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

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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.

1 **Projection of age of individuals living with HIV and time since ART**

2 **initiation in 2030: estimates for France**

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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.

55   **Conclusions:** By 2030, in France, close to 20% of the aPDHIV will be aged 70+, of which

56   >40% would have started ART more than 30 years ago. These estimates are essential to

57   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

5

83   occurrence of side-effects of long-term treatment.

84   So far, none of the studies that projected the number and age structure of PLHIV

85   accounted for the issue of the ART initiation period [10–16]. In this study, we propose to

86   fill this gap, and project the demographic profile of the adult population living with

87   diagnosed HIV (aPLdHIV) in France until 2030. For this purpose, we estimated mortality

88   rates according to ART initiation period, and considered several scenarios for the

89   numbers of new HIV cases that will be diagnosed by 2030. We also used mortality rate

90   estimates to provide updated estimates of LE for PLHIV currently on ART, by sex and ART

91   initiation period, and compared these estimates to those for the French general

92   population.

93 **Methods**

94 **Data Sources**

95 Three data sources were used. First, the permanent beneficiary sample (Échantillon

96 Généraliste des Bénéficiaires, EGB) is a representative cohort of the population covered

97 by the main health insurance schemes, which monitors beneficiaries' health care

98 consumption and long-term illness status. It is a sample of 1/97th of the insured

99 individuals in France [17]. Second, the French Hospital Database on HIV (ANRS CO4-

100 FHDH) is a nationwide open hospital cohort created, in 1989, to enroll adult PLHIV

101 receiving medical care, in currently 182 hospitals located throughout France [18]. The

102 FHDH is representative of PLHIV receiving care in France [18]. Data, including

103 demographic characteristics, biological markers, and ART regimen, are collected

104 prospectively, at each outpatient visit or hospital admission, using standardized forms. By

105 2019, FHDH included data on ~210,000 individuals aged ≥18 years, including ~106,000

106 with at least one follow-up visit in 2019. Third, routine national surveillance on

107 individuals newly diagnosed with HIV is managed by Santé publique France [19].

108

109 **Projecting the demographic profile of aPLdHIV**

110 To determine the demographic profile of aPLdHIV (i.e. age, sex and ART initiation period)

111 by 2030, we first needed data, estimates or assumptions on three parameters: (i) the

112 demographic profile of aPLdHIV in 2018, (ii) the number and age distribution of newly

113 diagnosed HIV cases over 2019-2030, and (iii) the mortality rates of aPLdHIV in 2018 and

114 of new cases diagnosed beyond 2018. Only adults (i.e. aged ≥18 years) were included in

115 the analysis. Specifically, we considered 14 age groups: 18-19, 20-24, 25-29, 30-34, 35-

116 39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, ≥80.

117   *Demographic profile of aPLdHIV in 2018*

118   To estimate the number and age distribution of aPLdHIV in 2018, we used data from EGB

119   and an algorithm initially developed by the general health scheme fund to study chronic

120   diseases (including HIV) in terms of numbers, prevalence rates, etc. [20]. For HIV, the

121   algorithm relies on long-term illness status, dispensations of HIV-specific drugs and

122   biological exams, as well as HIV diagnosis during hospital stays (see details in the

123   supplemental material, section A). We first used the algorithm to determine the numbers

124   of beneficiaries, by sex and age group, managed for HIV at least once over 2014-2018 and

125   still alive in 2018. We then extrapolated these numbers to the whole population of France,

126   by dividing them by the EGB representativeness (i.e. 1/97) and the proportion of the

127   population covered by the health insurance schemes included in the EGB (i.e. 95.6% of

128   the whole population). Then we used data from EGB and FHDH to determine for each

129   individual his/her date of ART initiation (supplemental material, section B). We

130   considered five ART initiation periods: 1985-1996, 1997-2005, 2006-2010, 2011-2016

131   and ≥2017; the choice of the periods was mainly based on the amount of available data

132   and changes in ART eligibility criteria (supplemental material, section B). Individuals who

133   had not started ART by 2018 were assumed to initiate ART in 2019, as median time

134   between care entry and ART initiation was less than 1 month (FHDH data).

135

136   *New HIV cases over 2019-2030*

137   To set the annual numbers of newly diagnosed HIV cases over 2019-2030, we projected

138   the mean annual number of newly diagnosed cases over 2015-2018 according to three

139   scenarios: a 30% decrease scenario (scenario 1, reference scenario), i.e. a linear decrease

140   with 30% fewer cases in 2030 compared to 2015-2018, a status quo scenario (scenario 2,

141   pessimistic scenario), with a steady annual number of cases over 2019-2030, and an

142   epidemic elimination scenario (scenario 3, optimistic scenario), with a linear decrease in

143   the number of cases until zero case in 2030 (supplemental material, section C, figure S1).

144   Scenario 1 was set as the reference as it is a broad extrapolation of the temporal trend in

145   newly diagnosed HIV cases observed over 2012-2018. Age distribution of newly

146   diagnosed cases over 2019-2030 was obtained by extrapolating that of cases newly

147   diagnosed over 2010-2018 (supplemental material, section C, Figure S2). We assumed

148   that newly diagnosed individuals would initiate ART within their diagnosis year.

149

150   *Mortality rates in 2018 and beyond*

151   To estimate mortality rates for aPLdHIV still alive in 2018, according to ART initiation

152   period, we used data on aPLdHIV enrolled in the FHDH who had at least one follow-up

153   visit between January 1, 2017 and December 31, 2019 and a known date of ART initiation.

154   Person-years were calculated for each sex and ART initiation period separately. They

155   were accumulated from January 1, 2017 or cohort enrolment, until death, loss to follow-

156   up (LTFU, defined as no clinical visit for 18 months, in line with French HIV guidelines

157   [21], supplemental material section D), or December 31, 2019, whichever came first. For

158   LTFU patients, follow-up stopped 6 months after the last visit. Patients with a clinical visit

159   within the 6-month period before December 31, 2019 were censored on December 31,

160   2019.

161   As the number of deaths is underreported in the FHDH [22], it was adjusted using data

162   from the health insurance schemes on beneficiaries living with HIV (supplemental

163   material, section E).

164   We then used a Poisson model, with age reached in 2018 by aPLdHIV and ART initiation

165   period as covariates, to estimate mortality rates by sex and age group, stratified by ART

166   initiation period.

9

167   It was not possible to estimate mortality rate for individuals who started ART from 2017

168   due to lack of follow-up data after ART initiation. Then for these individuals and for newly

169   diagnosed cases over 2019-2030, mortality rates were assumed, conservatively, to be the

170   same as those for individuals who started ART during 2011-2016. Likewise, due to data

171   scarcity, mortality rate for individuals aged 18-19 years were assumed to be the same as

172   those for individuals aged 20-24 years.

173

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

175   We used a matrix population model to project the size of aPLdHIV until 2030, using

176   estimates for aPLdHIV in 2018, scenarios on newly diagnosed cases over 2019-2030, and

177   estimates of mortality rates (supplemental material, section F). Distributions of time since

178   ART initiation were also projected, together with age distributions, stratified by ART

179   initiation period, using the same matrix model.

180

181   **Life Expectancy**

182   Using estimated mortality rates and life table method [23], we estimated LE for PLHIV on

183   ART, by sex, age and ART initiation period. LE at a given age is defined as the expected

184   number of years of life remaining for those surviving to that age (supplemental material,

185   section H). LE for the general population at age 20, 40 and 60 years in 2018 were obtained

186   from the Human Mortality Database (https://www.mortality.org).

187

188   **Ethical statement**

189   The ANRS CO4-FHDH project was approved by CNIL (French data protection authority)

190   on November 27, 1991, Journal Officiel, January 17, 1992. To conform to new regulations,

191   the ANRS CO4-FHDH was then approved by the CEREES (Expertise Committee for

192   Research, Studies and Evaluations in the field of Health) on July 20, 2018 and as a hospital

193   datawarehouse by CNIL on February 19, 2021. The cohort received authorization to

194   conduct research projects on the datawarehouse by CNIL on March 30, 2021. All ANRS

195   CO4-FHDH participants signed informed consent forms mentioning use of data for

196   research purposes. INSERM has a regulatory permanent access to EGB data, according to

197   Article R1431-13 of the French Public Health Code, as modified by the Decree 2021-848

198   of June 22, 2021. All data were deidentified, thus informed consent was not necessary.

199   **Results**

200   Demographic characteristics (age, sex, country of birth) of participants to the three data

201   sources are provided in Table 1.

202

203   **Mortality rates and life expectancies**

204   We used data on 104,042 adults (35% women), enrolled in the FHDH, who initiated ART

205   before 2017 and had at least one follow-up visit between January 1, 2017 and December

206   31, 2019 to estimate mortality rates (<mark>supplemental material</mark>, figure S3), as well as LE,

207   which are presented in Table 2 together with LE for the general population. For instance,

208   LE for individuals aged 40 in 2018 who started ART over 2011-2016 was 39.2 years for

209   men and 40.2 years for women. In comparison, it was respectively 40.9 and 46.3 years for

210   the general population. In general, whatever the age group, LE was higher for individuals

211   who initiated ART over 2011-2016, i.e. the most recent period, compared to those who

212   initiated ART earlier. Whatever the period and age group, women had higher LE than men,

213   however this difference tended to decrease over time, from 7 to 10% for women who

214   started ART over 1985-1996 to 3 to 4% for women who started ART over 2011-2016. In

215   addition, for individuals who initiated ART over 2011-2016, i.e. those with the highest LE,

216   the gap in LE compared to the general population was higher for women than for men,

217   whatever the age group, ranging from 3.8 to 6.8 years for women and from 0.4 to 2.4 for

218   men.

219

220   **Demographic profile of aPLdHIV in 2030**

221   In 2018, an estimated 161,125 adults (33% women) were living with diagnosed HIV.

222   Assuming a 30% decrease in the annual number of newly diagnosed cases over 2019-

223   2030 (scenario 1), and using the population matrix model together with mortality rate

224   estimates, we estimated that 195,246 adults (33% women) would be living with

225   diagnosed HIV in 2030, i.e. an increase of 21% of the epidemic size. It was 207,972

226   assuming a steady number of newly diagnosed cases until 2030 (scenario 2) and 167,221

227   under the epidemic elimination scenario (scenario 3).

228   For all scenarios, we found that age distribution of aPLdHIV would shift towards older

229   ages in 2030 (Figure 1). For scenario 1, the proportion of individuals aged ≥50 increased

230   between 2018 and 2030, from 61% to 68% for men, and from 44% to 63% for women.

231   The proportion of individuals aged ≥60 doubled, from 24% to 47% for men, and from

232   17% to 36% for women, like the proportion of individuals aged ≥70, from 8% to 18% for

233   men, 7% to 14% for women. These proportions were slightly lower for scenario 2 (Figure

234   1, C-D) and slightly higher for scenario 3 (Figure 1, E-F). Whatever the scenario, we

235   estimated that, in 2030, there would be ~83,400 individuals (~28% women) aged ≥60

236   and ~33,100 individuals aged ≥70 (~27% women); in comparison, in 2018, it was

237   respectively 35,715 (~25% women) and 12,582 (~27% women).

238

239   **Projected time since ART initiation**

240   Proportions of individuals who started ART more than 20 or 30 years ago will increase

241   over 2018-2030 (Figure 2), especially for older age groups. For brevity, we only present

242   results for scenario 1, results for other scenarios are described in the supplemental

243   material, section I. Proportions of individuals with ≥20 years of ART exposure will

244   increase from 27% to 42% for men, and from 21% to 44% for women. In particular, for

245   individuals aged ≥60, these proportions will increase from 43% to 68% for men, and from

246   33% to 67% for women. Proportions of individuals with ≥30 years of ART exposure will

247   increase from <1% to 21% for men, and from <1% to 18% for women. In particular, for

248   individuals aged ≥60, these proportions will increase from 1% to 39% for men, and from

249   <mark><1% to 37% for women.</mark> In consequence, median time since ART initiation will increase,

250   especially for older age groups. For individuals aged ≥60, it will increase from 18.4 (IQR

251   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-

252   33.1) for women, while for individuals aged <60, it will only increase from 9.8 (4.8-19.0)

253   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

254   women.

