) and Pfizer (2022) for lectures, outside the submitted work.

LM, AR, SG and YD declare no conflicts of interest.

Authorship: LM and VS designed the research; LM performed the research; all authors analyzed the data; LM and VS drafted the manuscript; all authors critically revised the manuscript for important intellectual content.

Acknowledgements: LM is grateful for the financial support of the ANRS, in the form of a postdoctoral research fellowship. All authors thank Adam Trickey for his help on the methodology of life expectancy estimation. We are grateful to all ANRS CO4-French Hospital Database on HIV (FHDH) participants and research assistants, without whom this work would not have been possible. Members of FHDH-ANRS CO4 are listed at https://anrs-co4.fhdh.fr/.

Financial support: FHDH is funded by the ANRS-MIE, the Institut National de la Santé et de la Recherche Médicale (INSERM), and the French Ministry of Health.

References

1. Mocroft A, Vella S, Benfield T, Chiesi A, Miller V, Gargalianos P, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. The Lancet. 1998;352(9142):1725–30.

2. Antiretroviral Therapy Cohort Collaboration. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. Lancet HIV. 2017;4(8):e349–56.

3. Samji H, Cescon A, Hogg RS, Modur SP, Althoff KN, Buchacz K, et al. Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. PloS One. 2013;8(12):e81355.

4. Gueler A, Moser A, Calmy A, Günthard HF, Bernasconi E, Furrer H, et al. Life expectancy in HIV-positive persons in Switzerland: matched comparison with general population. AIDS Lond Engl. 2017;31(3):427–36.

5. Joint United Nations Programme on HIV/AIDS. HIV and aging. [Internet]. 2013 [cited 2021 Oct 2]. Available from: http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2013/20131101_JC2563_hiv-and-aging_en.pdf

6. Guaraldi G, Orlando G, Zona S, Menozzi M, Carli F, Garlassi E, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. Clin Infect Dis. 2011;53(11):1120–6.

7. Justice AC, Gordon KS, Romero J, Edelman EJ, Garcia BJ, Jones P, et al. Polypharmacy-associated risk of hospitalisation among people ageing with and without HIV: an observational study. Lancet Healthy Longev. 2021;2(10):e639–50.

8. Rasmussen LD, May MT, Kronborg G, Larsen CS, Pedersen C, Gerstoft J, et al. Time trends for risk of severe age-related diseases in individuals with and without HIV infection

410 in Denmark: a nationwide population-based cohort study. Lancet HIV. 2015;2(7):e288-
411 98.
412 9. Guaraldi G, Zona S, Brothers TD, Carli F, Stentarelli C, Dolci G, et al. Aging with HIV
413 vs. HIV seroconversion at older age: a diverse population with distinct comorbidity
414 profiles. PloS One. 2015;10(4):e0118531.
415 10. Bretaña NA, Gray R, Law M, Guy R. Aging of the HIV population in Australia: a
416 modeling study. J Acquir Immune Defic Syndr. 2018;79(5):e115–6.
417 11. Kasaie P, Stewart C, Humes E, Gerace L, Zhang J, Silverberg MJ, et al. Projecting the
418 age-distribution of men who have sex with men receiving HIV treatment in the United
419 States. Ann Epidemiol. 2021;
420 12. Murray JM, McDonald AM, Law MG. Rapidly ageing HIV epidemic among men who
421 have sex with men in Australia. Sex Health. 2009;6(1):83–6.
422 13. Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, Sighem A van, et al. Future
423 challenges for clinical care of an ageing population infected with HIV: a modelling study.
424 Lancet Infect Dis. 2015;15(7):810–8.
425 14. Smit M, Cassidy R, Cozzi-Lepri A, Quiros-Roldan E, Girardi E, Mammone A, et al.
426 Projections of non-communicable disease and health care costs among HIV-positive
427 persons in Italy and the U.S.A.: A modelling study. PLOS ONE. 2017;12(10):e0186638.
428 15. Jansson J, Wilson DP. Projected demographic profile of people living with HIV in
429 Australia: planning for an older generation. PLoS ONE. 2012;7(8):e38334.
430 16. Althoff KN, Stewart CN, Humes E, Zhang J, Gerace L, Boyd CM, et al. The shifting age
431 distribution of people with HIV using antiretroviral therapy in the United States, 2020 to
432 2030. AIDS Lond Engl [Internet]. 2021 [cited 2022 Jan 17]; Available from:
433 https://doi.org/10.1097/QAD.0000000000003128
434 17. Tuppin P, Rudant J, Constantinou P, Gastaldi-Ménager C, Rachas A, de Roquefeuil

435 L, et al. Value of a national administrative database to guide public decisions: from the
436 système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the
437 système national des données de santé (SNDS) in France. Rev Epidemiol Sante Publique.
438 2017;65 Suppl 4:S149–67.
439 18. Mary-Krause M, Grabar S, Lièvre L, Abgrall S, Billaud E, Boué F, et al. Cohort Profile:
440 French hospital database on HIV (FHDH-ANRS CO4). Int J Epidemiol. 2014 Oct
441 1;43(5):1425–36.
442 19. Lot F, Semaille C, Cazein F, Barin F, Pinget R, Pillonel J, et al. Preliminary results
443 from the new HIV surveillance system in France. Euro Surveill. 2004;9(10):34–7.
444 20. Sécurité Sociale - l'Assurance maladie. Cartographie des pathologies et des
445 dépenses de l'Assurance Maladie [Internet]. Available from: https://assurance-
446 maladie.ameli.fr/etudes-et-donnees/par-theme/pathologies/cartographie-assurance-
447 maladie
448 21. Fournier AL, Yazdanpanah Y, Verdon R, Lariven S, Mackoumbou-Nkouka C, Phung
449 BC, et al. Incidence of and risk factors for medical care interruption in people living with
450 HIV in recent years. PLoS ONE. 2019;14(3):e0213526.
451 22. Lewden C, Jougla E, Alioum A, Pavillon G, Lievre L, Morlat P, et al. Number of deaths
452 among HIV-infected adults in France in 2000, three-source capture-recapture estimation.
453 Epidemiol Infect. 2006;134(6).
454 23. Chiang CL. The life table and its construction. In: Introduction to stochastic
455 processes in Biostatistics. New York: John Wiley and Sons; 1968. p. 198–214.
456 24. Carr A. Cardiovascular risk factors in HIV-infected patients. J Acquir Immune Defic
457 Syndr. 2003;34 Suppl 1:S73-8.
458 25. Mallal SA, John M, Moore CB, James IR, McKinnon EJ. Contribution of nucleoside
459 analogue reverse transcriptase inhibitors to subcutaneous fat wasting in patients with

460 HIV infection. AIDS Lond Engl. 2000;14(10):1309–16.
461 26. McGowan J, Sherr L, Rodger A, Fisher M, Miners A, Anderson J, et al. Age, time living
462 with diagnosed HIV infection, and self-rated health. HIV Med. 2017;18(2):89–103.
463 27. Sabranski M, Erdbeer G, Sonntag I, Stoehr A, Horst HA, Plettenberg A, et al. Physical
464 and mental health in HIV-infected patients with virological success and long-term
465 exposure to antiretroviral therapy. AIDS Care. 2021;33(4):453–61.
466 28. Jansson J, Wilson DP, Carr A, Petoumenos K, Boyd MA. Currently available
467 medications in resource-rich settings may not be sufficient for lifelong treatment of HIV.
468 AIDS Lond Engl. 2013 May 15;27(8):1245–51.
469 29. Hood JE, Golden MR, Hughes JP, Goodreau SM, Siddiqi AEA, Buskin SE, et al.
470 Projected demographic composition of the United States population of people living with
471 diagnosed HIV. AIDS Care. 2017;29(12):1543–50.
472 30. Marcus JL, Leyden WA, Alexeeff SE, Anderson AN, Hechter RC, Hu H, et al.
473 Comparison of overall and comorbidity-free life expectancy between insured adults with
474 and without HIV Infection, 2000-2016. JAMA Netw Open. 2020;3(6):e207954.
475 31. Marcus JL, Chao CR, Leyden WA, Xu L, Quesenberry CP, Klein DB, et al. Narrowing
476 the gap in life expectancy between HIV-infected and HIV-uninfected individuals with
477 access to care. J Acquir Immune Defic Syndr 1999. 2016;73(1):39–46.
478 32. Marty L, Cazein F, Panjo H, Pillonel J, Costagliola D, Supervie V, et al. Revealing
479 geographical and population heterogeneity in HIV incidence, undiagnosed HIV prevalence
480 and time to diagnosis to improve prevention and care: estimates for France. J Int AIDS Soc.
481 2018;21(3):e25100.
482 33. Supervie V, Marty L, Lacombe JM, Dray-Spira R, Costagliola D, FHDH-ANRS CO4
483 study group. Looking beyond the cascade of HIV care to end the AIDS epidemic: estimation
484 of the time interval from HIV infection to viral suppression. J Acquir Immune Defic Syndr.

2016;73(3):348–55.

34. Simard EP, Fransua M, Naishadham D, Jemal A. The influence of sex, race/ethnicity, and educational attainment on Human Immunodeficiency Virus death rates among adults, 1993-2007. Arch Intern Med. 2012;172(20):1591.

35. Collins LF, Sheth AN, Mehta CC, Naggie S, Golub ET, Anastos K, et al. The prevalence and burden of non-AIDS comorbidities among women living with or at risk for Human Immunodeficiency Virus infection in the United States. Clin Infect Dis Off Publ Infect Dis Soc Am. 2020;72(8):1301–11.

36. Justice AC, Goetz MB, Stewart CN, Hogan BC, Humes E, Luz PM, et al. Delayed presentation of HIV among older individuals: a growing problem. Lancet HIV. 2022;9(4):e269–80.

37. Althoff KN, Chandran A, Zhang J, Arevalo WM, Gange SJ, Sterling TR, et al. Life-Expectancy disparities among adults with HIV in the United States and Canada: the impact of a reduction in drug- and alcohol-related deaths using the lives saved simulation model. Am J Epidemiol. 2019 Dec;188(12):2097–109.

501 **Table 1: Sex, age, and country of birth distributions of participants to the three data**
502 **sources**

	EGB – 2014-2018		ANRS CO4-FHDH - 2017 - 2019[1]		HIV surveillance - 2015-2018	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Total	108,871	52,253	67,721	36,321	17,141	7,997
Age N (%)						
18-19	304 (0.3)	102 (0.2)	19 (0.0)	24 (0.1)	286 (1.7)	142 (1.8)
20-24	1,522 (1.4)	1,522 (2.9)	734 (1.1)	535 (1.5)	1,741 (10.2)	633 (7.9)
25-29	3,450 (3.2)	2,638 (5.0)	2,061 (3.0)	1,246 (3.4)	2,523 (14.7)	1,231 (15.4)
30-34	5,682 (5.2)	3,145 (6.0)	3,536 (5.2)	2,587 (7.1)	2,490 (14.5)	1,445 (18.1)
35-39	9,233 (8.5)	6,189 (11.8)	4,816 (7.1)	4,536 (12.5)	2,297 (13.4)	1,384 (17.3)
40-44	9,538 (8.8)	8,726 (16.7)	6,773 (10.0)	5,832 (16.1)	2,014 (11.7)	1,021 (12.8)
45-49	13,190 (12.1)	7,102 (13.6)	9,994 (14.8)	6,108 (16.8)	1,936 (11.3)	681 (8.5)
50-54	21,003 (19.3)	7,407 (14.2)	13,136 (19.4)	5,959 (16.4)	1,554 (9.1)	545 (6.8)
55-59	18,264 (16.8)	6,392 (12.2)	11,504 (17.0)	4,371 (12.0)	1,021 (6.0)	384 (4.8)
60-64	10,451 (9.6)	3,856 (7.4)	6,711 (9.9)	2,382 (6.6)	177 (3.6)	276 (3.4)
65-69	7,102 (6.5)	1,725 (3.3)	4,326 (6.4)	1,326 (3.7)	611 (2.3)	160 (2.0)
70-74	5,682 (5.2)	1,623 (3.1)	2,453 (3.6)	820 (2.3)	387 (1.1)	64 (0.8)
75-79	1,826 (1.7)	913 (1.7)	1,060 (1.6)	363 (1.0)	65 (0.4)	21 (0.3)
80+	1,623 (1.5)	913 (1.7)	598 (0.9)	232 (0.6)	31 (0.2)	10 (0.1)
Country of birth[2] (%)						
France			48,252 (71.3)	13,304 (36.6)	10,678 (61.4)	431 (21.9)
Sub-saharan Africa			9,427 (13.9)	17,704 (48.7)	3,566 (20.5)	5,453 (63.9)

Europe		2,969 (4.4)	933 (2.6)	870 (5.0)	247 (2.9)
America / Haïti		2,778 (4.1)	2,143 (5.9)	1,232 (7.1)	639 (7.5)
Other (North Africa / Asia / Oceania)		4,295 (6.3)	2,237 (6.2)	1,034 (6.01,865)	324 (3.8)

(1) Individuals enrolled in the FHDH, who initiated ART before 2017 and had at least one follow-up visit between January 1, 2017 and December 31, 2019.

(2) No data on country of birth are available in the EGB.

Table 2. Remaining life expectancy (in years) according to the age reached in 2018, for the general population* and for people living with HIV (PLHIV) men and women who initiated ART, by period of ART initiation. Mean remaining life expectancy (and 95% confidence interval) for PLVHIV individuals were estimated from mortality event among PLHIV individuals enrolled in the French Hospital Database on HIV (ANRS CO4-FHDH) who had at least one follow-up clinical visit between January 1, 2017 and December 31, 2019. *Values for the general population were obtained from the Human Mortality Database (https://www.mortality.org)

Period of ART initiation	Age reached in 2018					
	20 years		40 years		60 years	
	Men	Women	Men	Women	Men	Women
1985 – 1996	x	x	35.0 (33.7 – 36.3)	37.4 (35.8 – 39.0)	19.7 (19.1 – 20.3)	21.6 (20.4 – 22.8)
1997 – 2005	54.4 (52.1 – 56.7)	56.9 (54.9 – 58.9)	36.2 (35.5 – 36.9)	38.2 (37.3 – 39.1)	20.5 (20.0 – 21.0)	22.1 (21.2 – 23.0)
2006 – 2010	56.8 (53.9 – 59.7)	60.0 (57.7 – 62.3)	38.4 (37.4 – 39.4)	41.0 (39.6 – 42.4)	22.5 (21.5 – 23.5)	24.4 (23.1 – 25.7)
2011 - 2016	57.7 (56.5 – 58.9)	59.1 (57.3 – 60.9)	39.2 (38.1 – 40.3)	40.2 (38.6 – 41.8)	22.9 (21.8 – 24.0)	23.9 (22.3 – 25.5)
General population*	60.1	65.9	40.9	46.3	23.3	27.7

Figure 1. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, according to different scenarios. Numbers and age distributions for men (A) and for women (B), in 2018 (in red) and in 2030 (in turquoise) for scenario 1 (i.e. 30% decrease in newly diagnosed HIV cases between 2018 and 2030). Comparison of the numbers and age distributions of adults living with diagnosed HIV in 2030 for scenario 1 (in turquoise) and scenario 2 (i.e. status quo situation with a steady annual number of new HIV cases over 2019-2030, black diagonal stripes) for men (C) and for women (D), and for scenario 1 and scenario 3 (i.e. epidemic elimination with zero new HIV cases in 2030, black diagonal stripes) for men (E) and for women (F). Detailed assumptions made for the number and age of newly-diagnosed HIV cases in 2019-2030 can be found the supplemental material, section C.