255   Of note, we estimated that, in 2030, 83,659 individuals (34% women) would have started

256   ART ≥20 years ago and 38,492 individuals (30% women) would have started ART ≥30

257   years ago - versus respectively 40,667 and 573 in 2018 (Figure 2). Among men who

258   started ART ≥20 years ago, 77% would be aged ≥60, 33% ≥70, 8% ≥80. It was respectively

259   54%, 21% and 4% for women. Among men who started ART ≥30 years, 89% would be

260   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.

15

286 To the best of our knowledge, our study is the first to project time spent since ART

287 initiation for an HIV population. However, previous studies emphasized other important

288 aspects for the projected demographic profile of HIV populations, which we were unable

289 to take into account. First, a study investigating the capacity of current cART to offer long-

290 term HIV control found that median time until exhaustion of treatment options was 45.5

291 years (IQR 34.0–61.0 years) [28]. Furthermore, some studies showed important

292 heterogeneity in the projections of PLHIV according to race/ethnicity, with older

293 projected population of white PLHIV compared to Black and Hispanic minorities [11,29].

294 Other studies [13,14] focused on the burden and prevalence of age-related co-

295 morbidities: Smit et al. [13] predicted that in 2030, 84% of PLHIV in the Netherlands will

296 have at least one age-related non-communicable disease, with 28% having three or more,

297 mainly due to cardiovascular disease. This could generate complications due to drug-drug

298 interactions for 40% of patients with the currently recommended first-line HIV regimen.

299 Finally, a study for Australia [15] highlighted that the number of PLHIV in non-

300 metropolitan areas, where PLHIV median age is higher, are expected to increase at a

301 greater rate than that in the major cities.

302

303 We also found that LE of adults who started ART from 2011 onwards was either equal or

304 approaching that of the general population: for instance, at age 60 in 2018 it was ~23 and

305 ~24 years for respectively men and women living with diagnosed HIV versus respectively

306 ~23 and ~28 years in the general population. Individuals who started ART in 2005 or

307 earlier, and still alive in 2018, had lower LE, but the difference was only 2 to 4 years. This

308 can have important implications for health-related insurance policies for PLHIV. Marcus

309 et al. [30] reported an overall LE of 56.0 years at age 21 over 2014-2016, close to our

310 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-

17

336   reporting, with potential inaccurate adjustments (supplemental material, section G for

337   details). As health insurance schemes do not collect data on HIV exposure group, this

338   factor could not be accounted for. Third, we could not include individuals aged <18 years

339   for population size estimates. According to health insurance and HIV surveillance data,

340   this could represent ~5200 individuals in 2030, comprising ~4000 individuals aged <18

341   years living with diagnosed HIV in 2018, plus ~100 individuals who could be newly

342   diagnosed each year over 2019-2030. Fourth, our global LE estimates do not capture the

343   comorbidity-free LE. This was estimated to remain much lower for PLHIV than for the

344   general population (9.5 years difference in a US cohort of insured adults [30]). Finally, HIV

345   becoming more prevalent among older adults, transmission risk of higher age groups

346   might increase, if for instance older PLHIV are not adherent to their treatment. This may

347   impact the age distribution of individuals becoming newly infected, with for instance

348   more individuals seroconverting at an older age. As a consequence, interventions

349   explicitly targeting older individuals may be needed, as older individuals were recently

350   shown to be at increased risk of delayed presentation for HIV care [36].

351

352   **CONCLUSIONS**

353   By 2030, in France, close to 20% of the adult population living with diagnosed HIV will be

354   aged ≥70 (i.e. ~33,000 individuals), of which >40% would have started ART more than 30

355   years. Ageing of HIV population has important implications for care, generating an

356   increase in comorbidity prevalence and treatment complexity. Our findings can help to

357   measure the burden of ageing, and anticipate health care needs, resource provision and

358   screening guidelines in HIV care, in France but also in other high-income countries.

359   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.

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385   **References**

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500

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)

26

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)

503 [1] Individuals enrolled in the FHDH, who initiated ART before 2017 and had at least one

504 follow-up visit between January 1, 2017 and December 31, 2019.

505 [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

28

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.
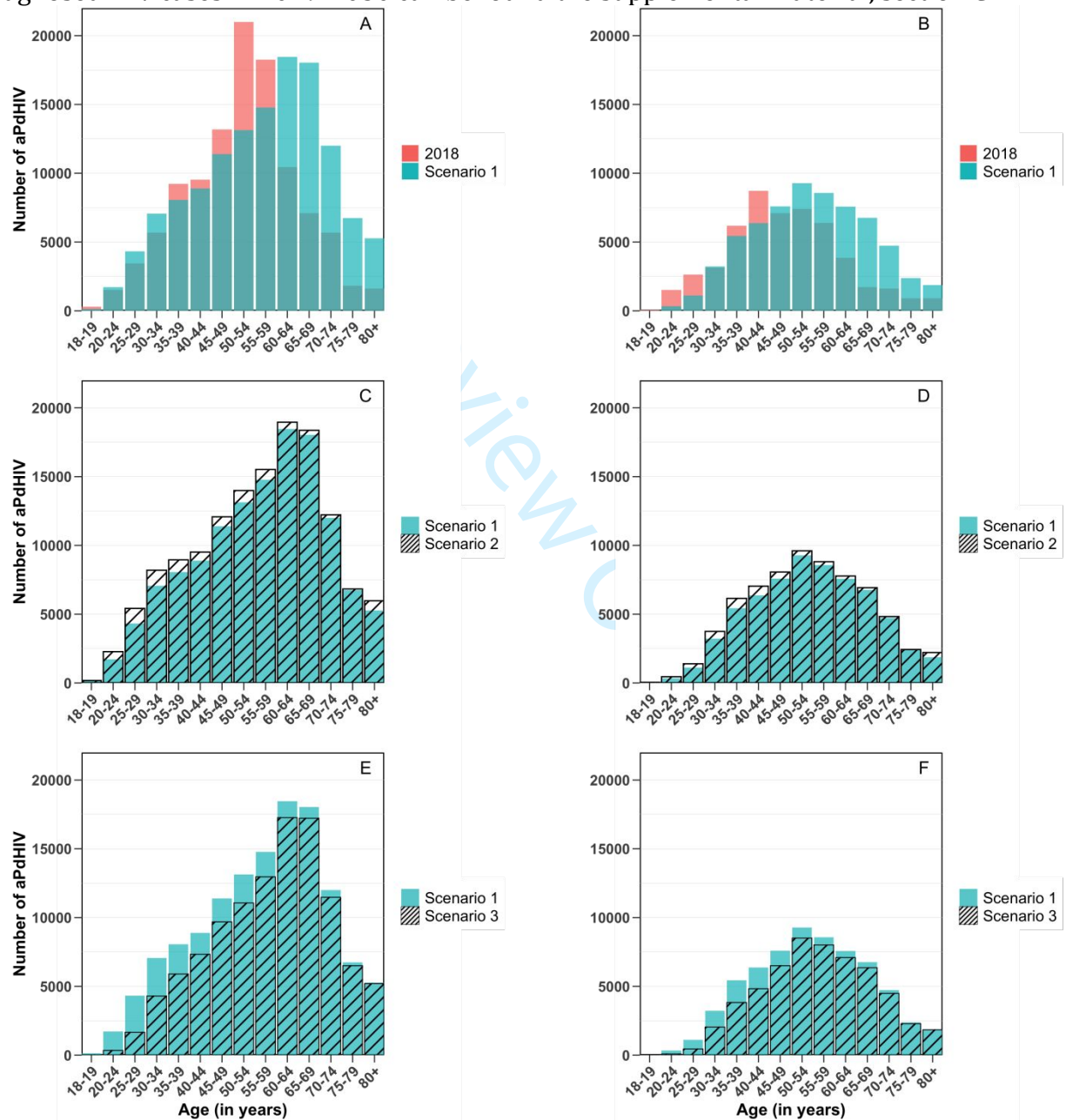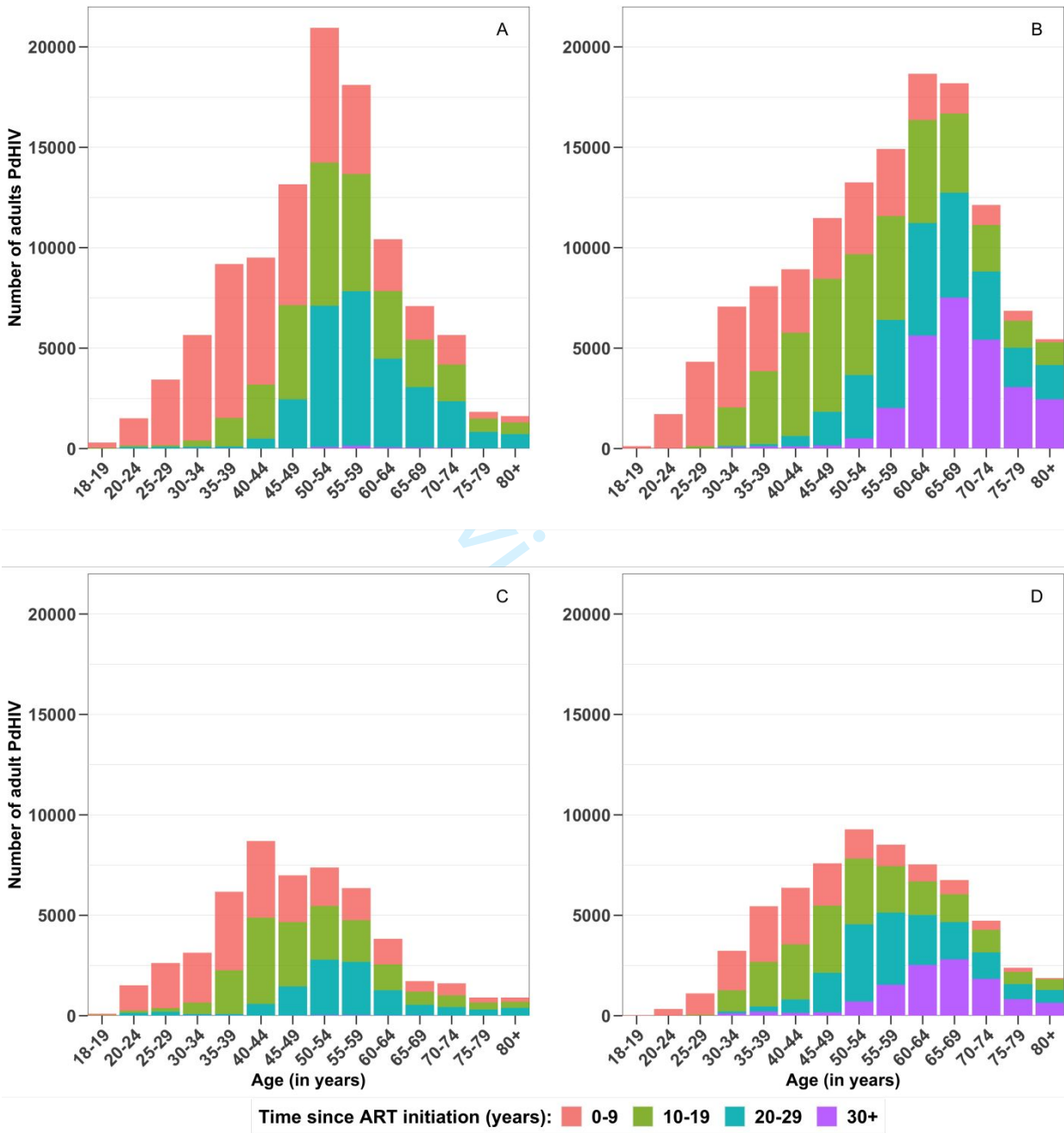

29

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.

30

1 **Projection of age of individuals living with HIV and time since ART**

2 **initiation in 2030: estimates for France**

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31 **Abstract**

32 **Introduction:** Thanks to antiretroviral treatment (ART), people living with HIV (PLHIV)

33 are living longer and ageing. However, ageing involves increased risks of co-morbidities,

34 which also depend on when PLHIV individuals started ART. To tackle the HIV age-related

35 upcoming challenges, knowledge of current and future age structure of HIV population is

36 needed. Here, we forecast the demographic profile of the adult population diagnosed with

37 HIV (aPDHIV) in France until 2030, accounting for the impact of ART initiation period on

38 mortality.

39 **Methods:** We used national data from the French Hospital Database on HIV (ANRS CO4-

40 FHDH) and a sample of the National Health Data System to, first, characterize the aPDHIV

41 in 2018 and estimate their mortality rates according to age, sex, and ART initiation period.

42 Second, we used national HIV surveillance data to define three scenarios for the numbers

43 of newly diagnosed HIV cases over 2019-2030: 30% decrease in HIV cases (S1), status

44 quo situation (S2), and epidemic elimination (S3). We then combined these data using a

45 matrix model, to project the age structure of aPDHIV, and time since ART initiation.

46 **Results:** In 2018, there was an estimated 161,125 aPDHIV (33% women), of which 55%

47 were aged 50 or older (50+), 22% aged 60+ and 8% aged 70+. In 2030, the aPDHIV would

48 grow to 195,246 for S1, 207,972 for S2 and 167,221 for S3. Whatever the scenario, in

49 2030, estimated median time since ART initiation would increase and age distribution

50 would shift towards older ages: with 65 to 72% aPDHIV aged 50+, 42-48% 60+ and 17-

51 19% 70+. This corresponds to ~83,400 aPDHIV (28% women) aged 60+, among which

52 ~69% started ART more than 20 years ago (i.e. before 2010) and ~39% >=30 years ago

53 (i.e. before 2000), and to ~33,100 aPDHIV (27% women) aged 70+, among which ~72%

54 started ART >=20 years ago and ~43% >=30 years ago.

55   **Conclusions:** By 2030, in France, close to 20% of the aPDHIV will be aged 70+, of which

56   >40% would have started ART more than 30 years ago. These estimates are essential to

57   adapt co-morbidities screening and anticipate resource provision in the aged care sector.

4

58 **Introduction**

59 Since the beginning of the HIV epidemic, great progress has been made to improve the

60 health of people living with HIV (PLHIV). The introduction of combination antiretroviral

61 therapy (cART) in 1996 has led to rapid decrease in mortality [1]. With increased cART

62 efficacy and tolerability over time, life expectancy (LE) within 3 years of cART initiation

63 further increased, and continued to increase even in the late cART era [2]. Currently the

64 LE of treated PLHIV approaches that of the general population [3,4].

65 Consequently, HIV populations are ageing. According to UNAIDS estimates, in high-

66 income countries, one-third of PLHIV were aged 50 or more in 2013 [5]. Ageing will

67 involve new care challenges. First, age is associated with chronic conditions like non-AIDS

68 defining cancers, cardiovascular, renal, liver, bone, and neurological diseases, and HIV

69 infection further increases the risk of these conditions [6]. Increased burden of

70 polypharmacy and risk of drug-drug interactions with cART could therefore represent an

71 upcoming issue in HIV care [7,8]. Second, ageing PLHIV will possibly need access to

72 assisted living facility for elderly people. Resource provision in the aged care sector will

73 thus need to be addressed in the coming years, including specific HIV care training for

74 medical staff.

75 To anticipate for needs and resources, it is essential to foresee the number and age of

76 PLHIV. Beyond age-related chronic morbidities, the period at which PLHIV started ART is

77 also key, as it reflects the type of ART regimen to which individuals had been exposed, the

78 level of immune dysfunction reached before ART initiation, which varied according to

79 ART guidelines, and indirectly the lifetime duration with HIV. At any age, comorbidity and

80 mortality risks are higher for individuals ageing with a longer duration of HIV infection

81 than for individuals who seroconverted at an older age [9]. The period of ART initiation is

82 thus likely to influence mortality risk, but also comorbidity risk and the potential

5

83   occurrence of side-effects of long-term treatment.

84   So far, none of the studies that projected the number and age structure of PLHIV

85   accounted for the issue of the ART initiation period [10–16]. In this study, we propose to

86   fill this gap, and project the demographic profile of the adult population living with

87   diagnosed HIV (aPLdHIV) in France until 2030. For this purpose, we estimated mortality

88   rates according to ART initiation period, and considered several scenarios for the

89   numbers of new HIV cases that will be diagnosed by 2030. We also used mortality rate

90   estimates to provide updated estimates of LE for PLHIV currently on ART, by sex and ART

91   initiation period, and compared these estimates to those for the French general

92   population.

93   **Methods**

94   **Data Sources**

95   Three data sources were used. First, the permanent beneficiary sample (Échantillon

96   Généraliste des Bénéficiaires, EGB) is a representative cohort of the population covered

97   by the main health insurance schemes, which monitors beneficiaries' health care

98   consumption and long-term illness status. It is a sample of 1/97th of the insured

99   individuals in France [17]. Second, the French Hospital Database on HIV (ANRS CO4-

100   FHDH) is a nationwide open hospital cohort created, in 1989, to enroll adult PLHIV

101   receiving medical care, in currently 182 hospitals located throughout France [18]. The

102   FHDH is representative of PLHIV receiving care in France [18]. Data, including

103   demographic characteristics, biological markers, and ART regimen, are collected

104   prospectively, at each outpatient visit or hospital admission, using standardized forms. By

105   2019, FHDH included data on ~210,000 individuals aged ≥18 years, including ~106,000

106   with at least one follow-up visit in 2019. Third, routine national surveillance on

107   individuals newly diagnosed with HIV is managed by Santé publique France [19].

108

109   **Projecting the demographic profile of aPLdHIV**

110   To determine the demographic profile of aPLdHIV (i.e. age, sex and ART initiation period)

111   by 2030, we first needed data, estimates or assumptions on three parameters: (i) the

112   demographic profile of aPLdHIV in 2018, (ii) the number and age distribution of newly

113   diagnosed HIV cases over 2019-2030, and (iii) the mortality rates of aPLdHIV in 2018 and

114   of new cases diagnosed beyond 2018. Only adults (i.e. aged ≥18 years) were included in

115   the analysis. Specifically, we considered 14 age groups: 18-19, 20-24, 25-29, 30-34, 35-

116   39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, ≥80.

117 *Demographic profile of aPLdHIV in 2018*

118 To estimate the number and age distribution of aPLdHIV in 2018, we used data from EGB

119 and an algorithm initially developed by the general health scheme fund to study chronic

120 diseases (including HIV) in terms of numbers, prevalence rates, etc. [20]. For HIV, the

121 algorithm relies on long-term illness status, dispensations of HIV-specific drugs and

122 biological exams, as well as HIV diagnosis during hospital stays (see details in the

123 supplemental material, section A). We first used the algorithm to determine the numbers

124 of beneficiaries, by sex and age group, managed for HIV at least once over 2014-2018 and

125 still alive in 2018. We then extrapolated these numbers to the whole population of France,

126 by dividing them by the EGB representativeness (i.e. 1/97) and the proportion of the

127 population covered by the health insurance schemes included in the EGB (i.e. 95.6% of

128 the whole population). Then we used data from EGB and FHDH to determine for each

129 individual his/her date of ART initiation (supplemental material, section B). We

130 considered five ART initiation periods: 1985-1996, 1997-2005, 2006-2010, 2011-2016

131 and ≥2017; the choice of the periods was mainly based on the amount of available data

132 and changes in ART eligibility criteria (supplemental material, section C). Individuals who

133 had not started ART by 2018 were assumed to initiate ART in 2019, as median time

134 between care entry and ART initiation was less than 1 month (FHDH data).

135

136 *New HIV cases over 2019-2030*

137 To set the annual numbers of newly diagnosed HIV cases over 2019-2030, we projected

138 the mean annual number of newly diagnosed cases over 2015-2018 according to three

139 scenarios: a 30% decrease scenario (scenario 1, reference scenario), i.e. a linear decrease

140 with 30% fewer cases in 2030 compared to 2015-2018, a status quo scenario (scenario 2,

141 pessimistic scenario), with a steady annual number of cases over 2019-2030, and an

142 epidemic elimination scenario (scenario 3, optimistic scenario), with a linear decrease in

143 the number of cases until zero case in 2030 (supplemental material, section C, figure S1).

144 Scenario 1 was set as the reference as it is a broad extrapolation of the temporal trend in

145 newly diagnosed HIV cases observed over 2012-2018. Age distribution of newly

146 diagnosed cases over 2019-2030 was obtained by extrapolating that of cases newly

147 diagnosed over 2010-2018 (supplemental material, section C, Figure S2). We assumed

148 that newly diagnosed individuals would initiate ART within their diagnosis year.

149

150 *Mortality rates in 2018 and beyond*

151 To estimate mortality rates for aPLdHIV still alive in 2018, according to ART initiation

152 period, we used data on aPLdHIV enrolled in the FHDH who had at least one follow-up

153 visit between January 1, 2017 and December 31, 2019 and a known date of ART initiation.

154 Person-years were calculated for each sex and ART initiation period separately. They

155 were accumulated from January 1, 2017 or cohort enrolment, until death, loss to follow-

156 up (LTFU, defined as no clinical visit for 18 months, in line with French HIV guidelines

157 [21], supplemental material section D), or December 31, 2019, whichever came first. For

158 LTFU patients, follow-up stopped 6 months after the last visit. Patients with a clinical visit

159 within the 6-month period before December 31, 2019 were censored on December 31,

160 2019 (supplemental material, section B).

161 As the number of deaths is underreported in the FHDH [22], it was adjusted using data

162 from the health insurance schemes on beneficiaries living with HIV (supplemental

163 material, section E).

164 We then used a Poisson model, with age reached in 2018 by aPLdHIV and ART initiation

165 period as covariates, to estimate mortality rates by sex and age group, stratified by ART

166 initiation period.

167   It was not possible to estimate mortality rate for individuals who started ART from 2017

168   due to lack of follow-up data after ART initiation. Then for these individuals and for newly

169   diagnosed cases over 2019-2030, mortality rates were assumed, conservatively, to be the

170   same as those for individuals who started ART during 2011-2016. Likewise, due to data

171   scarcity, mortality rate for individuals aged 18-19 years were assumed to be the same as

172   those for individuals aged 20-24 years.

173

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

175   We used a matrix population model to project the size of aPLdHIV until 2030, using

176   estimates for aPLdHIV in 2018, scenarios on newly diagnosed cases over 2019-2030, and

177   estimates of mortality rates (supplemental material, section F). Distributions of time since

178   ART initiation were also projected, together with age distributions, stratified by ART

179   initiation period, using the same matrix model.

180

181   **Life Expectancy**

182   Using estimated mortality rates and life table method [23], we estimated LE for PLHIV on

183   ART, by sex, age and ART initiation period. LE at a given age is defined as the expected

184   number of years of life remaining for those surviving to that age (supplemental material,

185   section H). LE for the general population at age 20, 40 and 60 years in 2018 were obtained

186   from the Human Mortality Database (https://www.mortality.org).

187

188   **Ethical statement**

189   The ANRS CO4-FHDH project was approved by CNIL (French data protection authority)

190   on November 27, 1991, Journal Officiel, January 17, 1992. To conform to new regulations,

191   the ANRS CO4-FHDH was then approved by the CEREES (Expertise Committee for

10

192   Research, Studies and Evaluations in the field of Health) on July 20, 2018 and as a hospital

193   datawarehouse by CNIL on February 19, 2021. The cohort received authorization to

194   conduct research projects on the datawarehouse by CNIL on March 30, 2021. All ANRS

195   CO4-FHDH participants signed informed consent forms mentioning use of data for

196   research purposes. INSERM has a regulatory permanent access to EGB data, according to

197   Article R1431-13 of the French Public Health Code, as modified by the Decree 2021-848

198   of June 22, 2021. All data were deidentified, thus informed consent was not necessary.

199   **Results**

200   Demographic characteristics (age, sex, country of birth) of participants to the three data

201   sources are provided in Table 1.