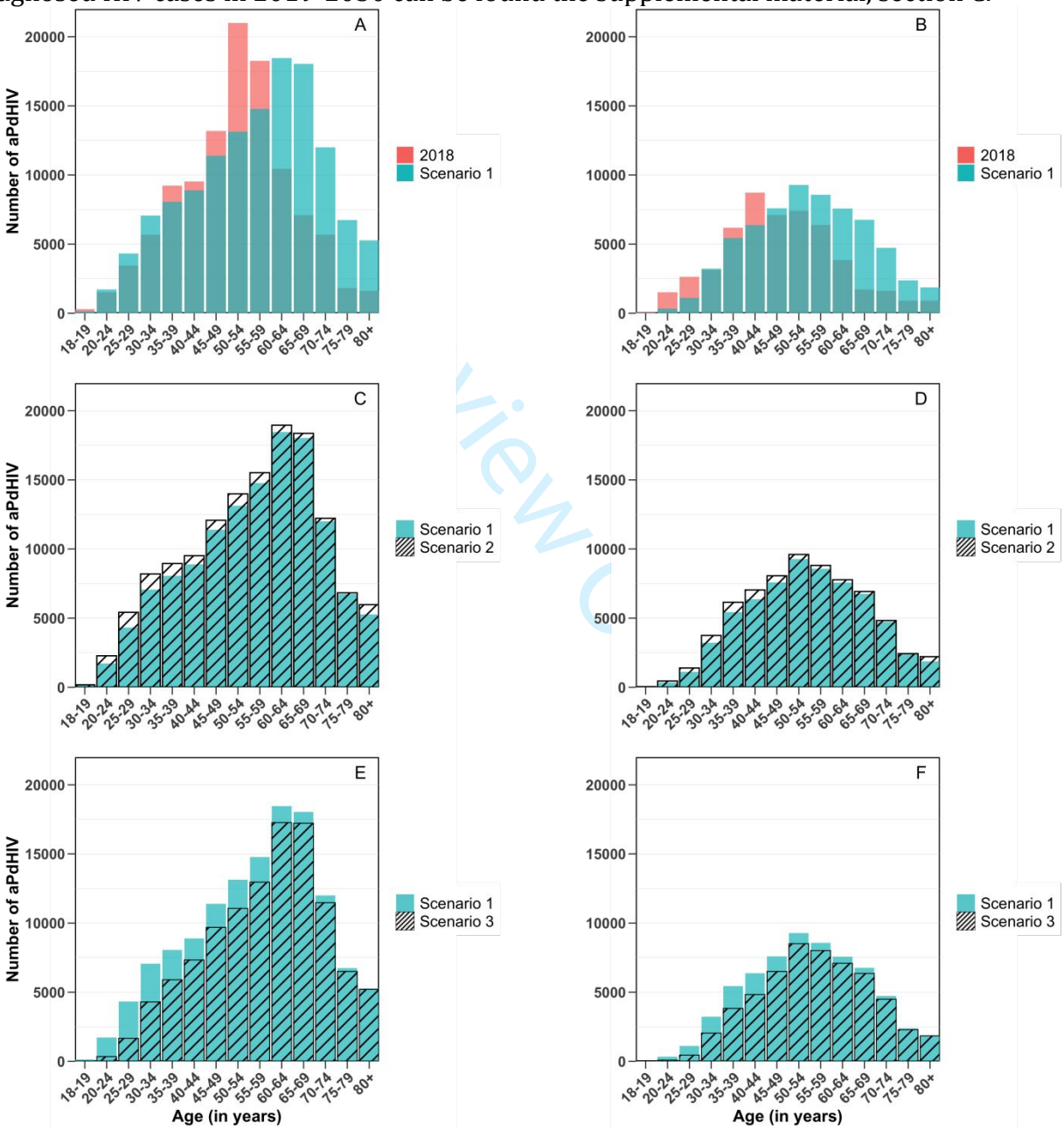
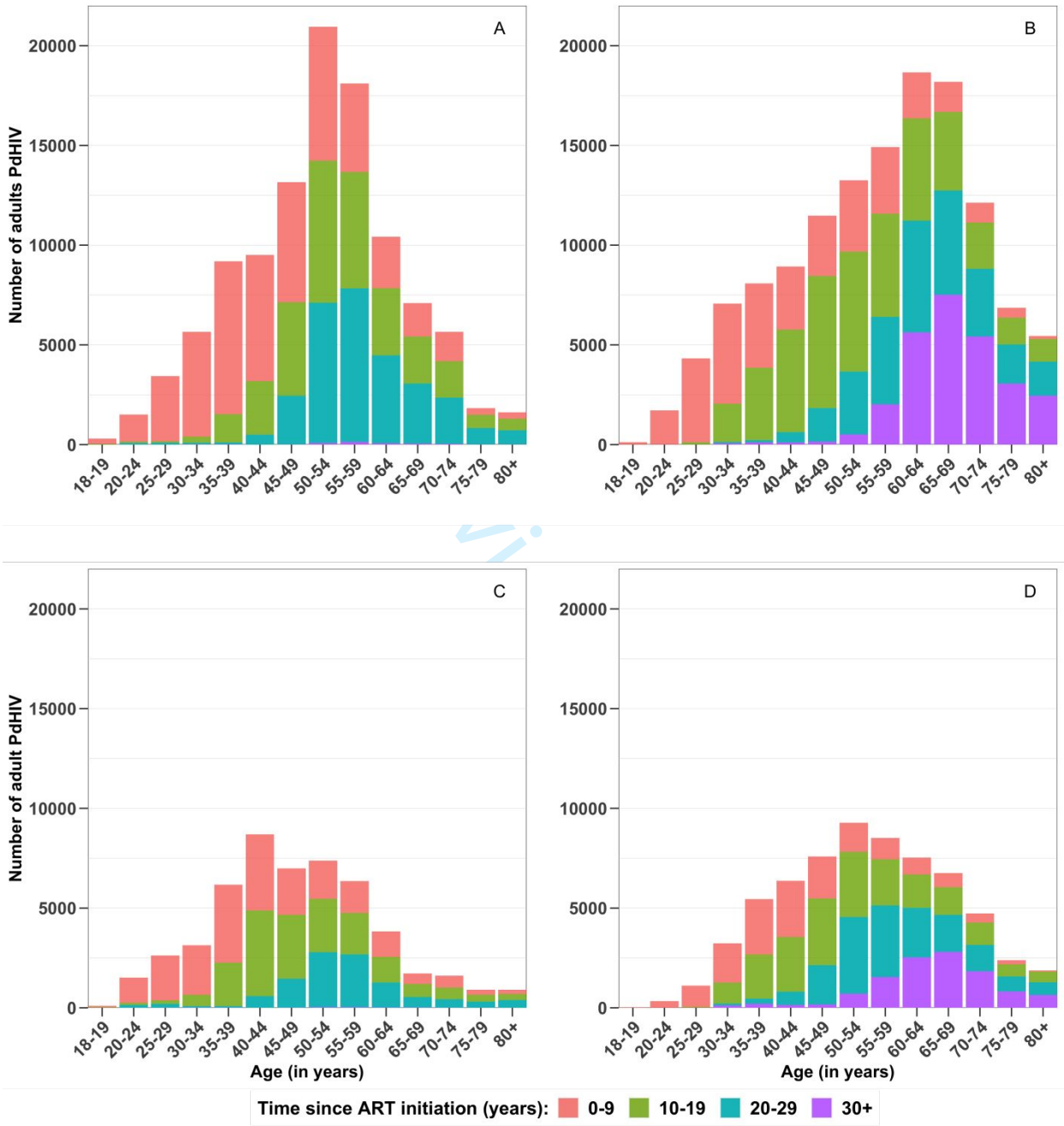


Figure 2. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D) for scenario 1 (i.e. 30% decrease in newly diagnosed HIV cases between 2018 and 2030). Results for other scenarios can be found in the supplemental material, section E and figures S4 and S5.



Projection of age of individuals living with HIV and time since ART initiation in 2030: estimates for France

Lise Marty[1§], Yakhara Diawara[1], Antoine Rachas[2], Sophie Grabar[3], Dominique Costagliola[4], Virginie Supervie[1]

[1] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, F75012, Paris, France

[2] Direction de la Stratégie, des Etudes et des Statistiques, CNAM, F-75000 Paris, France

[3] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, AP-HP, Hôpital St Antoine, F75012, Paris, France

[4] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, F75013, Paris, France

[§]Corresponding author: Lise Marty 27 rue de Chaligny Paris, F75012, France

Phone number: +33(0)185347257 Lise.marty@iplesp.upmc.fr

E-mail addresses of authors:

LM: lise.marty@iplesp.upmc.fr

YD: yakharadiawara@yahoo.com

AR: antoine.rachas@assurance-maladie.fr

SG: sophie.grabar@iplesp.upmc.fr

DC: dominique.costagliola@iplesp.upmc.fr

VS: virginie.supervie@inserm.fr

Keywords : HIV ; ageing ; demographic profile ; time since treatment initiation ; modelling.

Word count:

Text: 3713/3500;

Abstract 350/350;

Abstract

Introduction: Thanks to antiretroviral treatment (ART), people living with HIV (PLHIV) are living longer and ageing. However, ageing involves increased risks of co-morbidities, which also depend on when PLHIV individuals started ART. To tackle the HIV age-related upcoming challenges, knowledge of current and future age structure of HIV population is needed. Here, we forecast the demographic profile of the adult population diagnosed with HIV (aPDHIV) in France until 2030, accounting for the impact of ART initiation period on mortality.

Methods: We used national data from the French Hospital Database on HIV (ANRS CO4-FHDH) and a sample of the National Health Data System to, first, characterize the aPDHIV in 2018 and estimate their mortality rates according to age, sex, and ART initiation period. Second, we used national HIV surveillance data to define three scenarios for the numbers of newly diagnosed HIV cases over 2019-2030: 30% decrease in HIV cases (S1), status quo situation (S2), and epidemic elimination (S3). We then combined these data using a matrix model, to project the age structure of aPDHIV, and time since ART initiation.

Results: In 2018, there was an estimated 161,125 aPDHIV (33% women), of which 55% were aged 50 or older (50+), 22% aged 60+ and 8% aged 70+. In 2030, the aPDHIV would grow to 195,246 for S1, 207,972 for S2 and 167,221 for S3. Whatever the scenario, in 2030, estimated median time since ART initiation would increase and age distribution would shift towards older ages: with 65 to 72% aPDHIV aged 50+, 42-48% 60+ and 17-19% 70+. This corresponds to ~83,400 aPDHIV (28% women) aged 60+, among which ~69% started ART more than 20 years ago (i.e. before 2010) and ~39% >=30 years ago (i.e. before 2000), and to ~33,100 aPDHIV (27% women) aged 70+, among which ~72% started ART >=20 years ago and ~43% >=30 years ago.

Conclusions: By 2030, in France, close to 20% of the aPDHIV will be aged 70+, of which >40% would have started ART more than 30 years ago. These estimates are essential to adapt co-morbidities screening and anticipate resource provision in the aged care sector.

Introduction

Since the beginning of the HIV epidemic, great progress has been made to improve the health of people living with HIV (PLHIV). The introduction of combination antiretroviral therapy (cART) in 1996 has led to rapid decrease in mortality [1]. With increased cART efficacy and tolerability over time, life expectancy (LE) within 3 years of cART initiation further increased, and continued to increase even in the late cART era [2]. Currently the LE of treated PLHIV approaches that of the general population [3,4].

Consequently, HIV populations are ageing. According to UNAIDS estimates, in high-income countries, one-third of PLHIV were aged 50 or more in 2013 [5]. Ageing will involve new care challenges. First, age is associated with chronic conditions like non-AIDS defining cancers, cardiovascular, renal, liver, bone, and neurological diseases, and HIV infection further increases the risk of these conditions [6]. Increased burden of polypharmacy and risk of drug-drug interactions with cART could therefore represent an upcoming issue in HIV care [7,8]. Second, ageing PLHIV will possibly need access to assisted living facility for elderly people. Resource provision in the aged care sector will thus need to be addressed in the coming years, including specific HIV care training for medical staff.

To anticipate for needs and resources, it is essential to foresee the number and age of PLHIV. Beyond age-related chronic morbidities, the period at which PLHIV started ART is also key, as it reflects the type of ART regimen to which individuals had been exposed, the level of immune dysfunction reached before ART initiation, which varied according to ART guidelines, and indirectly the lifetime duration with HIV. At any age, comorbidity and mortality risks are higher for individuals ageing with a longer duration of HIV infection than for individuals who seroconverted at an older age [9]. The period of ART initiation is thus likely to influence mortality risk, but also comorbidity risk and the potential

occurrence of side-effects of long-term treatment.

So far, none of the studies that projected the number and age structure of PLHIV accounted for the issue of the ART initiation period [10–16]. In this study, we propose to fill this gap, and project the demographic profile of the adult population living with diagnosed HIV (aPLdHIV) in France until 2030. For this purpose, we estimated mortality rates according to ART initiation period, and considered several scenarios for the numbers of new HIV cases that will be diagnosed by 2030. We also used mortality rate estimates to provide updated estimates of LE for PLHIV currently on ART, by sex and ART initiation period, and compared these estimates to those for the French general population.