202

203   **Mortality rates and life expectancies**

204   We used data on 104,042 adults (35% women), enrolled in the FHDH, who initiated ART

205   before 2017 and had at least one follow-up visit between January 1, 2017 and December

206   31, 2019 to estimate mortality rates (supplemental material, figure S3), as well as LE,

207   which are presented in Table 2 together with LE for the general population. For instance,

208   LE for individuals aged 40 in 2018 who started ART over 2011-2016 was 39.2 years for

209   men and 40.2 years for women. In comparison, it was respectively 40.9 and 46.3 years for

210   the general population. In general, whatever the age group, LE was higher for individuals

211   who initiated ART over 2011-2016, i.e. the most recent period, compared to those who

212   initiated ART earlier. Whatever the period and age group, women had higher LE than men,

213   however this difference tended to decrease over time, from 7 to 10% for women who

214   started ART over 1985-1996 to 3 to 4% for women who started ART over 2011-2016. In

215   addition, for individuals who initiated ART over 2011-2016, i.e. those with the highest LE,

216   the gap in LE compared to the general population was higher for women than for men,

217   whatever the age group, ranging from 3.8 to 6.8 years for women and from 0.4 to 2.4 for

218   men.

219

220   **Demographic profile of aPLdHIV in 2030**

221   In 2018, an estimated 161,125 adults (33% women) were living with diagnosed HIV.

222   Assuming a 30% decrease in the annual number of newly diagnosed cases over 2019-

223   2030 (scenario 1), and using the population matrix model together with mortality rate

12

224 estimates, we estimated that 195,246 adults (33% women) would be living with

225 diagnosed HIV in 2030, i.e. an increase of 21% of the epidemic size. It was 207,972

226 assuming a steady number of newly diagnosed cases until 2030 (scenario 2) and 167,221

227 under the epidemic elimination scenario (scenario 3).

228 For all scenarios, we found that age distribution of aPLdHIV would shift towards older

229 ages in 2030 (Figure 1). For scenario 1, the proportion of individuals aged ≥50 increased

230 between 2018 and 2030, from 61% to 68% for men, and from 44% to 63% for women.

231 The proportion of individuals aged ≥60 doubled, from 24% to 47% for men, and from

232 17% to 36% for women, like the proportion of individuals aged ≥70, from 8% to 18% for

233 men, 7% to 14% for women. These proportions were slightly lower for scenario 2 (Figure

234 1, C-D) and slightly higher for scenario 3 (Figure 1, E-F). Whatever the scenario, we

235 estimated that, in 2030, there would be ~83,400 individuals (~28% women) aged ≥60

236 and ~33,100 individuals aged ≥70 (~27% women); in comparison, in 2018, it was

237 respectively 35,715 (~25% women) and 12,582 (~27% women).

238

239 **Projected time since ART initiation**

240 Proportions of individuals who started ART more than 20 or 30 years ago will increase

241 over 2018-2030 (Figure 2), especially for older age groups. For brevity, we only present

242 results for scenario 1, results for other scenarios are described in the supplemental

243 material, section I. Proportions of individuals with ≥20 years of ART exposure will

244 increase from 27% to 42% for men, and from 21% to 44% for women. In particular, for

245 individuals aged ≥60, these proportions will increase from 43% to 68% for men, and from

246 33% to 67% for women. Proportions of individuals with ≥30 years of ART exposure will

247 increase from <1% to 21% for men, and from <1% to 18% for women. In particular, for

248 individuals aged ≥60, these proportions will increase from 1% to 39% for men, and from

13

249 <1% to 37% for women. In consequence, median time since ART initiation will increase,

250 especially for older age groups. For individuals aged ≥60, it will increase from 18.4 (IQR

251 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-

252 33.1) for women, while for individuals aged <60, it will only increase from 9.8 (4.8-19.0)

253 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

254 women.

255 Of note, we estimated that, in 2030, 83,659 individuals (34% women) would have started

256 ART ≥20 years ago and 38,492 individuals (30% women) would have started ART ≥30

257 years ago - versus respectively 40,667 and 573 in 2018 (Figure 2). Among men who

258 started ART ≥20 years ago, 77% would be aged ≥60, 33% ≥70, 8% ≥80. It was respectively

259 54%, 21% and 4% for women. Among men who started ART ≥30 years, 89% would be

260 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.

15

286 To the best of our knowledge, our study is the first to project time spent since ART

287 initiation for an HIV population. However, previous studies emphasized other important

288 aspects for the projected demographic profile of HIV populations, which we were unable

289 to take into account. First, a study investigating the capacity of current cART to offer long-

290 term HIV control found that median time until exhaustion of treatment options was 45.5

291 years (IQR 34.0–61.0 years) [28]. Furthermore, some studies showed important

292 heterogeneity in the projections of PLHIV according to race/ethnicity, with older

293 projected population of white PLHIV compared to Black and Hispanic minorities [11,29].

294 Other studies [13,14] focused on the burden and prevalence of age-related co-

295 morbidities: Smit et al. [13] predicted that in 2030, 84% of PLHIV in the Netherlands will

296 have at least one age-related non-communicable disease, with 28% having three or more,

297 mainly due to cardiovascular disease. This could generate complications due to drug-drug

298 interactions for 40% of patients with the currently recommended first-line HIV regimen.

299 Finally, a study for Australia [15] highlighted that the number of PLHIV in non-

300 metropolitan areas, where PLHIV median age is higher, are expected to increase at a

301 greater rate than that in the major cities.

302

303 We also found that LE of adults who started ART from 2011 onwards was either equal or

304 approaching that of the general population: for instance, at age 60 in 2018 it was ~23 and

305 ~24 years for respectively men and women living with diagnosed HIV versus respectively

306 ~23 and ~28 years in the general population. Individuals who started ART in 2005 or

307 earlier, and still alive in 2018, had lower LE, but the difference was only 2 to 4 years. This

308 can have important implications for health-related insurance policies for PLHIV. Marcus

309 et al. [30] reported an overall LE of 56.0 years at age 21 over 2014-2016, close to our

310 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-

336   reporting, with potential inaccurate adjustments (supplemental material, section G for

337   details). As health insurance schemes do not collect data on HIV exposure group, this

338   factor could not be accounted for. Third, we could not include individuals aged <18 years

339   for population size estimates. According to health insurance and HIV surveillance data,

340   this could represent ∼5200 individuals in 2030, comprising ∼4000 individuals aged <18

341   years living with diagnosed HIV in 2018, plus ∼100 individuals who could be newly

342   diagnosed each year over 2019-2030. Fourth, our global LE estimates do not capture the

343   comorbidity-free LE. This was estimated to remain much lower for PLHIV than for the

344   general population (9.5 years difference in a US cohort of insured adults [30]). Finally, HIV

345   becoming more prevalent among older adults, transmission risk of higher age groups

346   might increase, if for instance older PLHIV are not adherent to their treatment. This may

347   impact the age distribution of individuals becoming newly infected, with for instance

348   more individuals seroconverting at an older age. As a consequence, interventions

349   explicitly targeting older individuals may be needed, as older individuals were recently

350   shown to be at increased risk of delayed presentation for HIV care [36].

351

352   **CONCLUSIONS**

353   By 2030, in France, close to 20% of the adult population living with diagnosed HIV will be

354   aged ≥70 (i.e. ∼33,000 individuals), of which >40% would have started ART more than 30

355   years. Ageing of HIV population has important implications for care, generating an

356   increase in comorbidity prevalence and treatment complexity. Our findings can help to

357   measure the burden of ageing, and anticipate health care needs, resource provision and

358   screening guidelines in HIV care, in France but also in other high-income countries.

359   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.

19

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500

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)

503 (1) Individuals enrolled in the FHDH, who initiated ART before 2017 and had at least one

504 follow-up visit between January 1, 2017 and December 31, 2019.

505 (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

28

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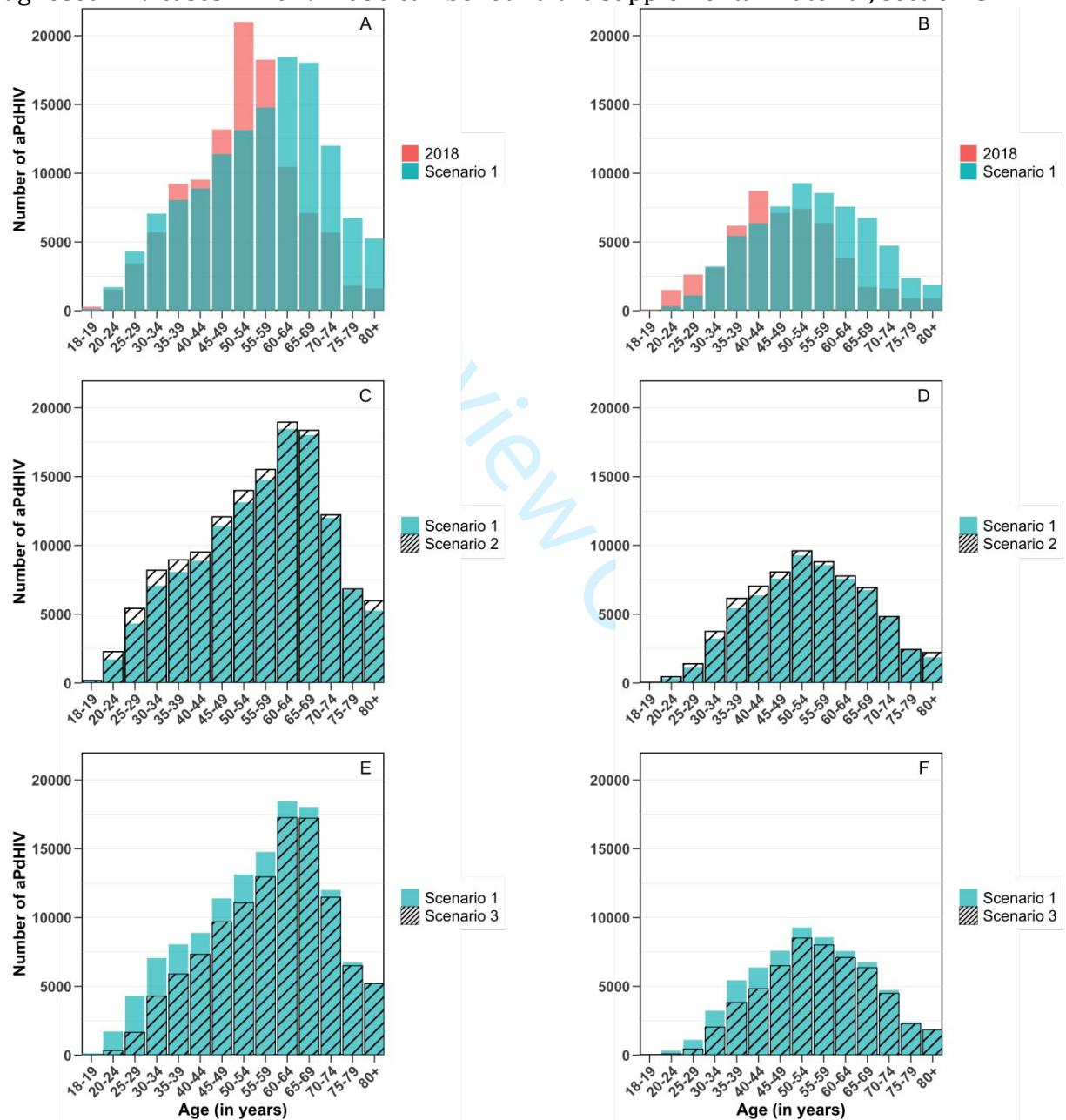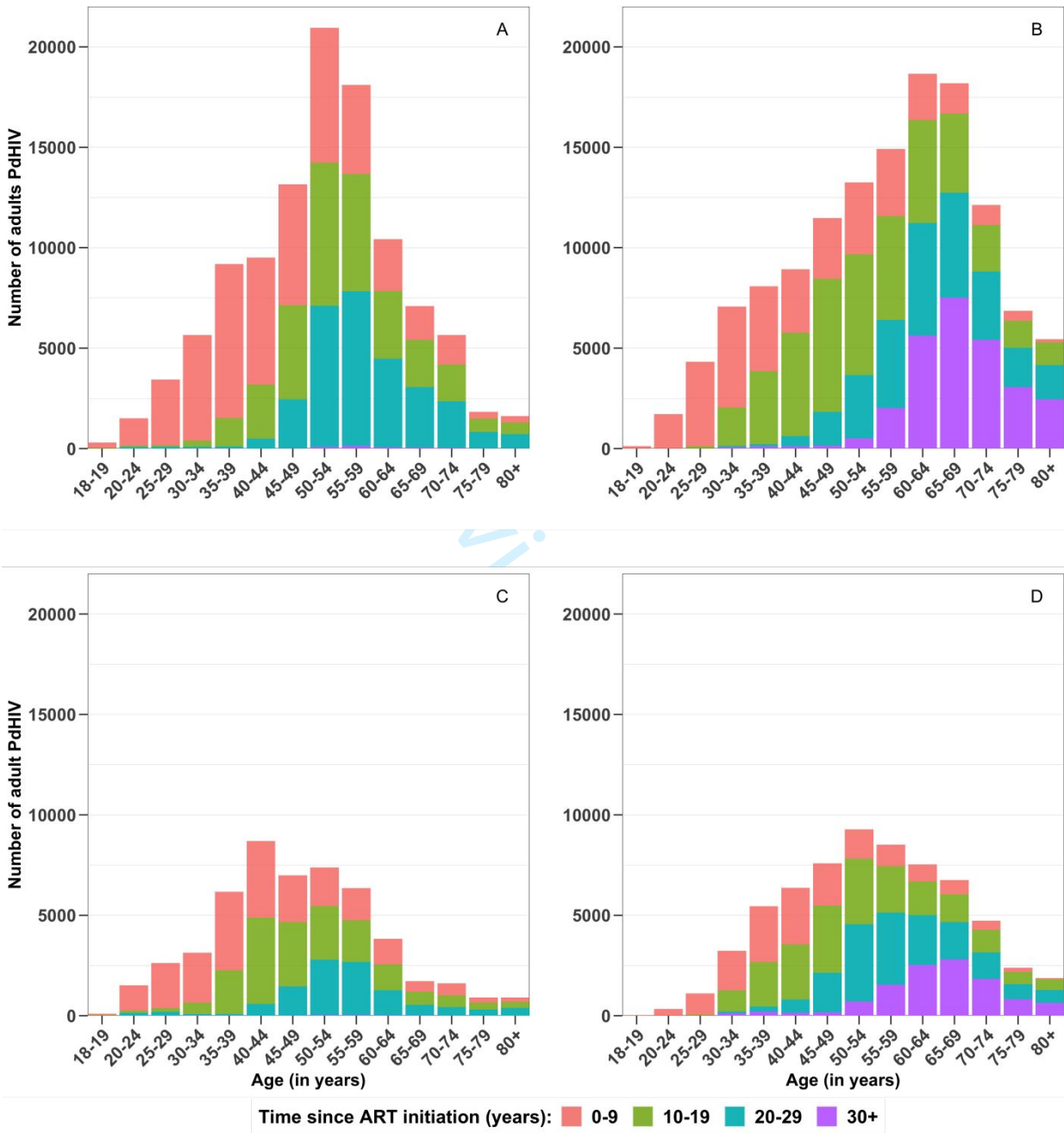
Figure 2. Numbers and age distributions of adults aged ≥18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D) for scenario 1 (i.e. 30% decrease in newly diagnosed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

30

1   **Supplementary Material**

2

3   **Projection of age of individuals living with HIV and time since ART initiation in 2030:**

4   **estimates for France**

5

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

17   Adapting a method initially developed by the general health scheme fund to study several

18   chronic diseases (including HIV) [1], in terms of numbers, prevalence rates, etc., we used the

19   following criteria to estimate, from a representative sample of the national health data system

20   (Échantillon Généraliste des Bénéficiaires, EGB), the number of individuals living with

21   diagnosed HIV in 2018:

22   -   Persons with long-term illness status (ALD, qualifying for 100% reimbursement of

23   medical expenses), with ICD 10 code for HIV, in any year over 2014-2018, and still

24   alive in 2018;

25   -   and/or persons hospitalized in medicine, surgery, obstetrics, with HIV as the main or

26   associated diagnosis (i.e. with ICD 10 code for HIV) at admission, in any year over

27   2014-2018, and still alive in 2018;

28   -   and/or persons hospitalized in medicine, surgery, obstetrics with HIV infection as

29   complication or associated morbidity (main, related, or associated diagnosis from the

30   hospital discharge database) in any year over 2014-2018, and still alive in 2018;

31   -   and/or persons with at least three dispensations of HIV-specific treatment at different

32   point in time within one year, in any year over 2014-2018, and still alive in 2018

33   (excluding Truvada dual therapy and Hepatitis B specific treatments);

34   -   and/or persons with at least one HIV-specific medical biology exam (including

35   antiretroviral genotypic resistance tests, antiretroviral plasma concentration

36   measurement, viral load quantification) in any year over 2014-2018;

37   We applied this set of criteria over the year 2014-2018, in order to identify all individuals living

38   with diagnosed HIV, whether engaged in care or not in 2018. Indeed, applying this set of criteria

39   only for the year 2018 would have only allowed identifying individuals living with diagnosed

40   HIV if they were engaged in HIV care and/or have been hospitalized in 2018, whereas

41   individuals who had interrupted their follow-up and did not have any hospitalizations in 2018

42   would have remained unidentified.

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

2

44

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.

71   The choice of the periods was based on the amount of data available and changes in ART

72   eligibility criteria. Treat-all strategy was adopted at the end of 2013 in France, but due to lack

73   of follow-up data we did not consider a group of patients who initiated ART over 2014-2016.

74   The two other milestones in terms of treatment guidelines that we considered are the following

75   ones:

76   -   1997: advent of cART;

77   -   2010: change in CD4 count eligibility from 350 to 500;

78   Since the period from 1997 to 2010 was large, and overall mortality was steadily decreasing

79   throughout this period, we split it into two, 1997-2005 and 2006-2010, in order to provide more

80   precise mortality estimates, as the amount of data allowed it. All together we thus consider

81   four periods: before 1997, 1997-2005 and 2006-2010 and 2011-2016. Beyond 2016, we

82   assumed that mortality rates would be the same as the mortality rates for individuals who had

83   started ART during 2011-2016.

84

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

86   The projected mean annual numbers of new HIV cases diagnosed over 2019-2030 according

87   to the three scenarios are presented in Figure S1: a 30% decrease in the annual number of

88   cases by 2030 (scenario 1), a status quo scenario, with a steady annual number of cases over

89   2019-2030 (scenario 2), and an epidemic elimination scenario (scenario 3), with a linear

90   decrease in the number of cases up to zero case in 2030.

91   To set age distributions of cases over 2019-2030, we first performed, for each sex, a linear

92   regression of the annual numbers of newly diagnosed HIV cases over 2010-2018 against time,

93   with age as a categorical covariable. Estimated regression coefficients were then used to

94   project, by sex, age distributions of new cases from 2019 to 2030. Using these age distributions

95   (figure S2) and the scenario-dependent annual numbers of new cases over 2019-2030 (figure

96   S1), we then obtained the annual numbers of new HIV diagnoses by age group over 2019-

97   2030.

98

4

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

100   We chose an 18-month period to define patients lost to follow-up because French HIV

101   guidelines have moved towards fewer laboratory tests and medical visits to health care centers

102   per year [2]. Specifically, the 2013 French guidelines recommend administration of ART to

103   each PLHIV whatever the CD4 count; a once-a-year visit to an infectious disease specialist for

104   patients on ART whose HIV infection has been under control (undetectable viral load and CD4

105   T cell count >500 cells/mm3) for one year without comorbidity; and a clinical and immuno-

106   virological check-up at least every 6 months, which can be performed by the primary care

107   physician.

108   **E.   Correction of the reported number of death cases**

109   The numbers of deaths reported in the FHDH over 2017-2019 (Table S1) were adjusted for

110   under-reporting, using data from the health insurance schemes on beneficiaries living with

111   diagnosed HIV (BLHIV); personal communication from A. Rachas. To do so, we first estimated

112   the coverage of FHDH, i.e. the proportion of all individuals living with diagnosed HIV in France

113   who are enrolled in FHDH. Second, we estimated the total number of death cases among

114   individuals living with diagnosed HIV in France. We then used these two estimates to obtain

115   the correction factor to adjust for under-reporting of deaths in FHDH.

116

117   The coverage of FHDH for each age group a and year t, noted $\rho_{a,t}$, was estimated using the

118   ratio of the number of individuals living with diagnosed HIV enrolled in FHDH database over

119   the total number of BLHIV from all health insurance schemes, for each year and age group

120   (Table S1):

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

122   where $N^{\mathrm{F}}_{a,t}$ is the number of individuals living with diagnosed HIV with at least one medical visit

123   registered in the FHDH and $N_{a,t}$ the total number of BLHIV from all insurance schemes (Table

124   S1);

125

126   The total number of death cases among individuals living with diagnosed HIV in France for

127   each year t and age group a, noted $D_{a,t}$, had to be estimated using data on deaths among

128   BLHIV from the main health insurance scheme, also called the general Social Security

129   scheme, because data on deaths are not complete for the other insurance schemes.

130   Specifically, we extrapolated the number of deaths reported among BLHIV of the main health

131   insurance scheme to all insurance schemes using the ratio of the number of BLHIV of the

132   general Social Security scheme over the total number of BLHIV from all insurance schemes,

133   for each year and age group:

134
$$D_{a,t} = D'_{a,t} \frac{N'_{a,t}}{N_{a,t}} \tag{2}$$

135   with $D'_{a,t}$ the number of deaths among BLHIV of the general Social Security scheme, $N'_{a,t}$ the

136   number of BLHIV of the general Social Security scheme and $N_{a,t}$, as aforementioned, the total

137   number of BLHIV from all insurance schemes (Table S2).

138

139    $\rho_{a,t}$, and $D_{a,t}$, obtained from equations (1) and (2), were then used to estimate a factor to correct

140   unreported deaths for each age group a and year t, noted $\delta_{a,t}$, using the following formula :

141
$$\delta_{a,t} = \rho_{a,t} \frac{D_{a,t}}{D^{F}_{a,t}} \tag{3}$$

142   where $D^{F}_{a,t}$ is the number of deaths reported in FHDH database for each age group a and year

143   t (Table S1).

144   Each death case in FHDH database were then multiplied by the factor $\delta_{a,t}$, obtained from

145   equation (3), to adjust for under-reporting of deaths.

146

147   **F. Age-structured projection matrix model**

148   The projection method was adapted from a Leslie matrix model for age-structured population.

149   Each year, the population was stratified by age and period of ART initiation. We divided age

150   into 63 age groups, i.e. one group for each age over ages 18-79 years and one group for the

151   last open-ended age group, ≥80 years, and the period of ART initiation into five periods (i.e.

152   1985-1996, 1997-2005, 2006-2010, 2011-2016 and ≥2017).

153   From 2019 to 2030, the number of individuals living with diagnosed HIV in age group a in year

154   t, $N_{a,t}$, corresponds to (i) the sum over all ART initiation periods of individuals of age $a-1$

155   living with diagnosed HIV in year $t-1$ with ART initiation period k who aged one year and thus

156   survived up to year t, plus (ii) the number of new HIV cases of age a diagnosed in year t, who

157   initiated ART within the same year of their diagnosis, $D_{a,t,k}$:

158

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

160

161   with $s_{a-1,k}$ the probability of surviving from age $a-1$ to age a, for individuals who started ART

162   in time period k, which is defined as:

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

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

165   during the time period k.

166   Equation (4) was thus iterated 12 times (from 2019 to 2030) to obtain the number and age

167   distribution of aPLdHIV in 2030.