Methods

Data Sources

Three data sources were used. First, the permanent beneficiary sample (Échantillon Généraliste des Bénéficiaires, EGB) is a representative cohort of the population covered by the main health insurance schemes, which monitors beneficiaries' health care consumption and long-term illness status. It is a sample of 1/97th of the insured individuals in France [17]. Second, the French Hospital Database on HIV (ANRS CO4-FHDH) is a nationwide open hospital cohort created, in 1989, to enroll adult PLHIV receiving medical care, in currently 182 hospitals located throughout France [18]. The FHDH is representative of PLHIV receiving care in France [18]. Data, including demographic characteristics, biological markers, and ART regimen, are collected prospectively, at each outpatient visit or hospital admission, using standardized forms. By 2019, FHDH included data on ~210,000 individuals aged ≥18 years, including ~106,000 with at least one follow-up visit in 2019. Third, routine national surveillance on individuals newly diagnosed with HIV is managed by Santé publique France [19].

Projecting the demographic profile of aPLdHIV

To determine the demographic profile of aPLdHIV (i.e. age, sex and ART initiation period) by 2030, we first needed data, estimates or assumptions on three parameters: (i) the demographic profile of aPLdHIV in 2018, (ii) the number and age distribution of newly diagnosed HIV cases over 2019-2030, and (iii) the mortality rates of aPLdHIV in 2018 and of new cases diagnosed beyond 2018. Only adults (i.e. aged ≥18 years) were included in the analysis. Specifically, we considered 14 age groups: 18-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, ≥80.

Demographic profile of aPLdHIV in 2018

To estimate the number and age distribution of aPLdHIV in 2018, we used data from EGB and an algorithm initially developed by the general health scheme fund to study chronic diseases (including HIV) in terms of numbers, prevalence rates, etc. [20]. For HIV, the algorithm relies on long-term illness status, dispensations of HIV-specific drugs and biological exams, as well as HIV diagnosis during hospital stays (see details in the supplemental material, section A). We first used the algorithm to determine the numbers of beneficiaries, by sex and age group, managed for HIV at least once over 2014-2018 and still alive in 2018. We then extrapolated these numbers to the whole population of France, by dividing them by the EGB representativeness (i.e. 1/97) and the proportion of the population covered by the health insurance schemes included in the EGB (i.e. 95.6% of the whole population). Then we used data from EGB and FHDH to determine for each individual his/her date of ART initiation (supplemental material, section B). We considered five ART initiation periods: 1985-1996, 1997-2005, 2006-2010, 2011-2016 and ≥2017; the choice of the periods was mainly based on the amount of available data and changes in ART eligibility criteria (supplemental material, section C). Individuals who had not started ART by 2018 were assumed to initiate ART in 2019, as median time between care entry and ART initiation was less than 1 month (FHDH data).

New HIV cases over 2019-2030

To set the annual numbers of newly diagnosed HIV cases over 2019-2030, we projected the mean annual number of newly diagnosed cases over 2015-2018 according to three scenarios: a 30% decrease scenario (scenario 1, reference scenario), i.e. a linear decrease with 30% fewer cases in 2030 compared to 2015-2018, a status quo scenario (scenario 2, pessimistic scenario), with a steady annual number of cases over 2019-2030, and an

epidemic elimination scenario (scenario 3, optimistic scenario), with a linear decrease in the number of cases until zero case in 2030 (supplemental material, section C, figure S1). Scenario 1 was set as the reference as it is a broad extrapolation of the temporal trend in newly diagnosed HIV cases observed over 2012-2018. Age distribution of newly diagnosed cases over 2019-2030 was obtained by extrapolating that of cases newly diagnosed over 2010-2018 (supplemental material, section C, Figure S2). We assumed that newly diagnosed individuals would initiate ART within their diagnosis year.

Mortality rates in 2018 and beyond

To estimate mortality rates for aPLdHIV still alive in 2018, according to ART initiation period, we used data on aPLdHIV enrolled in the FHDH who had at least one follow-up visit between January 1, 2017 and December 31, 2019 and a known date of ART initiation. Person-years were calculated for each sex and ART initiation period separately. They were accumulated from January 1, 2017 or cohort enrolment, until death, loss to follow-up (LTFU, defined as no clinical visit for 18 months, in line with French HIV guidelines [21], supplemental material section D), or December 31, 2019, whichever came first. For LTFU patients, follow-up stopped 6 months after the last visit. Patients with a clinical visit within the 6-month period before December 31, 2019 were censored on December 31, 2019 (supplemental material, section B).

As the number of deaths is underreported in the FHDH [22], it was adjusted using data from the health insurance schemes on beneficiaries living with HIV (supplemental material, section E).

We then used a Poisson model, with age reached in 2018 by aPLdHIV and ART initiation period as covariates, to estimate mortality rates by sex and age group, stratified by ART initiation period.

It was not possible to estimate mortality rate for individuals who started ART from 2017 due to lack of follow-up data after ART initiation. Then for these individuals and for newly diagnosed cases over 2019-2030, mortality rates were assumed, conservatively, to be the same as those for individuals who started ART during 2011-2016. Likewise, due to data scarcity, mortality rate for individuals aged 18-19 years were assumed to be the same as those for individuals aged 20-24 years.

Projection matrix model and projection of age and time since ART initiation

We used a matrix population model to project the size of aPLdHIV until 2030, using estimates for aPLdHIV in 2018, scenarios on newly diagnosed cases over 2019-2030, and estimates of mortality rates (supplemental material, section F). Distributions of time since ART initiation were also projected, together with age distributions, stratified by ART initiation period, using the same matrix model.

Life Expectancy

Using estimated mortality rates and life table method [23], we estimated LE for PLHIV on ART, by sex, age and ART initiation period. LE at a given age is defined as the expected number of years of life remaining for those surviving to that age (supplemental material, section H). LE for the general population at age 20, 40 and 60 years in 2018 were obtained from the Human Mortality Database (https://www.mortality.org).

Ethical statement

The ANRS CO4-FHDH project was approved by CNIL (French data protection authority) on November 27, 1991, Journal Officiel, January 17, 1992. To conform to new regulations, the ANRS CO4-FHDH was then approved by the CEREES (Expertise Committee for

Research, Studies and Evaluations in the field of Health) on July 20, 2018 and as a hospital datawarehouse by CNIL on February 19, 2021. The cohort received authorization to conduct research projects on the datawarehouse by CNIL on March 30, 2021. All ANRS CO4-FHDH participants signed informed consent forms mentioning use of data for research purposes. INSERM has a regulatory permanent access to EGB data, according to Article R1431-13 of the French Public Health Code, as modified by the Decree 2021-848 of June 22, 2021. All data were deidentified, thus informed consent was not necessary.

Results

Demographic characteristics (age, sex, country of birth) of participants to the three data sources are provided in Table 1.

Mortality rates and life expectancies

We used data on 104,042 adults (35% women), enrolled in the FHDH, who initiated ART before 2017 and had at least one follow-up visit between January 1, 2017 and December 31, 2019 to estimate mortality rates (supplemental material, figure S3), as well as LE, which are presented in Table 2 together with LE for the general population. For instance, LE for individuals aged 40 in 2018 who started ART over 2011-2016 was 39.2 years for men and 40.2 years for women. In comparison, it was respectively 40.9 and 46.3 years for the general population. In general, whatever the age group, LE was higher for individuals who initiated ART over 2011-2016, i.e. the most recent period, compared to those who initiated ART earlier. Whatever the period and age group, women had higher LE than men, however this difference tended to decrease over time, from 7 to 10% for women who started ART over 1985-1996 to 3 to 4% for women who started ART over 2011-2016. In addition, for individuals who initiated ART over 2011-2016, i.e. those with the highest LE, the gap in LE compared to the general population was higher for women than for men, whatever the age group, ranging from 3.8 to 6.8 years for women and from 0.4 to 2.4 for men.

Demographic profile of aPLdHIV in 2030

In 2018, an estimated 161,125 adults (33% women) were living with diagnosed HIV. Assuming a 30% decrease in the annual number of newly diagnosed cases over 2019-2030 (scenario 1), and using the population matrix model together with mortality rate

estimates, we estimated that 195,246 adults (33% women) would be living with diagnosed HIV in 2030, i.e. an increase of 21% of the epidemic size. It was 207,972 assuming a steady number of newly diagnosed cases until 2030 (scenario 2) and 167,221 under the epidemic elimination scenario (scenario 3).

For all scenarios, we found that age distribution of aPLdHIV would shift towards older ages in 2030 (Figure 1). For scenario 1, the proportion of individuals aged ≥50 increased between 2018 and 2030, from 61% to 68% for men, and from 44% to 63% for women. The proportion of individuals aged ≥60 doubled, from 24% to 47% for men, and from 17% to 36% for women, like the proportion of individuals aged ≥70, from 8% to 18% for men, 7% to 14% for women. These proportions were slightly lower for scenario 2 (Figure 1, C-D) and slightly higher for scenario 3 (Figure 1, E-F). Whatever the scenario, we estimated that, in 2030, there would be ~83,400 individuals (~28% women) aged ≥60 and ~33,100 individuals aged ≥70 (~27% women); in comparison, in 2018, it was respectively 35,715 (~25% women) and 12,582 (~27% women).

Projected time since ART initiation

Proportions of individuals who started ART more than 20 or 30 years ago will increase over 2018-2030 (Figure 2), especially for older age groups. For brevity, we only present results for scenario 1, results for other scenarios are described in the supplemental material, section I. Proportions of individuals with ≥20 years of ART exposure will increase from 27% to 42% for men, and from 21% to 44% for women. In particular, for individuals aged ≥60, these proportions will increase from 43% to 68% for men, and from 33% to 67% for women. Proportions of individuals with ≥30 years of ART exposure will increase from <1% to 21% for men, and from <1% to 18% for women. In particular, for individuals aged ≥60, these proportions will increase from 1% to 39% for men, and from

<1% to 37% for women. In consequence, median time since ART initiation will increase, especially for older age groups. For individuals aged ≥60, it will increase from 18.4 (IQR 10.4-22.4) to 25.9 years (17.6-33.4) for men, and from 15.2 (7.9-21.4) to 25.8 years (16.8-33.1) for women, while for individuals aged <60, it will only increase from 9.8 (4.8-19.0) to 12.0 years (6.5-17.8) for men, and from 11.0 (5.2-17.7) to 14.5 years (7.5-21.8) for women.

Of note, we estimated that, in 2030, 83,659 individuals (34% women) would have started ART ≥20 years ago and 38,492 individuals (30% women) would have started ART ≥30 years ago - versus respectively 40,667 and 573 in 2018 (Figure 2). Among men who started ART ≥20 years ago, 77% would be aged ≥60, 33% ≥70, 8% ≥80. It was respectively 54%, 21% and 4% for women. Among men who started ART ≥30 years, 89% would be aged ≥60, 40% ≥70, 8% ≥80. It was respectively 75%, 29% and 6% for women.

Discussion

We projected that by 2030, the HIV epidemic in France would be growing, most likely by more than 20%, and ageing, with a doubling of the proportion of individuals aged ≥60 and ≥70. More than two-third of aPLdHIV would be aged ≥50, ~50% aged ≥60, and ~20% aged ≥70. Interestingly, whatever the scenario considered for the epidemic dynamics over 2019-2030, we estimated that ~83,000 individuals will be aged ≥60 in 2030, including ~33,000 aged ≥70. Our results are in line with studies forecasting the age structure of HIV population in other high-income countries [10,11,13,14,16]. It was estimated that the proportion of PLHIV on ART aged ≥50 would be 73% in 2030 in the Netherlands [13] and 54% in the United States (US) [16], and ~75% in 2035 in the US and in Italy [14]. Bretaña et al. [10] performed projections for Australia, considering three scenarios for the future number of newly diagnosed cases over 2018-2027. They highlighted that, whatever the scenario, the age distribution of PLHIV would have its highest peak in the 55-59 age group in 2027, which aligns with our findings of highest peak in the 60-64 age group for men, 50-54 for women.

In addition, our study predicts that in 2030, in France, there will be more than 38,000 individuals who would have started ART more than 30 years ago (i.e. before 2000), with most of them being aged ≥60 (85%, ~33,000), 37% aged ≥70 (~14,000) and 8% aged ≥80 (~3,000). These individuals were thus exposed to the first generation of nucleoside reverse transcriptase inhibitors (AZT, D4T) and protease inhibitors, which have been associated with body morphology changes and cardiovascular diseases [24,25]. In addition, ART duration and time living with diagnosed HIV infection have been associated with increased risk of multimorbidity [7,9], but also with psychological morbidity and lower quality of life [26,27], which should be considered as part as integrated HIV care.

To the best of our knowledge, our study is the first to project time spent since ART initiation for an HIV population. However, previous studies emphasized other important aspects for the projected demographic profile of HIV populations, which we were unable to take into account. First, a study investigating the capacity of current cART to offer long-term HIV control found that median time until exhaustion of treatment options was 45.5 years (IQR 34.0–61.0 years) [28]. Furthermore, some studies showed important heterogeneity in the projections of PLHIV according to race/ethnicity, with older projected population of white PLHIV compared to Black and Hispanic minorities [11,29]. Other studies [13,14] focused on the burden and prevalence of age-related co-morbidities: Smit et al. [13] predicted that in 2030, 84% of PLHIV in the Netherlands will have at least one age-related non-communicable disease, with 28% having three or more, mainly due to cardiovascular disease. This could generate complications due to drug-drug interactions for 40% of patients with the currently recommended first-line HIV regimen. Finally, a study for Australia [15] highlighted that the number of PLHIV in non-metropolitan areas, where PLHIV median age is higher, are expected to increase at a greater rate than that in the major cities.