168   Then the total count of individuals living with diagnosed HIV in each year t was obtained by

169   summing the count of individuals living with diagnosed HIV over all age groups a and over all

170   ART initiation periods k.

171

172   **G. Sources of uncertainty in the data and method**

173   Calculation steps presented in this study involve different data sources or estimates, and each

174   of them involves a certain degree of uncertainty.

175   First, EGB is a sample, covering 1/97th of the insured persons in France. However, it is a

176   representative sample, which allows us to make extrapolations to obtain the total number of

177   people identified as HIV-positive.

178   Second, number of deaths had to be adjusted for under-reporting: overall, we estimated that

179   under-reporting of death events was 37%. To adjust the number of deaths, we used data on

180   death events among people identified as HIV-positive who were insured in the general health

181   insurance scheme, as data on deaths are only exhaustive for this scheme. Data from the

182   general health insurance scheme are the most exhaustive data source in France, as

183   individuals are tracked until deaths or migration, which is a strength. Nevertheless, two sources

184   of uncertainty can arise in this process. First, the algorithm used to identify HIV-positive

185   persons is probably not perfect, although it is the reference to estimate HIV prevalence in

186   France. Second, we had to extrapolate the number of deaths observed among individuals

187   insured with the general health insurance scheme to obtain to the number of deaths among all

188   people identified as HIV-positive, not only those insured with the general health insurance

189   scheme. The general health insurance scheme includes 84% of people identified as HIV-

190   positive in all health insurance schemes, the uncertainty in this extrapolation is therefore quite

191   low.

192   Third, uncertainty lies in the number of newly diagnosed HIV cases that will be observed in the

193   future. This source of uncertainty has been taken into account by considering several

194   scenarios (see aforementioned answer).

195

196   **H. Life Expectancy**

197   Using estimated mortality rates and life table method [3], we estimated life expectancy for

198   PLHIV on ART in France, by sex, age and ART initiation period. For the oldest open-ended

199   age group (≥80), data on follow-up care and deaths were scarce. Therefore, following other

200   studies [4,5], we obtained an estimate of the mortality rate for individual aged ≥80 by

201   multiplying the French general population mortality rate for individuals aged ≥80 by an average

202   standardized mortality ratio (SMR), representing the ratio between PLHIV mortality rate and

203   general population mortality rate. The average SMR was obtained by first calculating SMRs

204   for age groups 70-74 and 75-79 and then by averaging these two values.

205

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

207   **a.   Scenario 2 : status quo situation with a steady annual number of new HIV**

208   **cases over 2019-2030**

209   We found that the proportions of individuals who started ART more than 20 and 30 years ago

210   will increase over 2018-2030 (Figure S4), especially for older age groups. The overall

211   proportions of individuals who started ART ≥20 years (respectively, ≥30 years) will increase

212   from 27% to 39% (respectively, from <1% to 19%) for men, and from 21% to 42% (respectively,

213   from <1% to 17%) for women. In particular, among those aged ≥60, these proportions will

214   increase from 43% to 67 % (respectively, from 1% to 38 %) for men, and from 33% to 66%

215   (respectively, from <1% to 36%) for women. In consequence, median time since ART initiation

216   will increase, especially for older age groups. In particular, for individuals aged ≥60, it will

217   increase from 18.4 (interquartile range (IQR) 10.4 – 22.4) to 25.5 years (IQR 17.0 – 33.3) for

218   men, and from 15.2 (IQR 7.9-21.4) to 25.3 years (IQR 15.8 – 32.9) for women, while for those

219   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,

220   and from 11.0 (IQR 5.2-17.7) to 13.3 years (IQR 6.5 – 21.3) for women.

221   Of note, we estimated that, in 2030, 83,659 individuals (34% women) would have started ART

222   ≥20 years ago, i.e. before 2010, including 38,492 individuals (30% women) that would have

223   started ART ≥30 years ago - versus respectively 40,667 and 573 in 2018 – with the vast

224   majority of them being aged ≥60 (Figure 2). For those who would have started ART ≥20 years

225   ago, for men, 77% would be aged ≥60, 33% ≥70, 8% ≥80, and for women, 54% would be ≥60,

226   21% ≥70, 4% ≥80, while for those who would have started ART ≥30 years ago, for men, 89%

227   would be aged ≥60, 40% ≥70, 8% ≥80, and for women, 75% being aged ≥60, 29% ≥70, 6%

228   ≥80.

229

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

231   We found that proportions of individuals who started ART more than 20 and 30 years ago will

232   increase over 2018-2030 (Figure S5), especially for older age groups. The overall proportions

233   of individuals who started ART more than 20 years (respectively, ≥30 years) will increase from

234   27% to 49% (respectively, from <1% to 24%) for men, and from 21% to 51% (respectively,

235   from <1% to 20%) for women. In particular, among those aged ≥60, these proportions will

236   increase from 43% to 72% (respectively, from 1% to 41%) for men, and from 33% to 71%

237   (respectively, from <1% to 39%) for women. In consequence, median time since ART initiation

238   will increase, especially for older age groups. In particular, for individuals aged ≥60, it will

239   increase from 18.4 (interquartile range (IQR) 10.4 – 22.4) to 26.8 years (IQR 18.9 – 33.5) for

240   men, and from 15.2 (IQR 7.9-21.4) to 26.6 years (IQR 18.4 – 33.3) for women, while for those

241   aged <60, it will only increase from 9.8 (IQR 4.8 – 19.0) to 14.8 years (IQR 10.5 – 19.6) for

242   men, and from 11.0 (IQR 5.2-17.7) to 16.9 years (IQR 11.5 – 23.5) for women.

243   Of note, we estimated that, in 2030, 83,659 individuals (34% women) would have started ART

244   ≥20 years ago, i.e. before 2010, including 38,492 individuals (30% women) that would have

245   started ART ≥30 years ago - versus respectively 40,667 and 573 in 2018 – with the vast

246   majority of them being aged ≥60 (Figure 2). For those who would have started ART ≥20 years

247   ago, for men, 77% would be aged ≥60, 33% ≥70, 8% ≥80, and for women, 54% would be ≥60,

248   21% ≥70, 4% ≥80, while for those who would have started ART ≥30 years ago, for men, 89%

249   would be aged ≥60, 40% ≥70, 8% ≥80, and for women, 75% being aged ≥60, 29% ≥70, 6%

250   ≥80.

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266

267 **Table S1. Data from the French National Health Data System and the FHDH for the years**
268 **2017, 2018 and 2019 on the number of individuals living with diagnosed HIV and deaths**
269 **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, $(N_{a,t}^{F})$	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, $(D_{a,t}^{F})$
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

270 BLHIV: beneficiaries living with diagnosed HIV ;
271 *five age groups (18-34, 35-54, 55-64, 65-74, 75+) to comply with available statistics from
272 the French National Health Data System.

273 ** estimated as $\rho_{a,t} = \frac{N_{a,t}^{F}}{N_{a,t}}$.

274

275 **Table S2. Data from the French National Health Data System for the years 2017, 2018**
276 **and 2019 on the number of beneficiaries living with diagnosed HIV (BLHIV) and deaths**
277 **among them, stratified by age group.**
278

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

301 *five
302 age groups (18-34, 35-54, 55-64, 65-74, 75+) to comply with available statistics from the
303 French National Health Data System.
304 ** includes data from the general Social Security scheme as well as all other schemes;
305 *** estimated as $D_{a,t} = D'_{a,t} \frac{N'_{a,t}}{N_{a,t}}$
306

13

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

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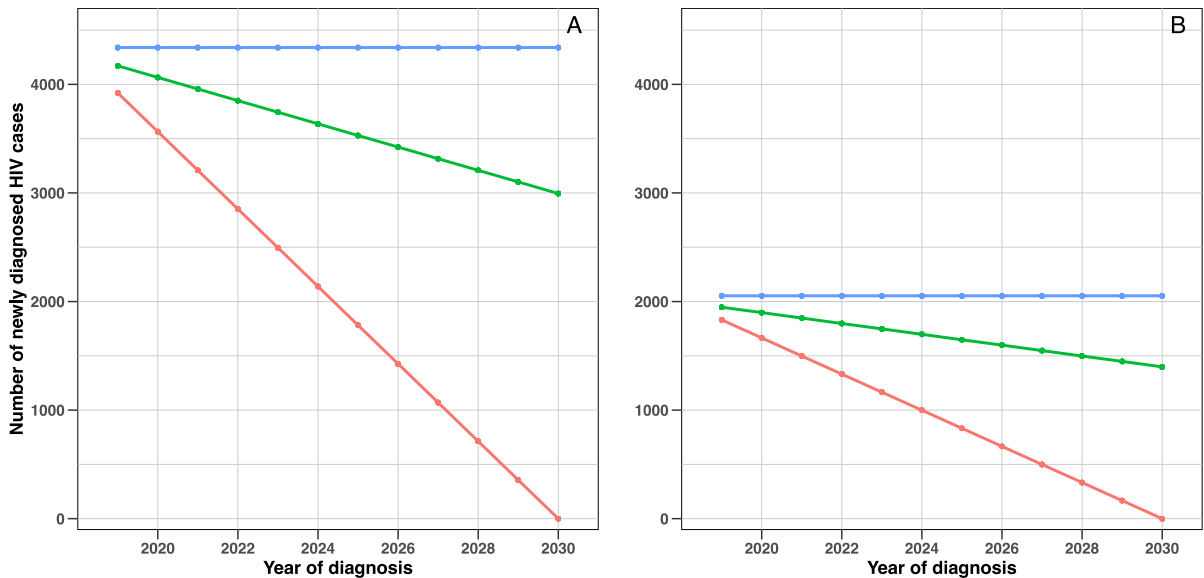
314 **Figure S2. Projected adult newly diagnosed HIV cases by age group at diagnosis over**

315 **2019-2030 for men (A) and for women (B).**

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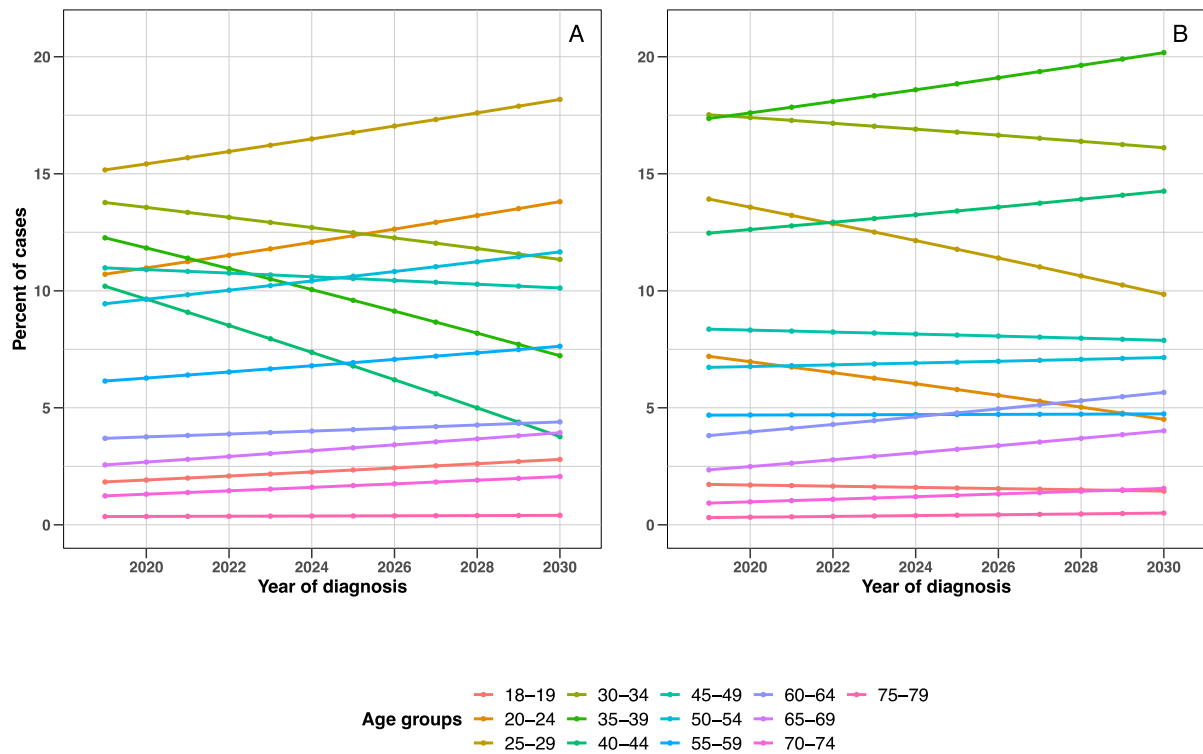
319 **Figure S3. Mortality rates of adults aged ≥20 years living with diagnosed HIV in**
320 **2018, according to age and ART initiation period, for men (A) and women (B).**