We also found that LE of adults who started ART from 2011 onwards was either equal or approaching that of the general population: for instance, at age 60 in 2018 it was ~23 and ~24 years for respectively men and women living with diagnosed HIV versus respectively ~23 and ~28 years in the general population. Individuals who started ART in 2005 or earlier, and still alive in 2018, had lower LE, but the difference was only 2 to 4 years. This can have important implications for health-related insurance policies for PLHIV. Marcus et al. [30] reported an overall LE of 56.0 years at age 21 over 2014-2016, close to our estimates for individuals of age 20 in 2018, ranging from 51.4 to 57.4 years. Studies that

311 estimated LE for earlier periods of follow-up found, expectedly, lower LE than ours [3,31].
312 We also found that although women living with diagnosed HIV had higher LE than men,
313 the gap in LE compared to the general population was higher for women than for men,
314 which is in line with previous results [2,3]. Potential explanations for this higher gap
315 include later access to HIV care for women than for men. However, in France, time
316 between infection and care entry was estimated to be shorter for women than for men
317 [32,33]. Another explanation is that among women living with diagnosed HIV in France, a
318 vast majority was born abroad (63%, of which 77% in sub-Saharan African countries,
319 Table 1), while among men a vast majority was born in France (71%). Hence, differences
320 in socio-economic levels and access to health care system between born-abroad and born-
321 in-France individuals, but also stigma, and marginalization, probably play an important
322 role in the observed sex difference in LE gap between PLHIV and the general population
323 [34,35].
324
325 The main novelty of our approach is that it accounts for the impact of ART initiation
326 period on mortality rates to project the demographic profile of HIV population. In
327 addition, our projections for the population size aged ≥60 are robust to assumptions
328 regarding epidemic dynamics over 2019-2020. However, our study has also a number of
329 limitations. First, the projection method and LE estimates rely on the assumption that age-
330 specific mortality rates estimated over 2017-2019 will remain constant over 2019-2030.
331 On one hand, lower mortality beyond 2019 would lead to higher LE estimates and larger
332 HIV population in 2030. On the other hand, higher mortality among older age groups, due
333 to covid-19 during 2020-2021 for instance, could lead to a decrease in LE, total population
334 size and proportions of older PLHIV in 2030. Second, several limitations affect HIV care
335 data. Data on deaths in FHDH were not comprehensive, and were adjusted for under-

reporting, with potential inaccurate adjustments (supplemental material, section G for details). As health insurance schemes do not collect data on HIV exposure group, this factor could not be accounted for. Third, we could not include individuals aged <18 years for population size estimates. According to health insurance and HIV surveillance data, this could represent ~5200 individuals in 2030, comprising ~4000 individuals aged <18 years living with diagnosed HIV in 2018, plus ~100 individuals who could be newly diagnosed each year over 2019-2030. Fourth, our global LE estimates do not capture the comorbidity-free LE. This was estimated to remain much lower for PLHIV than for the general population (9.5 years difference in a US cohort of insured adults [30]). Finally, HIV becoming more prevalent among older adults, transmission risk of higher age groups might increase, if for instance older PLHIV are not adherent to their treatment. This may impact the age distribution of individuals becoming newly infected, with for instance more individuals seroconverting at an older age. As a consequence, interventions explicitly targeting older individuals may be needed, as older individuals were recently shown to be at increased risk of delayed presentation for HIV care [36].

CONCLUSIONS

By 2030, in France, close to 20% of the adult population living with diagnosed HIV will be aged ≥70 (i.e. ~33,000 individuals), of which >40% would have started ART more than 30 years. Ageing of HIV population has important implications for care, generating an increase in comorbidity prevalence and treatment complexity. Our findings can help to measure the burden of ageing, and anticipate health care needs, resource provision and screening guidelines in HIV care, in France but also in other high-income countries. Indeed, our estimates probably provide a broad picture of what is likely to occur in term

360 of HIV population ageing in other settings, with similar historical access to ART and free
361 access to care.

Conflict of interest statement: VS reports lecture fees from ViiV (2019), Gilead (2019, 2020), and Janssen-Cilag (2020), outside the submitted work.

DC reports an HIV grant from Janssen (2019-2020), and personal fees from Gilead (2020) and Pfizer (2022) for lectures, outside the submitted work.

LM, AR, SG and YD declare no conflicts of interest.

Authorship: LM and VS designed the research; LM performed the research; all authors analyzed the data; LM and VS drafted the manuscript; all authors critically revised the manuscript for important intellectual content.

Acknowledgements: LM is grateful for the financial support of the ANRS, in the form of a postdoctoral research fellowship. All authors thank Adam Trickey for his help on the methodology of life expectancy estimation. We are grateful to all ANRS CO4-French Hospital Database on HIV (FHDH) participants and research assistants, without whom this work would not have been possible. Members of FHDH-ANRS CO4 are listed at https://anrs-co4.fhdh.fr/.

Financial support: FHDH is funded by the ANRS-MIE, the Institut National de la Santé et de la Recherche Médicale (INSERM), and the French Ministry of Health.

References

1. Mocroft A, Vella S, Benfield T, Chiesi A, Miller V, Gargalianos P, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. The Lancet. 1998;352(9142):1725–30.

2. Antiretroviral Therapy Cohort Collaboration. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. Lancet HIV. 2017;4(8):e349–56.

3. Samji H, Cescon A, Hogg RS, Modur SP, Althoff KN, Buchacz K, et al. Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. PloS One. 2013;8(12):e81355.

4. Gueler A, Moser A, Calmy A, Günthard HF, Bernasconi E, Furrer H, et al. Life expectancy in HIV-positive persons in Switzerland: matched comparison with general population. AIDS Lond Engl. 2017;31(3):427–36.

5. Joint United Nations Programme on HIV/AIDS. HIV and aging. [Internet]. 2013 [cited 2021 Oct 2]. Available from: http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2013/20131101_JC2563_hiv-and-aging_en.pdf

6. Guaraldi G, Orlando G, Zona S, Menozzi M, Carli F, Garlassi E, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. Clin Infect Dis. 2011;53(11):1120–6.

7. Justice AC, Gordon KS, Romero J, Edelman EJ, Garcia BJ, Jones P, et al. Polypharmacy-associated risk of hospitalisation among people ageing with and without HIV: an observational study. Lancet Healthy Longev. 2021;2(10):e639–50.

8. Rasmussen LD, May MT, Kronborg G, Larsen CS, Pedersen C, Gerstoft J, et al. Time trends for risk of severe age-related diseases in individuals with and without HIV infection

410 in Denmark: a nationwide population-based cohort study. Lancet HIV. 2015;2(7):e288-
411 98.
412 9. Guaraldi G, Zona S, Brothers TD, Carli F, Stentarelli C, Dolci G, et al. Aging with HIV
413 vs. HIV seroconversion at older age: a diverse population with distinct comorbidity
414 profiles. PloS One. 2015;10(4):e0118531.
415 10. Bretaña NA, Gray R, Law M, Guy R. Aging of the HIV population in Australia: a
416 modeling study. J Acquir Immune Defic Syndr. 2018;79(5):e115–6.
417 11. Kasaie P, Stewart C, Humes E, Gerace L, Zhang J, Silverberg MJ, et al. Projecting the
418 age-distribution of men who have sex with men receiving HIV treatment in the United
419 States. Ann Epidemiol. 2021;
420 12. Murray JM, McDonald AM, Law MG. Rapidly ageing HIV epidemic among men who
421 have sex with men in Australia. Sex Health. 2009;6(1):83–6.
422 13. Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, Sighem A van, et al. Future
423 challenges for clinical care of an ageing population infected with HIV: a modelling study.
424 Lancet Infect Dis. 2015;15(7):810–8.
425 14. Smit M, Cassidy R, Cozzi-Lepri A, Quiros-Roldan E, Girardi E, Mammone A, et al.
426 Projections of non-communicable disease and health care costs among HIV-positive
427 persons in Italy and the U.S.A.: A modelling study. PLOS ONE. 2017;12(10):e0186638.
428 15. Jansson J, Wilson DP. Projected demographic profile of people living with HIV in
429 Australia: planning for an older generation. PLoS ONE. 2012;7(8):e38334.
430 16. Althoff KN, Stewart CN, Humes E, Zhang J, Gerace L, Boyd CM, et al. The shifting age
431 distribution of people with HIV using antiretroviral therapy in the United States, 2020 to
432 2030. AIDS Lond Engl [Internet]. 2021 [cited 2022 Jan 17]; Available from:
433 https://doi.org/10.1097/QAD.0000000000003128
434 17. Tuppin P, Rudant J, Constantinou P, Gastaldi-Ménager C, Rachas A, de Roquefeuil

435 L, et al. Value of a national administrative database to guide public decisions: from the
436 système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the
437 système national des données de santé (SNDS) in France. Rev Epidemiol Sante Publique.
438 2017;65 Suppl 4:S149–67.
439 18. Mary-Krause M, Grabar S, Lièvre L, Abgrall S, Billaud E, Boué F, et al. Cohort Profile:
440 French hospital database on HIV (FHDH-ANRS CO4). Int J Epidemiol. 2014 Oct
441 1;43(5):1425–36.
442 19. Lot F, Semaille C, Cazein F, Barin F, Pinget R, Pillonel J, et al. Preliminary results
443 from the new HIV surveillance system in France. Euro Surveill. 2004;9(10):34–7.
444 20. Sécurité Sociale - l'Assurance maladie. Cartographie des pathologies et des
445 dépenses de l'Assurance Maladie [Internet]. Available from: https://assurance-
446 maladie.ameli.fr/etudes-et-donnees/par-theme/pathologies/cartographie-assurance-
447 maladie
448 21. Fournier AL, Yazdanpanah Y, Verdon R, Lariven S, Mackoumbou-Nkouka C, Phung
449 BC, et al. Incidence of and risk factors for medical care interruption in people living with
450 HIV in recent years. PLoS ONE. 2019;14(3):e0213526.
451 22. Lewden C, Jougla E, Alioum A, Pavillon G, Lievre L, Morlat P, et al. Number of deaths
452 among HIV-infected adults in France in 2000, three-source capture-recapture estimation.
453 Epidemiol Infect. 2006;134(6).
454 23. Chiang CL. The life table and its construction. In: Introduction to stochastic
455 processes in Biostatistics. New York: John Wiley and Sons; 1968. p. 198–214.
456 24. Carr A. Cardiovascular risk factors in HIV-infected patients. J Acquir Immune Defic
457 Syndr. 2003;34 Suppl 1:S73-8.
458 25. Mallal SA, John M, Moore CB, James IR, McKinnon EJ. Contribution of nucleoside
459 analogue reverse transcriptase inhibitors to subcutaneous fat wasting in patients with

460 HIV infection. AIDS Lond Engl. 2000;14(10):1309–16.
461 26. McGowan J, Sherr L, Rodger A, Fisher M, Miners A, Anderson J, et al. Age, time living
462 with diagnosed HIV infection, and self-rated health. HIV Med. 2017;18(2):89–103.
463 27. Sabranski M, Erdbeer G, Sonntag I, Stoehr A, Horst HA, Plettenberg A, et al. Physical
464 and mental health in HIV-infected patients with virological success and long-term
465 exposure to antiretroviral therapy. AIDS Care. 2021;33(4):453–61.
466 28. Jansson J, Wilson DP, Carr A, Petoumenos K, Boyd MA. Currently available
467 medications in resource-rich settings may not be sufficient for lifelong treatment of HIV.
468 AIDS Lond Engl. 2013 May 15;27(8):1245–51.
469 29. Hood JE, Golden MR, Hughes JP, Goodreau SM, Siddiqi AEA, Buskin SE, et al.
470 Projected demographic composition of the United States population of people living with
471 diagnosed HIV. AIDS Care. 2017;29(12):1543–50.
472 30. Marcus JL, Leyden WA, Alexeeff SE, Anderson AN, Hechter RC, Hu H, et al.
473 Comparison of overall and comorbidity-free life expectancy between insured adults with
474 and without HIV Infection, 2000-2016. JAMA Netw Open. 2020;3(6):e207954.
475 31. Marcus JL, Chao CR, Leyden WA, Xu L, Quesenberry CP, Klein DB, et al. Narrowing
476 the gap in life expectancy between HIV-infected and HIV-uninfected individuals with
477 access to care. J Acquir Immune Defic Syndr 1999. 2016;73(1):39–46.
478 32. Marty L, Cazein F, Panjo H, Pillonel J, Costagliola D, Supervie V, et al. Revealing
479 geographical and population heterogeneity in HIV incidence, undiagnosed HIV prevalence
480 and time to diagnosis to improve prevention and care: estimates for France. J Int AIDS Soc.
481 2018;21(3):e25100.
482 33. Supervie V, Marty L, Lacombe JM, Dray-Spira R, Costagliola D, FHDH-ANRS CO4
483 study group. Looking beyond the cascade of HIV care to end the AIDS epidemic: estimation
484 of the time interval from HIV infection to viral suppression. J Acquir Immune Defic Syndr.

2016;73(3):348–55.

34. Simard EP, Fransua M, Naishadham D, Jemal A. The influence of sex, race/ethnicity, and educational attainment on Human Immunodeficiency Virus death rates among adults, 1993-2007. Arch Intern Med. 2012;172(20):1591.

35. Collins LF, Sheth AN, Mehta CC, Naggie S, Golub ET, Anastos K, et al. The prevalence and burden of non-AIDS comorbidities among women living with or at risk for Human Immunodeficiency Virus infection in the United States. Clin Infect Dis Off Publ Infect Dis Soc Am. 2020;72(8):1301–11.

36. Justice AC, Goetz MB, Stewart CN, Hogan BC, Humes E, Luz PM, et al. Delayed presentation of HIV among older individuals: a growing problem. Lancet HIV. 2022;9(4):e269–80.

37. Althoff KN, Chandran A, Zhang J, Arevalo WM, Gange SJ, Sterling TR, et al. Life-Expectancy disparities among adults with HIV in the United States and Canada: the impact of a reduction in drug- and alcohol-related deaths using the lives saved simulation model. Am J Epidemiol. 2019 Dec;188(12):2097–109.

501 **Table 1: Sex, age, and country of birth distributions of participants to the three data**
502 **sources**

	EGB – 2014-2018		ANRS CO4-FHDH - 2017 - 2019[1]		HIV surveillance - 2015-2018	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Total	108,871	52,253	67,721	36,321	17,141	7,997
Age N (%)						
18-19	304 (0.3)	102 (0.2)	19 (0.0)	24 (0.1)	286 (1.7)	142 (1.8)
20-24	1,522 (1.4)	1,522 (2.9)	734 (1.1)	535 (1.5)	1,741 (10.2)	633 (7.9)
25-29	3,450 (3.2)	2,638 (5.0)	2,061 (3.0)	1,246 (3.4)	2,523 (14.7)	1,231 (15.4)
30-34	5,682 (5.2)	3,145 (6.0)	3,536 (5.2)	2,587 (7.1)	2,490 (14.5)	1,445 (18.1)
35-39	9,233 (8.5)	6,189 (11.8)	4,816 (7.1)	4,536 (12.5)	2,297 (13.4)	1,384 (17.3)
40-44	9,538 (8.8)	8,726 (16.7)	6,773 (10.0)	5,832 (16.1)	2,014 (11.7)	1,021 (12.8)
45-49	13,190 (12.1)	7,102 (13.6)	9,994 (14.8)	6,108 (16.8)	1,936 (11.3)	681 (8.5)
50-54	21,003 (19.3)	7,407 (14.2)	13,136 (19.4)	5,959 (16.4)	1,554 (9.1)	545 (6.8)
55-59	18,264 (16.8)	6,392 (12.2)	11,504 (17.0)	4,371 (12.0)	1,021 (6.0)	384 (4.8)
60-64	10,451 (9.6)	3,856 (7.4)	6,711 (9.9)	2,382 (6.6)	177 (3.6)	276 (3.4)
65-69	7,102 (6.5)	1,725 (3.3)	4,326 (6.4)	1,326 (3.7)	611 (2.3)	160 (2.0)
70-74	5,682 (5.2)	1,623 (3.1)	2,453 (3.6)	820 (2.3)	387 (1.1)	64 (0.8)
75-79	1,826 (1.7)	913 (1.7)	1,060 (1.6)	363 (1.0)	65 (0.4)	21 (0.3)
80+	1,623 (1.5)	913 (1.7)	598 (0.9)	232 (0.6)	31 (0.2)	10 (0.1)
Country of birth[2] (%)						
France			48,252 (71.3)	13,304 (36.6)	10,678 (61.4)	431 (21.9)
Sub-saharan Africa			9,427 (13.9)	17,704 (48.7)	3,566 (20.5)	5,453 (63.9)

Europe		2,969 (4.4)	933 (2.6)	870 (5.0)	247 (2.9)
America / Haïti		2,778 (4.1)	2,143 (5.9)	1,232 (7.1)	639 (7.5)
Other (North Africa / Asia / Oceania)		4,295 (6.3)	2,237 (6.2)	1,034 (6.01,865)	324 (3.8)

(1) Individuals enrolled in the FHDH, who initiated ART before 2017 and had at least one follow-up visit between January 1, 2017 and December 31, 2019.

(2) No data on country of birth are available in the EGB.

Table 2. Remaining life expectancy (in years) according to the age reached in 2018, for the general population* and for people living with HIV (PLHIV) men and women who initiated ART, by period of ART initiation. Mean remaining life expectancy (and 95% confidence interval) for PLVHIV individuals were estimated from mortality event among PLHIV individuals enrolled in the French Hospital Database on HIV (ANRS CO4-FHDH) who had at least one follow-up clinical visit between January 1, 2017 and December 31, 2019. *Values for the general population were obtained from the Human Mortality Database (https://www.mortality.org)

Period of ART initiation	Age reached in 2018					
	20 years		40 years		60 years	
	Men	Women	Men	Women	Men	Women
1985 – 1996	x	x	35.0 (33.7 – 36.3)	37.4 (35.8 – 39.0)	19.7 (19.1 – 20.3)	21.6 (20.4 – 22.8)
1997 – 2005	54.4 (52.1 – 56.7)	56.9 (54.9 – 58.9)	36.2 (35.5 – 36.9)	38.2 (37.3 – 39.1)	20.5 (20.0 – 21.0)	22.1 (21.2 – 23.0)
2006 – 2010	56.8 (53.9 – 59.7)	60.0 (57.7 – 62.3)	38.4 (37.4 – 39.4)	41.0 (39.6 – 42.4)	22.5 (21.5 – 23.5)	24.4 (23.1 – 25.7)
2011 - 2016	57.7 (56.5 – 58.9)	59.1 (57.3 – 60.9)	39.2 (38.1 – 40.3)	40.2 (38.6 – 41.8)	22.9 (21.8 – 24.0)	23.9 (22.3 – 25.5)
General population*	60.1	65.9	40.9	46.3	23.3	27.7

Figure 1. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, according to different scenarios. Numbers and age distributions for men (A) and for women (B), in 2018 (in red) and in 2030 (in turquoise) for scenario 1 (i.e. 30% decrease in newly diagnosed HIV cases between 2018 and 2030). Comparison of the numbers and age distributions of adults living with diagnosed HIV in 2030 for scenario 1 (in turquoise) and scenario 2 (i.e. status quo situation with a steady annual number of new HIV cases over 2019-2030, black diagonal stripes) for men (C) and for women (D), and for scenario 1 and scenario 3 (i.e. epidemic elimination with zero new HIV cases in 2030, black diagonal stripes) for men (E) and for women (F). Detailed assumptions made for the number and age of newly-diagnosed HIV cases in 2019-2030 can be found the supplemental material, section C.

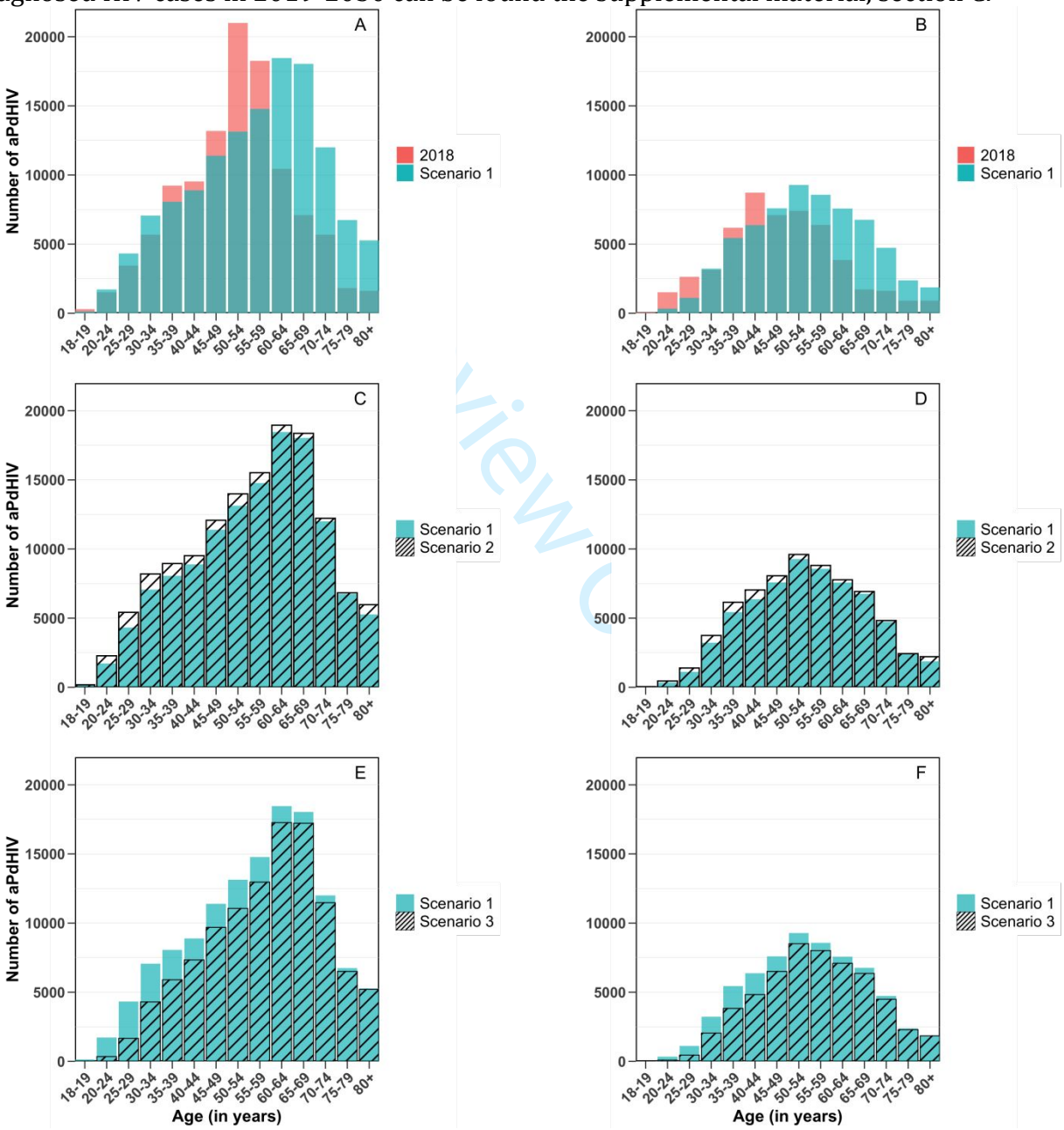
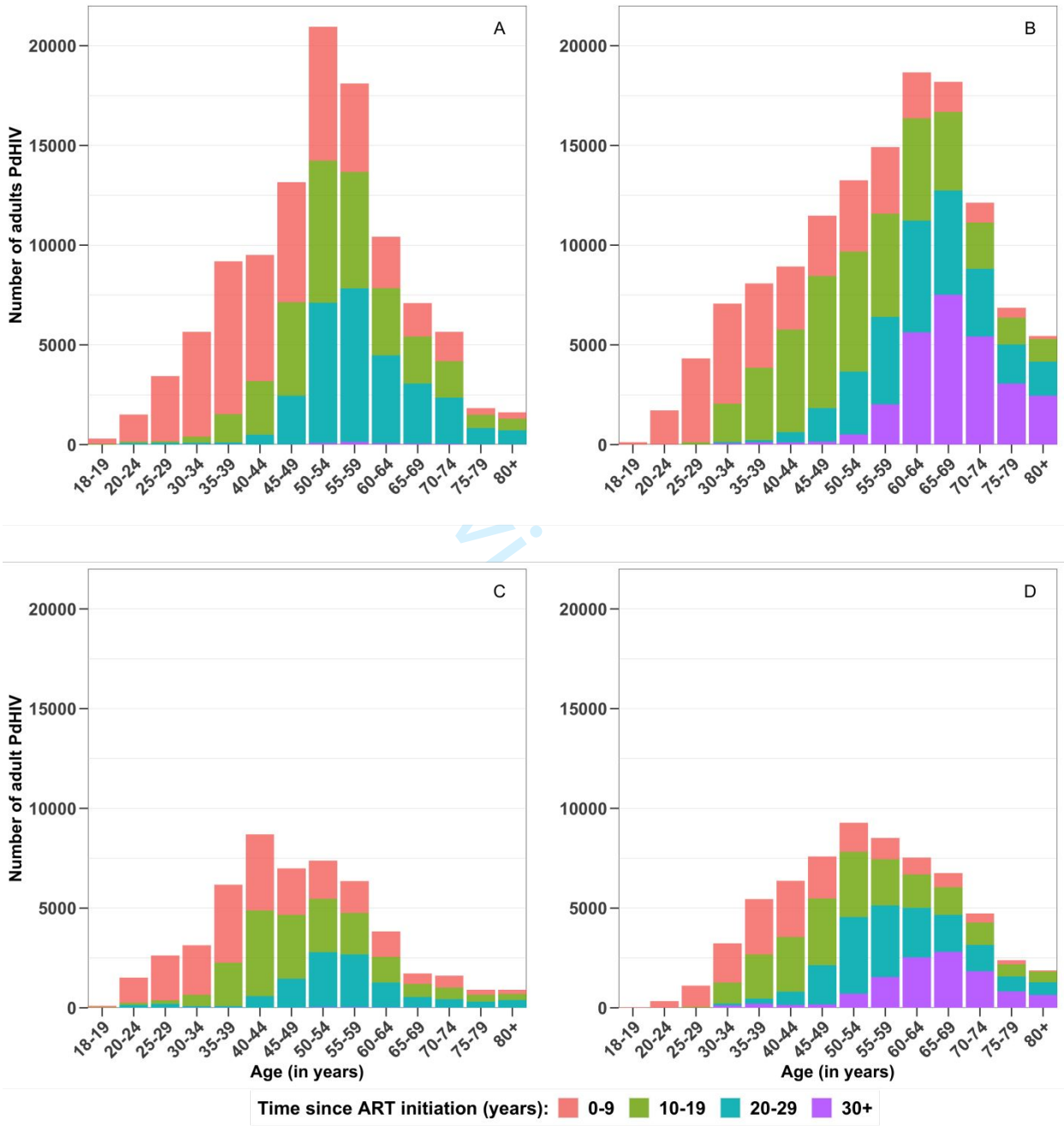


Figure 2. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D) for scenario 1 (i.e. 30% decrease in newly diagnosed HIV cases between 2018 and 2030). Results for other scenarios can be found in the supplemental material, section E and figures S4 and S5.



Supplementary Material

Projection of age of individuals living with HIV and time since ART initiation in 2030: estimates for France

Lise Marty[1], Yakhara Diawara[1], Antoine Rachas[2], Sophie Grabar[3], Dominique Costagliola[4], Virginie Supervie[1]

[1] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, F75012, Paris, France

[2] Direction de la Stratégie, des Etudes et des Statistiques, CNAM, F-75000 Paris, France

[3] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, AP-HP, Hôpital St Antoine, F75012, Paris, France

[4] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, F75013, Paris, France

A. Identification of individuals living with diagnosed HIV in 2018 from the EGB

Adapting a method initially developed by the general health scheme fund to study several chronic diseases (including HIV) [1], in terms of numbers, prevalence rates, etc., we used the following criteria to estimate, from a representative sample of the national health data system (Échantillon Généraliste des Bénéficiaires, EGB), the number of individuals living with diagnosed HIV in 2018:

- Persons with long-term illness status (ALD, qualifying for 100% reimbursement of medical expenses), with ICD 10 code for HIV, in any year over 2014-2018, and still alive in 2018;
- and/or persons hospitalized in medicine, surgery, obstetrics, with HIV as the main or associated diagnosis (i.e. with ICD 10 code for HIV) at admission, in any year over 2014-2018, and still alive in 2018;
- and/or persons hospitalized in medicine, surgery, obstetrics with HIV infection as complication or associated morbidity (main, related, or associated diagnosis from the hospital discharge database) in any year over 2014-2018, and still alive in 2018;
- and/or persons with at least three dispensations of HIV-specific treatment at different point in time within one year, in any year over 2014-2018, and still alive in 2018 (excluding Truvada dual therapy and Hepatitis B specific treatments);
- and/or persons with at least one HIV-specific medical biology exam (including antiretroviral genotypic resistance tests, antiretroviral plasma concentration measurement, viral load quantification) in any year over 2014-2018;

We applied this set of criteria over the year 2014-2018, in order to identify all individuals living with diagnosed HIV, whether engaged in care or not in 2018. Indeed, applying this set of criteria only for the year 2018 would have only allowed identifying individuals living with diagnosed HIV if they were engaged in HIV care and/or have been hospitalized in 2018, whereas individuals who had interrupted their follow-up and did not have any hospitalizations in 2018 would have remained unidentified.