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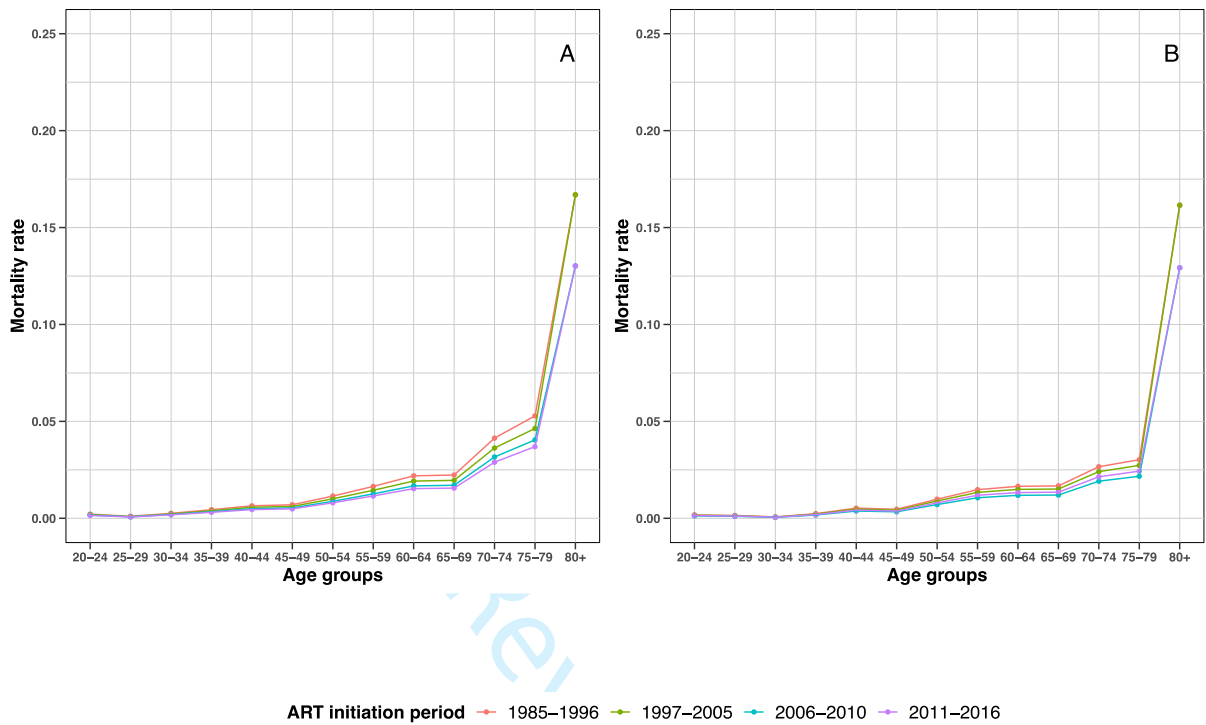
324 **Figure S4. Numbers and age distributions of adults aged ≥18 years living with**
325 **diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in**
326 **years):** for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D)
327 under scenario 2 (i.e. status quo situation with a steady annual number of new HIV cases over
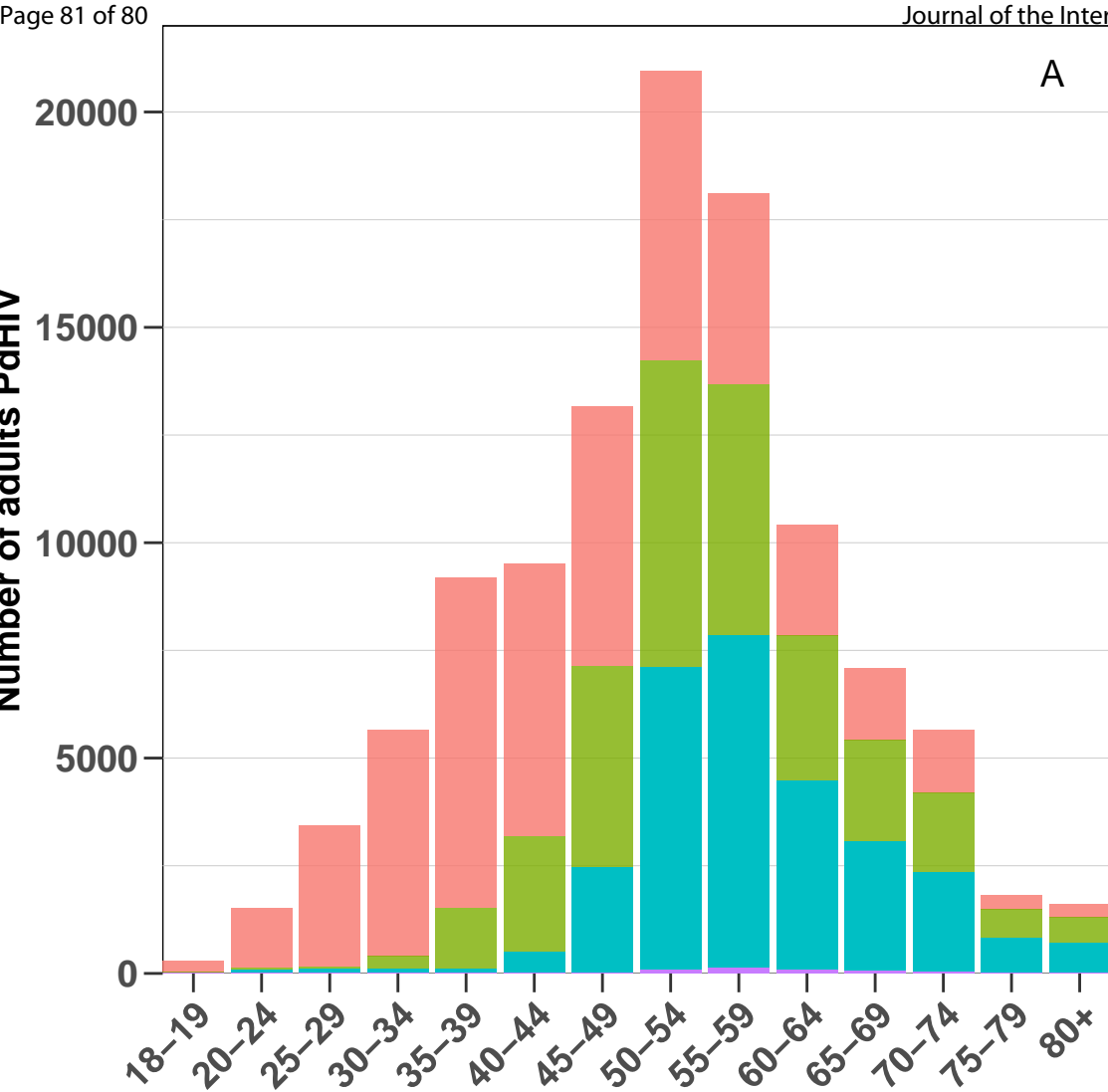328 2019-2030).
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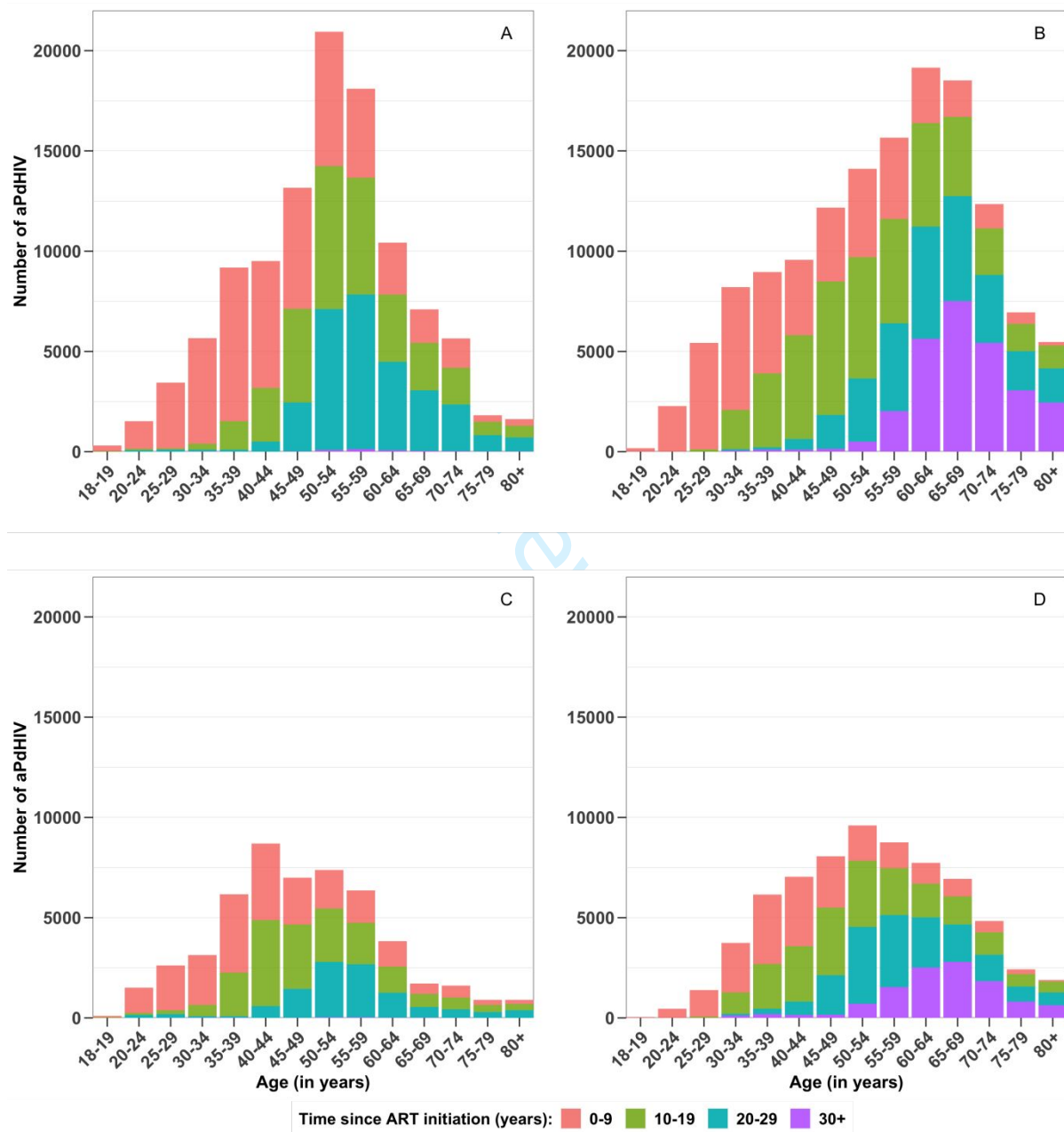
331 **Figure S5. Numbers and age distributions of adults aged ≥18 years living with**
332 **diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in**
333 **years):** for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D)
334 under scenario 3 (i.e. epidemic elimination with zero new HIV cases in 2030).