Age distribution was obtained by considering the age reached by the beneficiaries in 2018.

B. Extracting the date of ART initiation of individuals living with diagnosed HIV in 2018

We used data from the EGB and the FHDH cohort to determine for each individual living with diagnosed HIV in 2018 his/her date of ART initiation. These two data sources complement each other as follows. On one hand, information on the date of ART initiation in EGB is not complete (and less complete than in the FHDH cohort), since EGB was created in 2005, with retrospective care consumption data from 2004 only, while FHDH data are available since 1985. On the other hand, as with any patient cohort, FHDH collects information on individuals who are engaged in care but it loses track of patients who interrupt HIV care, whereas EGB includes all patients, whether they are engaged in care or not.

Therefore, individuals living with diagnosed HIV in 2018 were split into two groups, according to whether they were engaged in care in 2018 or not. For individuals who were engaged in care in 2018, we extracted the date of ART initiation from FHDH, and defined five periods of ART initiation (1985-1996, 1997-2005, 2006-2010, 2011-2016 and ≥2017). For individuals who were not engaged in care in 2018, we extracted the date of ART initiation from EGB, and defined only four periods of ART initiation, because of shorter data collection period (<2006, 2006-2010, 2011-2016 and ≥2017). For both groups, we assumed that individuals who had not initiated ART in 2018 would do so in 2019.

To identify the two groups (engaged in care in 2018 or not), we proceeded as follows. In a first step, we applied the set of criteria described in section A over the years 2014-2018, and as a second step, we applied the same set of criteria but only for the year 2018. Individuals identified with the first step correspond to the whole population of individuals living with diagnosed HIV in 2018 (engaged in care in 2018 or not) while individuals identified with the second step only correspond to those engaged in care in 2018. Then, from individuals identified in the first step but not in the second step, we determined those who were not engaged in care in 2018.

The choice of the periods was based on the amount of data available and changes in ART eligibility criteria. Treat-all strategy was adopted at the end of 2013 in France, but due to lack of follow-up data we did not consider a group of patients who initiated ART over 2014-2016. The two other milestones in terms of treatment guidelines that we considered are the following ones:

- 1997: advent of cART;
- 2010: change in CD4 count eligibility from 350 to 500;

Since the period from 1997 to 2010 was large, and overall mortality was steadily decreasing throughout this period, we split it into two, 1997-2005 and 2006-2010, in order to provide more precise mortality estimates, as the amount of data allowed it. All together we thus consider four periods: before 1997, 1997-2005 and 2006-2010 and 2011-2016. Beyond 2016, we assumed that mortality rates would be the same as the mortality rates for individuals who had started ART during 2011-2016.

C. Number and age of newly diagnosed HIV cases over 2019-2030

The projected mean annual numbers of new HIV cases diagnosed over 2019-2030 according to the three scenarios are presented in Figure S1: a 30% decrease in the annual number of cases by 2030 (scenario 1), a status quo scenario, with a steady annual number of cases over 2019-2030 (scenario 2), and an epidemic elimination scenario (scenario 3), with a linear decrease in the number of cases up to zero case in 2030.

To set age distributions of cases over 2019-2030, we first performed, for each sex, a linear regression of the annual numbers of newly diagnosed HIV cases over 2010-2018 against time, with age as a categorical covariable. Estimated regression coefficients were then used to project, by sex, age distributions of new cases from 2019 to 2030. Using these age distributions (figure S2) and the scenario-dependent annual numbers of new cases over 2019-2030 (figure S1), we then obtained the annual numbers of new HIV diagnoses by age group over 2019-2030.

D. Definition of patients lost to follow-up based on French HIV guidelines

We chose an 18-month period to define patients lost to follow-up because French HIV guidelines have moved towards fewer laboratory tests and medical visits to health care centers per year [2]. Specifically, the 2013 French guidelines recommend administration of ART to each PLHIV whatever the CD4 count; a once-a-year visit to an infectious disease specialist for patients on ART whose HIV infection has been under control (undetectable viral load and CD4 T cell count >500 cells/mm3) for one year without comorbidity; and a clinical and immuno-virological check-up at least every 6 months, which can be performed by the primary care physician.

E. Correction of the reported number of death cases

The numbers of deaths reported in the FHDH over 2017-2019 (Table S1) were adjusted for under-reporting, using data from the health insurance schemes on beneficiaries living with diagnosed HIV (BLHIV); personal communication from A. Rachas. To do so, we first estimated the coverage of FHDH, i.e. the proportion of all individuals living with diagnosed HIV in France who are enrolled in FHDH. Second, we estimated the total number of death cases among individuals living with diagnosed HIV in France. We then used these two estimates to obtain the correction factor to adjust for under-reporting of deaths in FHDH.

The coverage of FHDH for each age group a and year t, noted $\rho_{a,t}$, was estimated using the ratio of the number of individuals living with diagnosed HIV enrolled in FHDH database over the total number of BLHIV from all health insurance schemes, for each year and age group (Table S1):

$$\rho_{a,t} = \frac{N^{\mathrm{F}}_{a,t}}{N_{a,t}} \quad (1)$$

where $N^{\mathrm{F}}_{a,t}$ is the number of individuals living with diagnosed HIV with at least one medical visit registered in the FHDH and $N_{a,t}$ the total number of BLHIV from all insurance schemes (Table S1);

The total number of death cases among individuals living with diagnosed HIV in France for each year t and age group a, noted $D_{a,t}$, had to be estimated using data on deaths among BLHIV from the main health insurance scheme, also called the general Social Security scheme, because data on deaths are not complete for the other insurance schemes. Specifically, we extrapolated the number of deaths reported among BLHIV of the main health insurance scheme to all insurance schemes using the ratio of the number of BLHIV of the general Social Security scheme over the total number of BLHIV from all insurance schemes, for each year and age group:

$$D_{a,t} = D'_{a,t} \frac{N'_{a,t}}{N_{a,t}} \quad (2)$$

with $D'_{a,t}$ the number of deaths among BLHIV of the general Social Security scheme, $N'_{a,t}$ the number of BLHIV of the general Social Security scheme and $N_{a,t}$, as aforementioned, the total number of BLHIV from all insurance schemes (Table S2).

$\rho_{a,t}$, and $D_{a,t}$, obtained from equations (1) and (2), were then used to estimate a factor to correct unreported deaths for each age group a and year t, noted $\delta_{a,t}$, using the following formula :

$$\delta_{a,t} = \rho_{a,t} \frac{D_{a,t}}{D^{\mathrm{F}}_{a,t}} \quad (3)$$

where $D^{\mathrm{F}}_{a,t}$ is the number of deaths reported in FHDH database for each age group a and year t (Table S1).

Each death case in FHDH database were then multiplied by the factor $\delta_{a,t}$, obtained from equation (3), to adjust for under-reporting of deaths.

F. Age-structured projection matrix model

The projection method was adapted from a Leslie matrix model for age-structured population. Each year, the population was stratified by age and period of ART initiation. We divided age into 63 age groups, i.e. one group for each age over ages 18-79 years and one group for the

last open-ended age group, ≥80 years, and the period of ART initiation into five periods (i.e. 1985-1996, 1997-2005, 2006-2010, 2011-2016 and ≥2017).

From 2019 to 2030, the number of individuals living with diagnosed HIV in age group a in year t, $N_{\mathrm{a,t}}$, corresponds to (i) the sum over all ART initiation periods of individuals of age $a-1$ living with diagnosed HIV in year $t-1$ with ART initiation period k who aged one year and thus survived up to year t, plus (ii) the number of new HIV cases of age a diagnosed in year t, who initiated ART within the same year of their diagnosis, $D_{a,t,k}$:

$$N_{\mathrm{a,t}} = \sum_{k=1}^{5} N_{\mathrm{a}-1,\mathrm{t}-1,\mathrm{k}} s_{a-1,k} + D_{a,t,k}, \quad (4)$$

with $s_{a-1,k}$ the probability of surviving from age $a-1$ to age a, for individuals who started ART in time period k, which is defined as:

$$s_{a-1,k} = e^{-m_{a-1,k}},$$

where $m_{a-1,k}$ is the estimated mortality rate of individuals of age $a-1$ who initiated treatment during the time period k.

Equation (4) was thus iterated 12 times (from 2019 to 2030) to obtain the number and age distribution of aPLdHIV in 2030.

Then the total count of individuals living with diagnosed HIV in each year t was obtained by summing the count of individuals living with diagnosed HIV over all age groups a and over all ART initiation periods k.

G. Sources of uncertainty in the data and method

Calculation steps presented in this study involve different data sources or estimates, and each of them involves a certain degree of uncertainty.

First, EGB is a sample, covering 1/97th of the insured persons in France. However, it is a representative sample, which allows us to make extrapolations to obtain the total number of people identified as HIV-positive.

Second, number of deaths had to be adjusted for under-reporting: overall, we estimated that under-reporting of death events was 37%. To adjust the number of deaths, we used data on death events among people identified as HIV-positive who were insured in the general health insurance scheme, as data on deaths are only exhaustive for this scheme. Data from the general health insurance scheme are the most exhaustive data source in France, as individuals are tracked until deaths or migration, which is a strength. Nevertheless, two sources of uncertainty can arise in this process. First, the algorithm used to identify HIV-positive persons is probably not perfect, although it is the reference to estimate HIV prevalence in France. Second, we had to extrapolate the number of deaths observed among individuals insured with the general health insurance scheme to obtain to the number of deaths among all people identified as HIV-positive, not only those insured with the general health insurance scheme. The general health insurance scheme includes 84% of people identified as HIV-positive in all health insurance schemes, the uncertainty in this extrapolation is therefore quite low.

Third, uncertainty lies in the number of newly diagnosed HIV cases that will be observed in the future. This source of uncertainty has been taken into account by considering several scenarios (see aforementioned answer).

H. Life Expectancy

Using estimated mortality rates and life table method [3], we estimated life expectancy for PLHIV on ART in France, by sex, age and ART initiation period. For the oldest open-ended age group (≥80), data on follow-up care and deaths were scarce. Therefore, following other studies [4,5], we obtained an estimate of the mortality rate for individual aged ≥80 by multiplying the French general population mortality rate for individuals aged ≥80 by an average standardized mortality ratio (SMR), representing the ratio between PLHIV mortality rate and general population mortality rate. The average SMR was obtained by first calculating SMRs for age groups 70-74 and 75-79 and then by averaging these two values.

I. Projected time since ART initiation : results from scenarios 2 and 3

a. Scenario 2 : status quo situation with a steady annual number of new HIV cases over 2019-2030

We found that the proportions of individuals who started ART more than 20 and 30 years ago will increase over 2018-2030 (Figure S4), especially for older age groups. The overall proportions of individuals who started ART ≥20 years (respectively, ≥30 years) will increase from 27% to 39% (respectively, from <1% to 19%) for men, and from 21% to 42% (respectively, from <1% to 17%) for women. In particular, among those aged ≥60, these proportions will increase from 43% to 67 % (respectively, from 1% to 38 %) for men, and from 33% to 66% (respectively, from <1% to 36%) for women. In consequence, median time since ART initiation will increase, especially for older age groups. In particular, for individuals aged ≥60, it will increase from 18.4 (interquartile range (IQR) 10.4 – 22.4) to 25.5 years (IQR 17.0 – 33.3) for men, and from 15.2 (IQR 7.9-21.4) to 25.3 years (IQR 15.8 – 32.9) for women, while for those aged <60, it will only increase from 9.8 (IQR 4.8 – 19.0) to 10.5 years (IQR 5.5 – 17.3) for men, and from 11.0 (IQR 5.2-17.7) to 13.3 years (IQR 6.5 – 21.3) for women.

Of note, we estimated that, in 2030, 83,659 individuals (34% women) would have started ART ≥20 years ago, i.e. before 2010, including 38,492 individuals (30% women) that would have started ART ≥30 years ago - versus respectively 40,667 and 573 in 2018 – with the vast majority of them being aged ≥60 (Figure 2). For those who would have started ART ≥20 years ago, for men, 77% would be aged ≥60, 33% ≥70, 8% ≥80, and for women, 54% would be ≥60, 21% ≥70, 4% ≥80, while for those who would have started ART ≥30 years ago, for men, 89% would be aged ≥60, 40% ≥70, 8% ≥80, and for women, 75% being aged ≥60, 29% ≥70, 6% ≥80.

b. Scenario 3 : epidemic elimination with zero new HIV cases in 2030

We found that proportions of individuals who started ART more than 20 and 30 years ago will increase over 2018-2030 (Figure S5), especially for older age groups. The overall proportions of individuals who started ART more than 20 years (respectively, ≥30 years) will increase from

27% to 49% (respectively, from <1% to 24%) for men, and from 21% to 51% (respectively, from <1% to 20%) for women. In particular, among those aged ≥60, these proportions will increase from 43% to 72% (respectively, from 1% to 41%) for men, and from 33% to 71% (respectively, from <1% to 39%) for women. In consequence, median time since ART initiation will increase, especially for older age groups. In particular, for individuals aged ≥60, it will increase from 18.4 (interquartile range (IQR) 10.4 – 22.4) to 26.8 years (IQR 18.9 – 33.5) for men, and from 15.2 (IQR 7.9-21.4) to 26.6 years (IQR 18.4 – 33.3) for women, while for those aged <60, it will only increase from 9.8 (IQR 4.8 – 19.0) to 14.8 years (IQR 10.5 – 19.6) for men, and from 11.0 (IQR 5.2-17.7) to 16.9 years (IQR 11.5 – 23.5) for women.

Of note, we estimated that, in 2030, 83,659 individuals (34% women) would have started ART ≥20 years ago, i.e. before 2010, including 38,492 individuals (30% women) that would have started ART ≥30 years ago - versus respectively 40,667 and 573 in 2018 – with the vast majority of them being aged ≥60 (Figure 2). For those who would have started ART ≥20 years ago, for men, 77% would be aged ≥60, 33% ≥70, 8% ≥80, and for women, 54% would be ≥60, 21% ≥70, 4% ≥80, while for those who would have started ART ≥30 years ago, for men, 89% would be aged ≥60, 40% ≥70, 8% ≥80, and for women, 75% being aged ≥60, 29% ≥70, 6% ≥80.

References

1. Sécurité Sociale - l'Assurance maladie. Cartographie des pathologies et des dépenses de l'Assurance Maladie [Internet]. Available from: https://assurance-maladie.ameli.fr/etudes-et-donnees/par-theme/pathologies/cartographie-assurance-maladie

2. Fournier AL, Yazdanpanah Y, Verdon R, Lariven S, Mackoumbou-Nkouka C, Phung BC, et al. Incidence of and risk factors for medical care interruption in people living with HIV in recent years. PLoS One. 2019;14(3):e0213526.

3. Chiang CL. The life table and its construction. In: Introduction to stochastic processes in Biostatistics. New York: John Wiley and Sons; 1968. p. 198–214.

4. Antiretroviral Therapy Cohort Collaboration. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. Lancet. 2008;372:293–9.

5. Antiretroviral Therapy Cohort Collaboration. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. Lancet HIV. 2017;4(8):e349–56.

Table S1. Data from the French National Health Data System and the FHDH for the years 2017, 2018 and 2019 on the number of individuals living with diagnosed HIV and deaths among them, stratified by age group.

Year (t)	Age group* (a)	Number of individuals living with HIV with at least one medical visit registered in the FHDH, ($N^{F}_{a,t}$)	Number of BLHIV from all health insurance schemes, ($N_{a,t}$)	Coverage of the FHDH, ($\rho_{a,t}$)**	Number of deaths reported in the FHDH, ($D^{F}_{a,t}$)
2017	18-34	13250	17087	77.5%	12
2017	35-54	57521	78277	73.5%	282
2017	55-64	22928	32422	70.7%	232
2017	65-74	8152	11803	69.1%	124
2017	≥75	1898	3307	57.4%	72
2018	18-34	13410	17090	78.5%	26
2018	35-54	57563	76502	75.2%	254
2018	55-64	25570	35611	71.8%	249
2018	65-74	9158	12857	71.2%	121
2018	≥75	2203	3713	59.3%	88
2019	18-34	11854	17750	66.8%	15
2019	35-54	54362	74871	72.6%	205
2019	55-64	27310	39022	70.0%	233
2019	65-74	9747	14014	69.6%	144
2019	≥75	2494	4186	59.6%	84

BLHIV: beneficiaries living with diagnosed HIV ;
*five age groups (18-34, 35-54, 55-64, 65-74, 75+) to comply with available statistics from the French National Health Data System.
** estimated as $\rho_{a,t} = \frac{N^{F}_{a,t}}{N_{a,t}}$.

Table S2. Data from the French National Health Data System for the years 2017, 2018 and 2019 on the number of beneficiaries living with diagnosed HIV (BLHIV) and deaths among them, stratified by age group.

Year (t)	Age group* (a)	Number of BLHIV from all health insurance schemes**, ($N_{a,t}$)	Number of BLHIV of the general Social Security scheme, ($N'_{a,t}$)	Number of deaths among BLHIV of the general Social Security scheme, ($D'_{a,t}$)	Estimated number of deaths among BLHIV from all health insurance schemes***, ($D_{a,t}$)
2017	18-34	17087	14087	18	22
2017	35-54	78277	66482	451	531
2017	55-64	32422	26392	443	544
2017	65-74	11803	9388	202	254
2017	≥75	3307	2599	169	215
2018	18-34	17090	13871	22	27
2018	35-54	76502	65083	440	517
2018	55-64	35611	29446	451	545
2018	65-74	12857	10460	220	270
2018	≥75	3713	2968	169	211
2019	18-34	17750	15038	26	31
2019	35-54	74871	64752	336	389
2019	55-64	39022	33138	472	556
2019	65-74	14014	11770	289	344
2019	≥75	4186	3447	198	240

*five age groups (18-34, 35-54, 55-64, 65-74, 75+) to comply with available statistics from the French National Health Data System.

** includes data from the general Social Security scheme as well as all other schemes;

*** estimated as $D_{a,t} = D'_{a,t}\frac{N'_{a,t}}{N_{a,t}}$

Figure S1. Annual number of newly diagnosed HIV cases over 2019-2030 according to the three scenarios, for men (A) and for women (B). In green: linear decrease with 30% fewer cases in 2030 compared to 2015-2018 (scenario 1). In blue: status quo situation with a steady annual number of new HIV cases over 2019-2030 (scenario 2). In red: epidemic elimination with zero new HIV cases in 2030 (scenario 3).

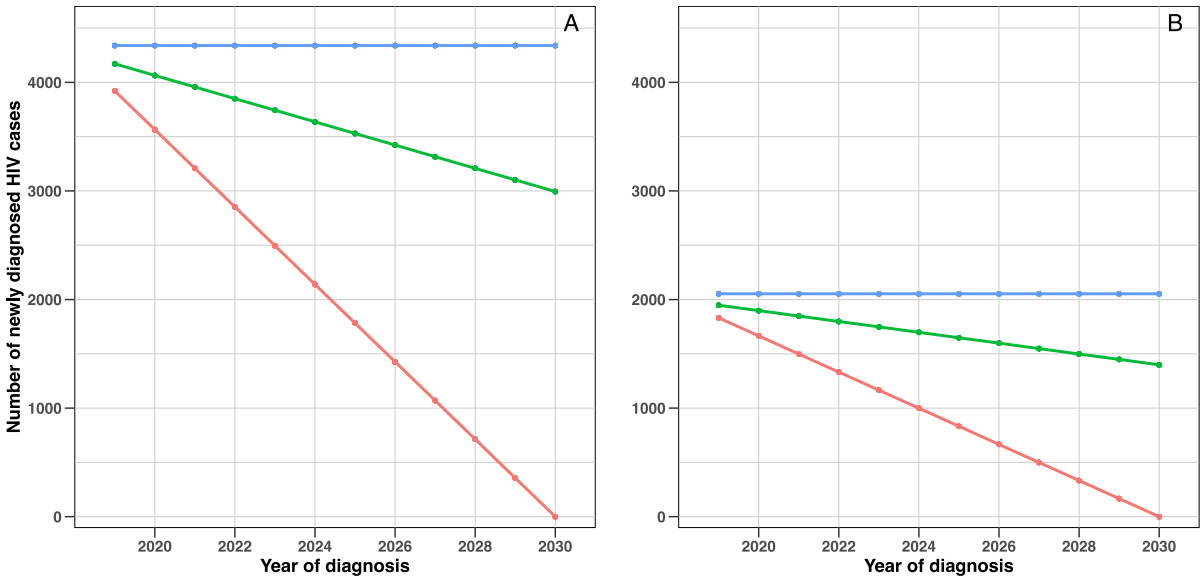


Figure S2. Projected adult newly diagnosed HIV cases by age group at diagnosis over 2019-2030 for men (A) and for women (B).

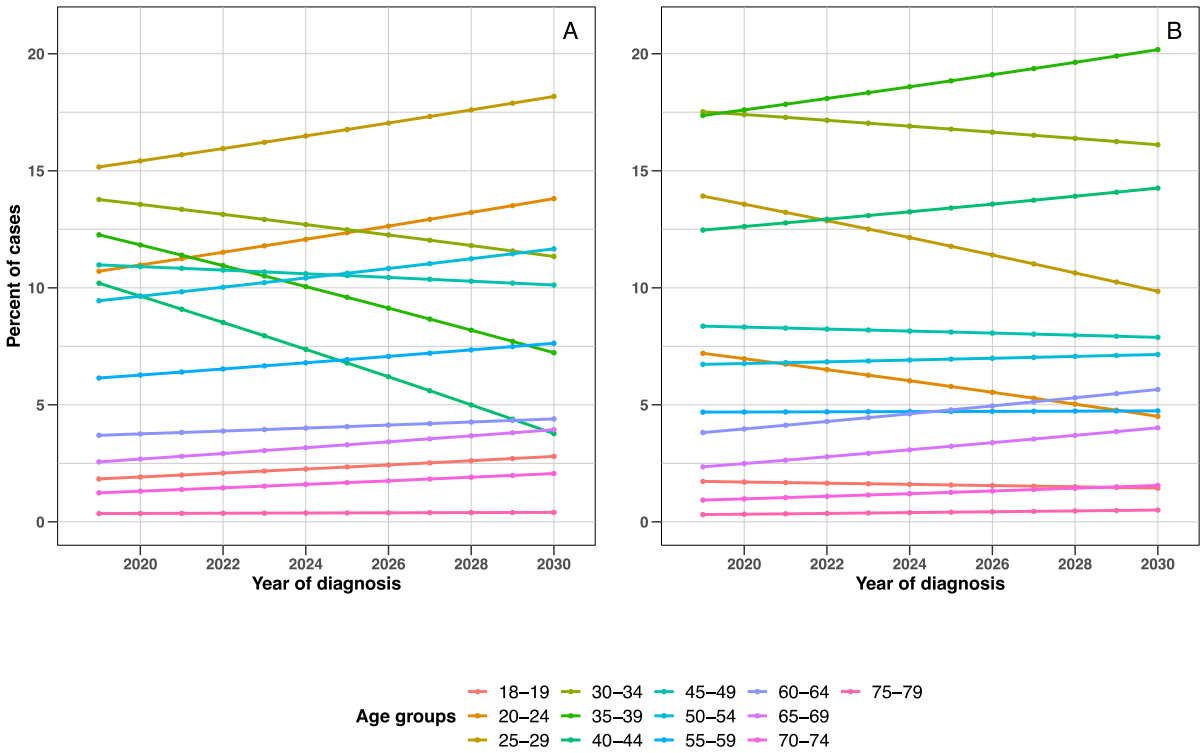


Figure S3. Mortality rates of adults aged ≥20 years living with diagnosed HIV in 2018, according to age and ART initiation period, for men (A) and women (B).

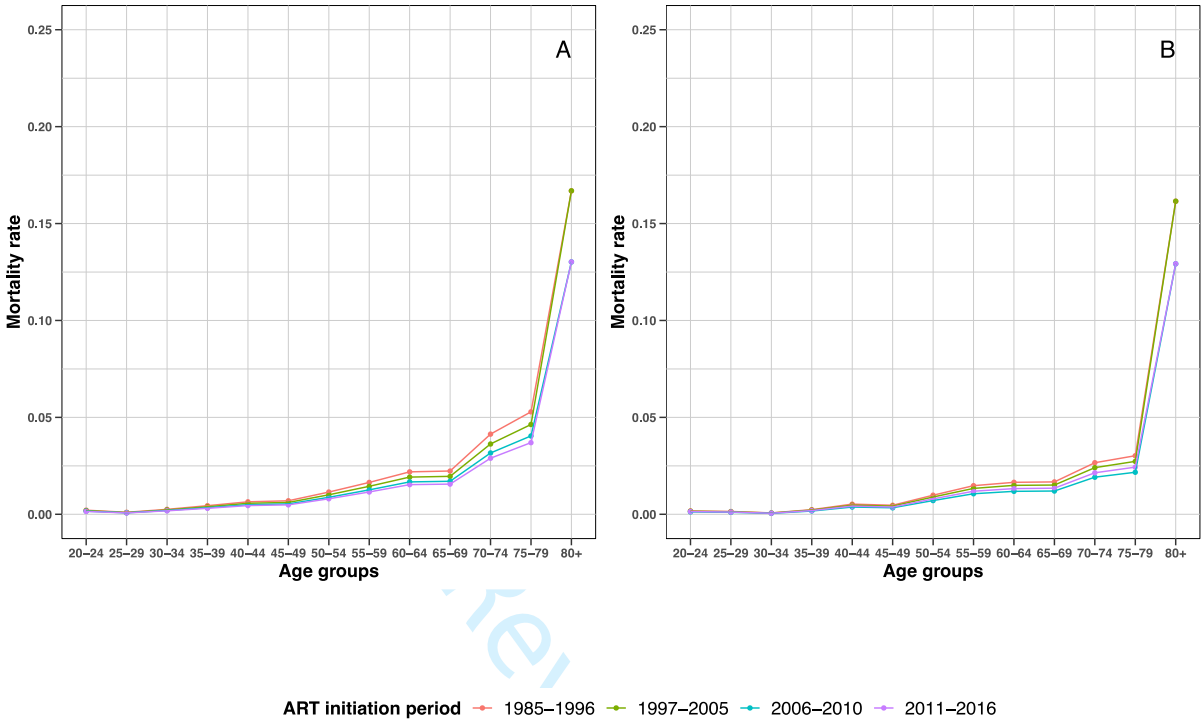


Figure S4. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D) under scenario 2 (i.e. status quo situation with a steady annual number of new HIV cases over 2019-2030).

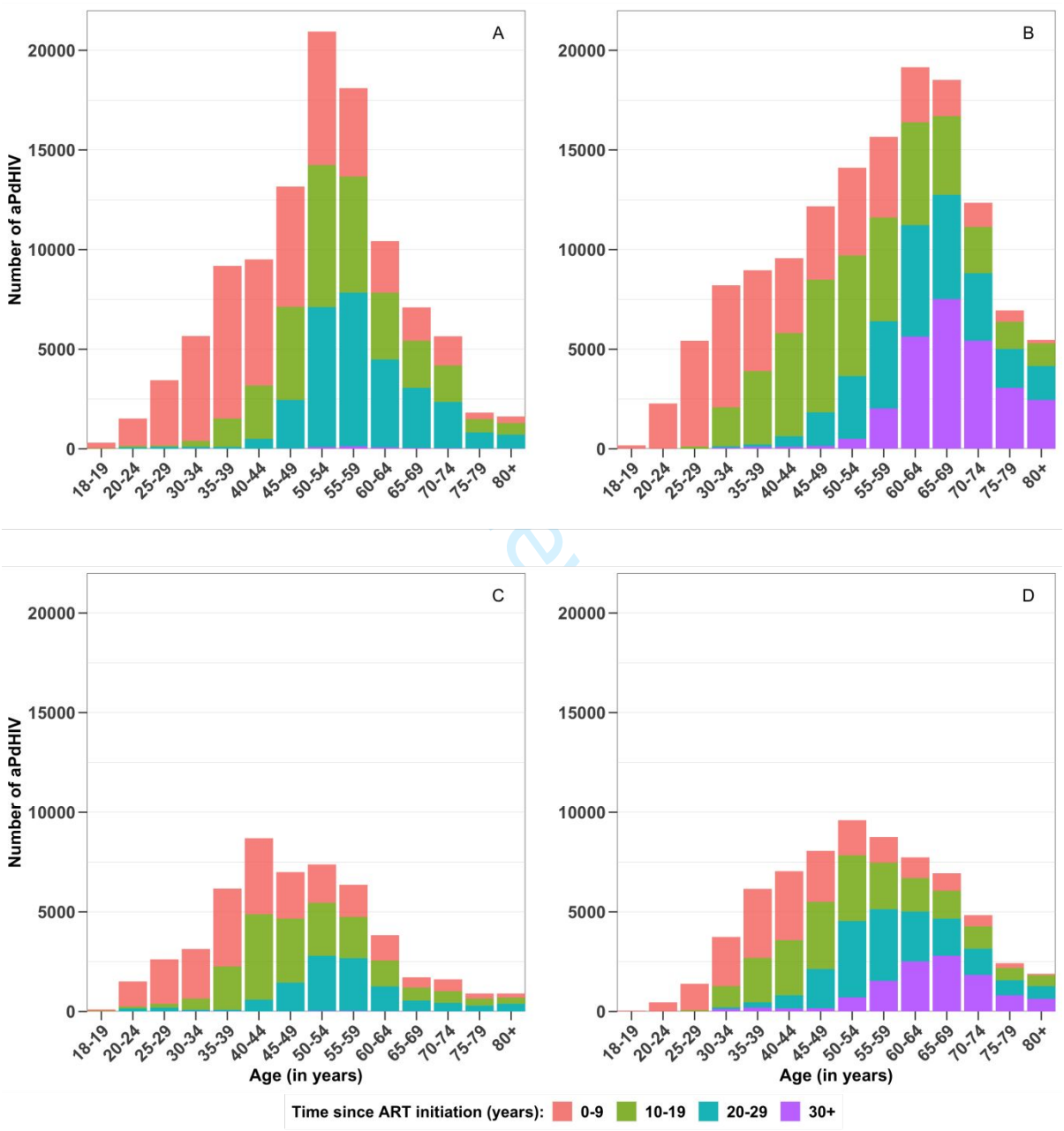
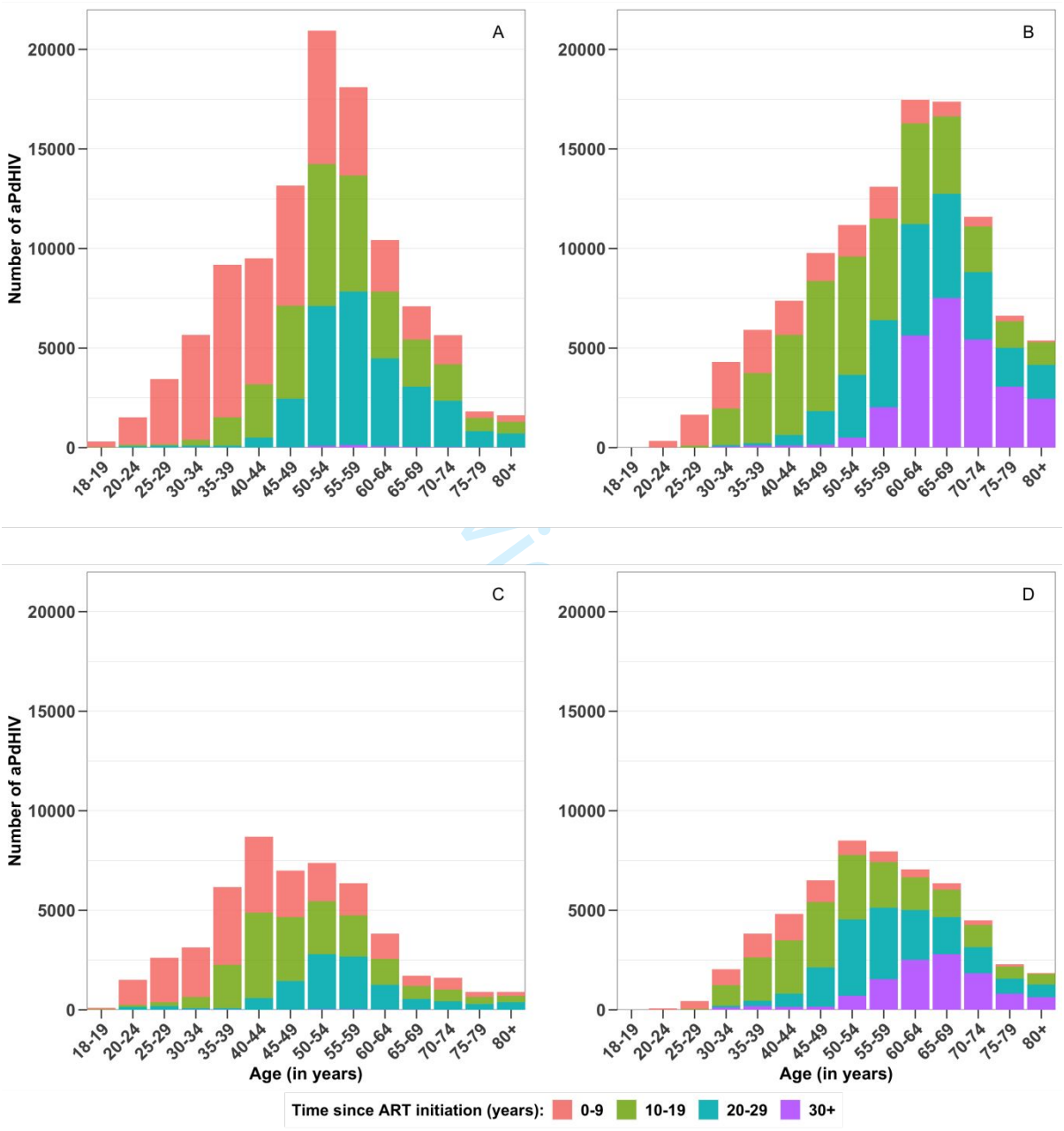
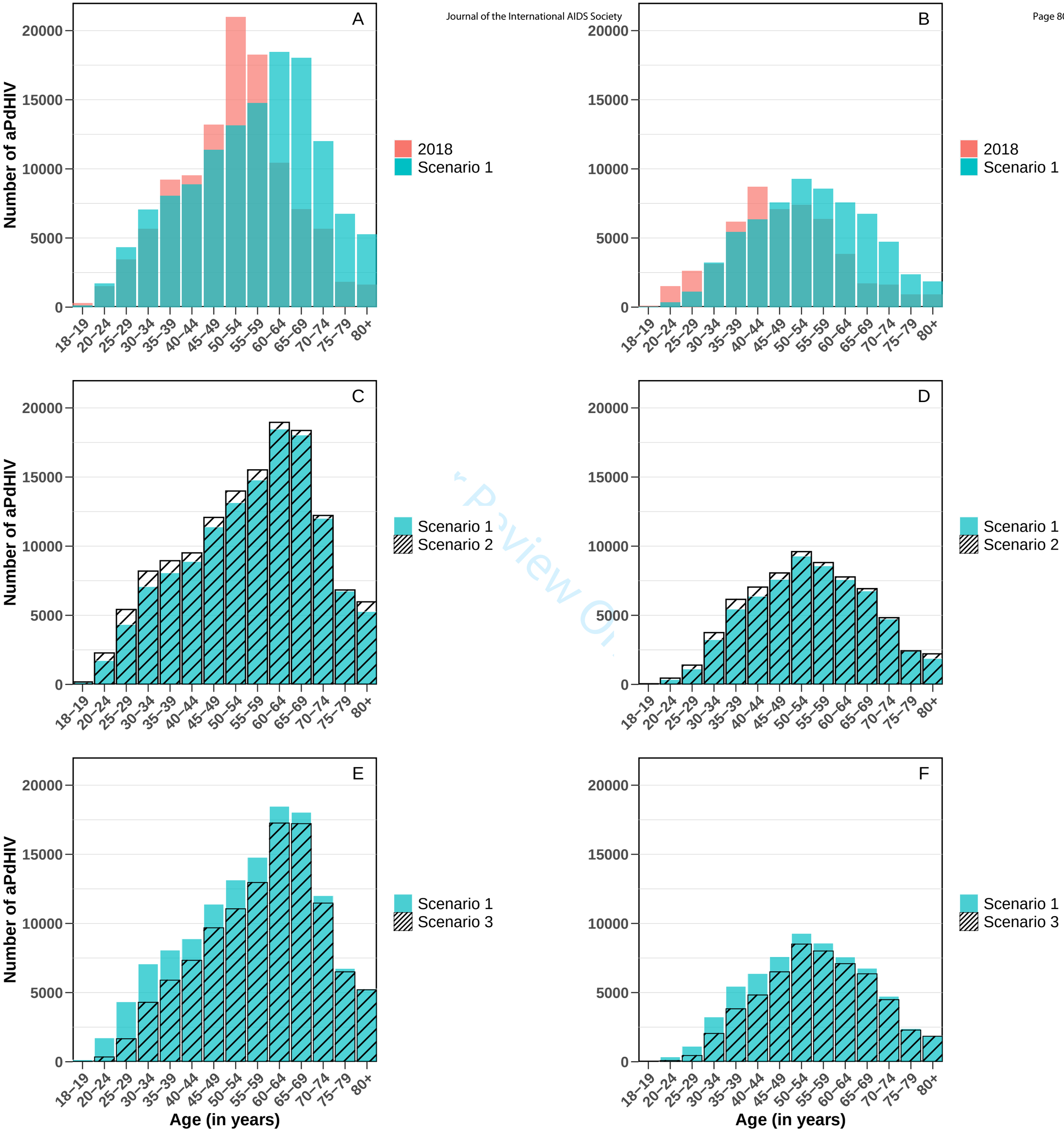
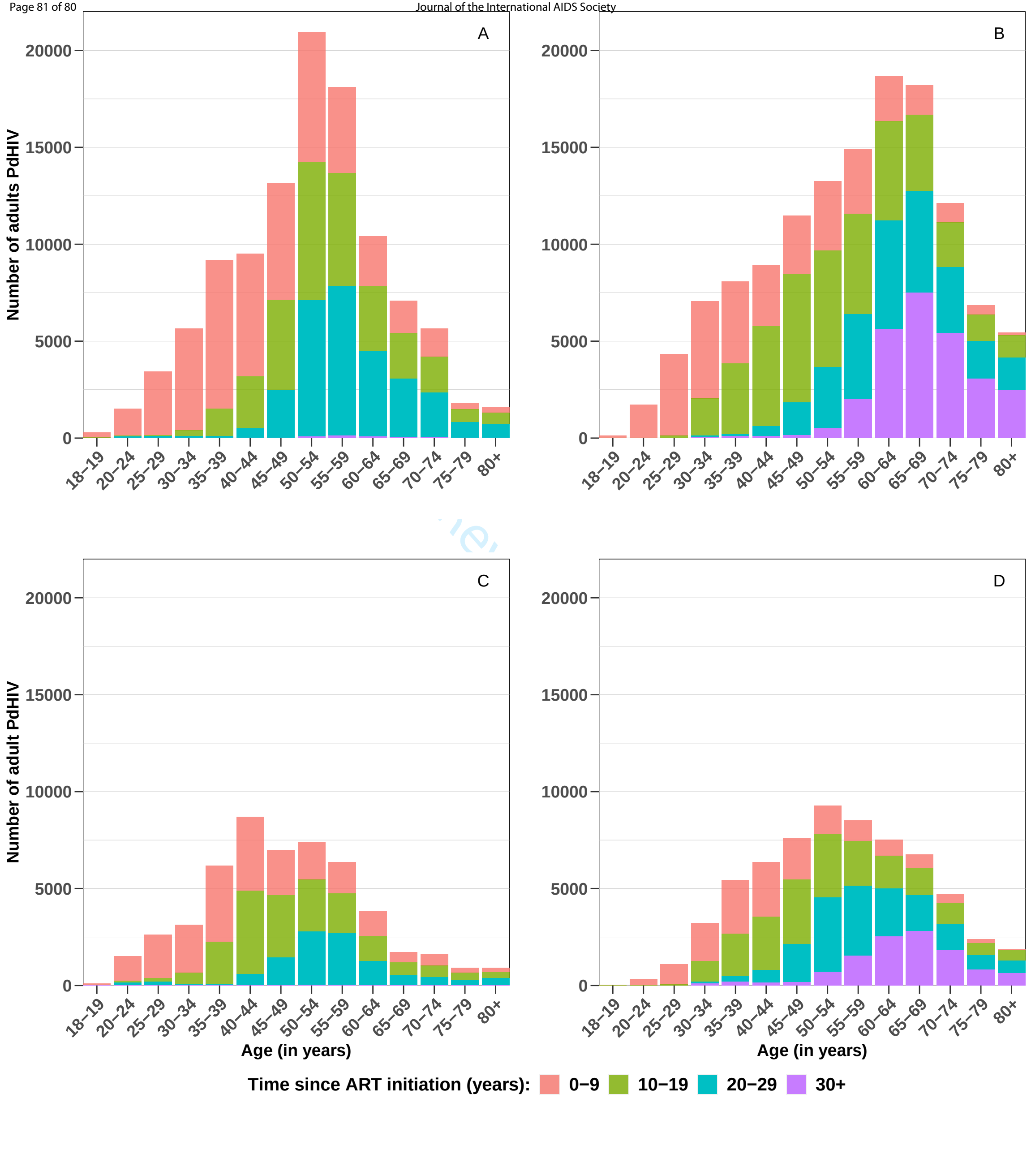


Figure S5. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D) under scenario 3 (i.e. epidemic elimination with zero new HIV cases in 2030).




A
B
C
D
E
F
Number of aPdHIV
Age (in years)
0
5000
10000
15000
20000
18–19
20–24
25–29
30–34
35–39
40–44
45–49
50–54
55–59
60–64
65–69
70–74
75–79
80+
2018
Scenario 1
Scenario 2
Scenario 3


A
B
C
D
Number of adults PdHIV
Number of adult PdHIV
20000
15000
10000
5000
0
18–19
20–24
25–29
30–34
35–39
40–44
45–49
50–54
55–59
60–64
65–69
70–74
75–79
80+
Age (in years)
Time since ART initiation (years):
0–9
10–19
20–29
30+