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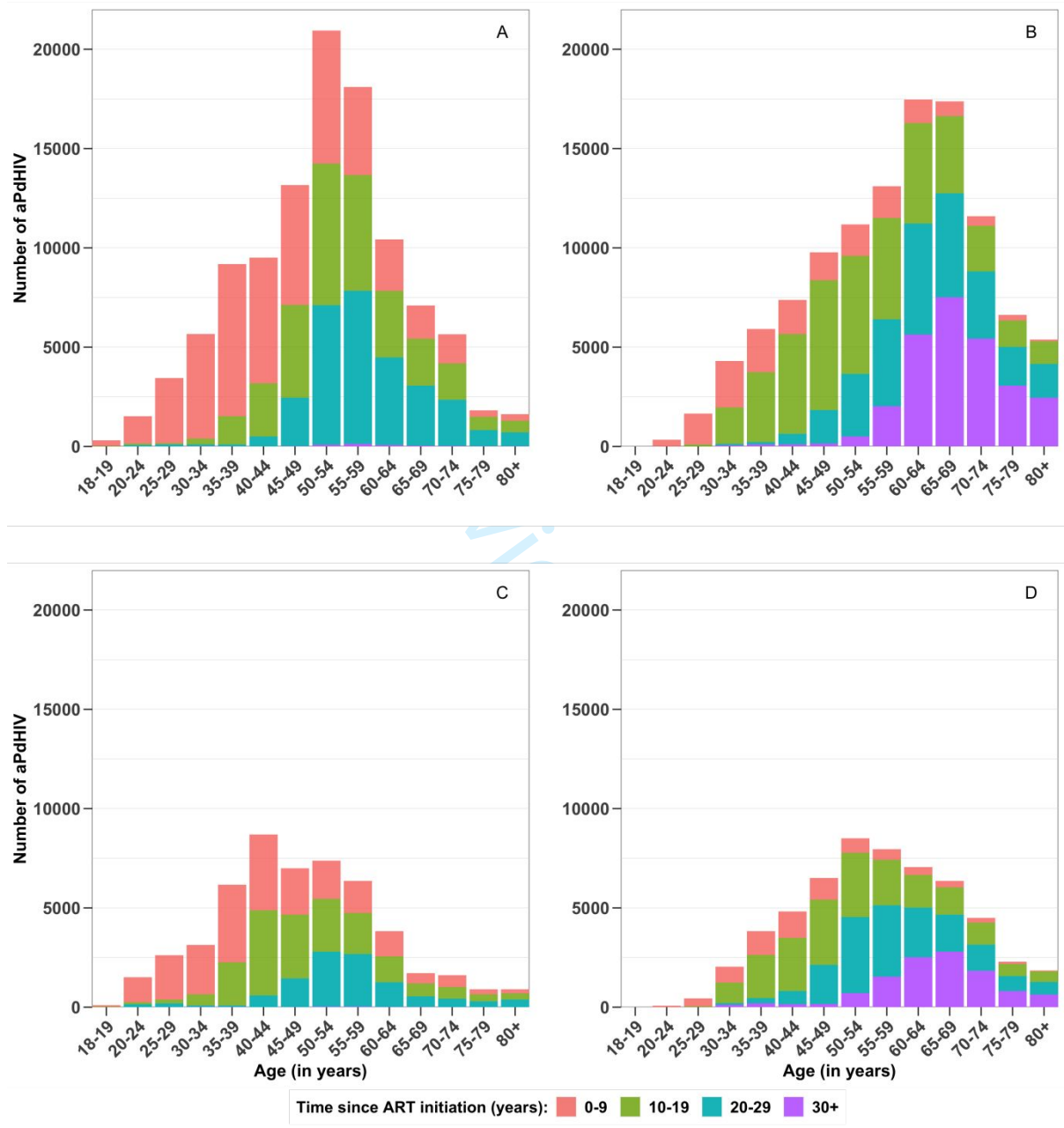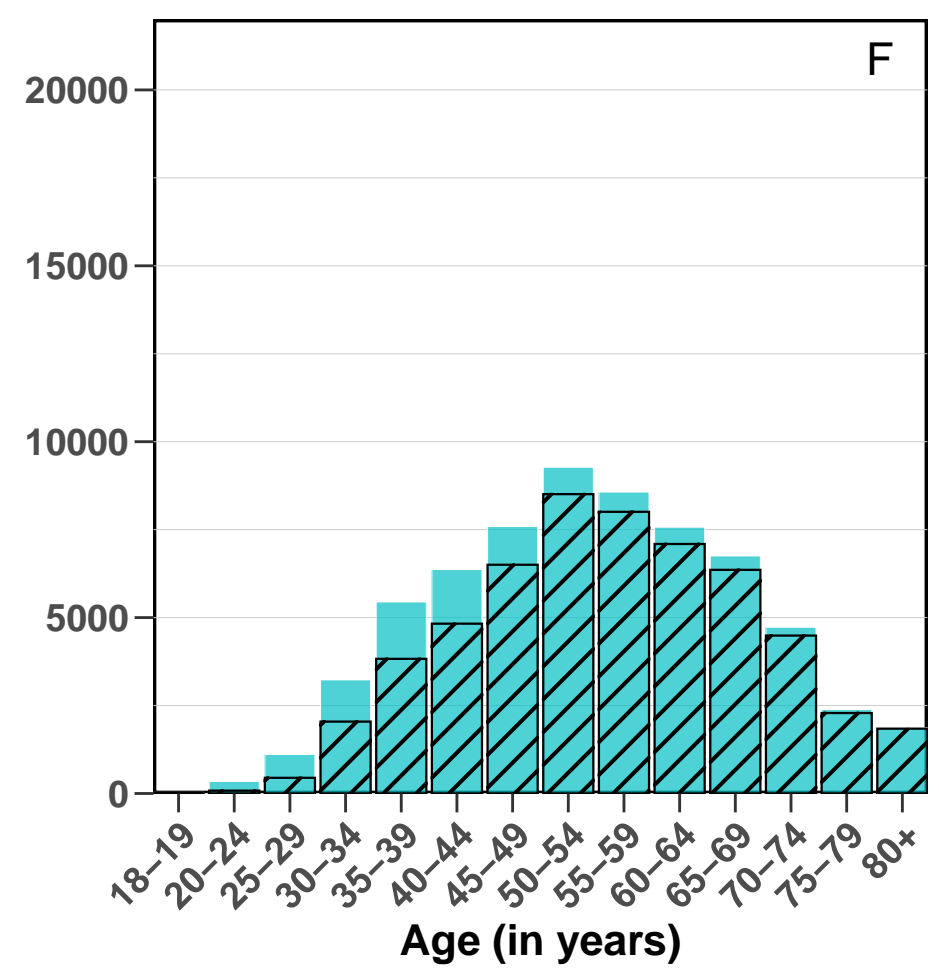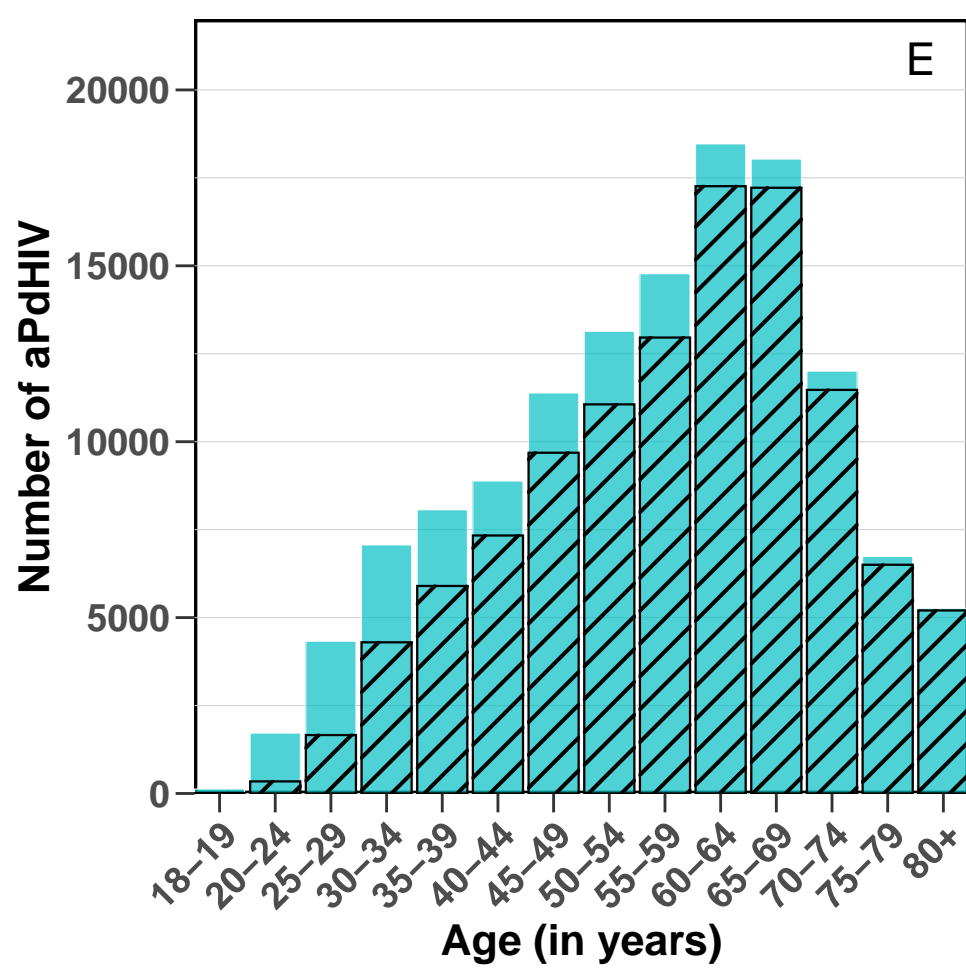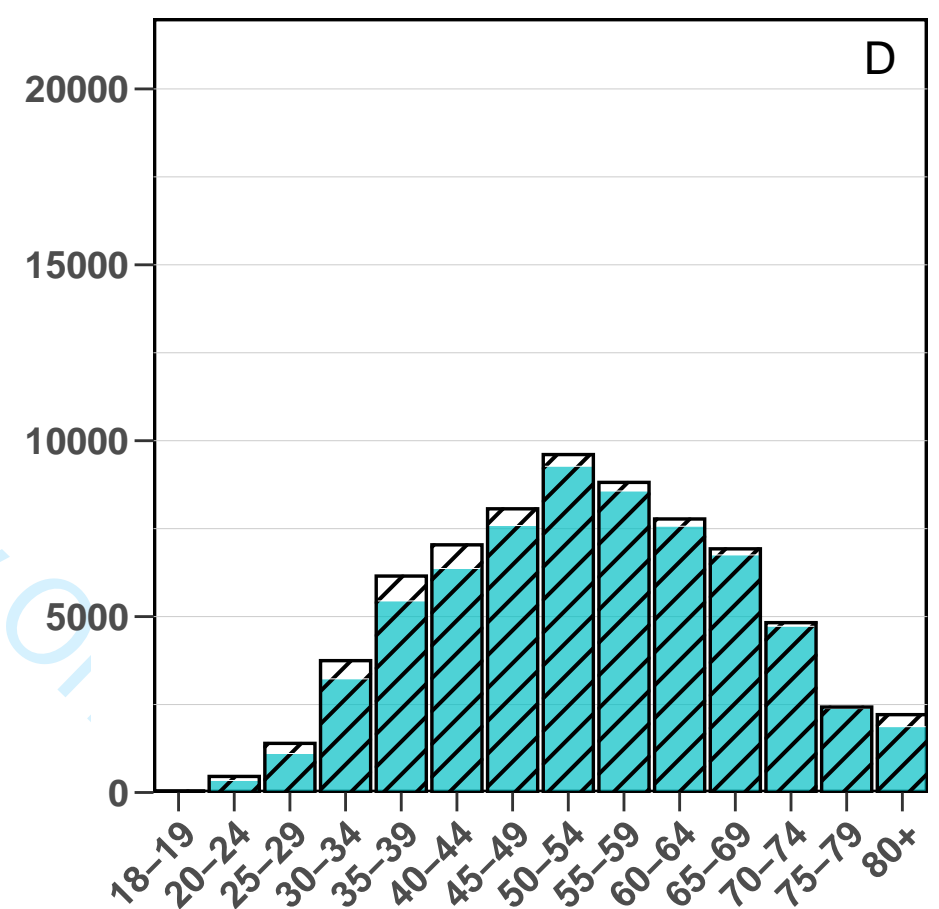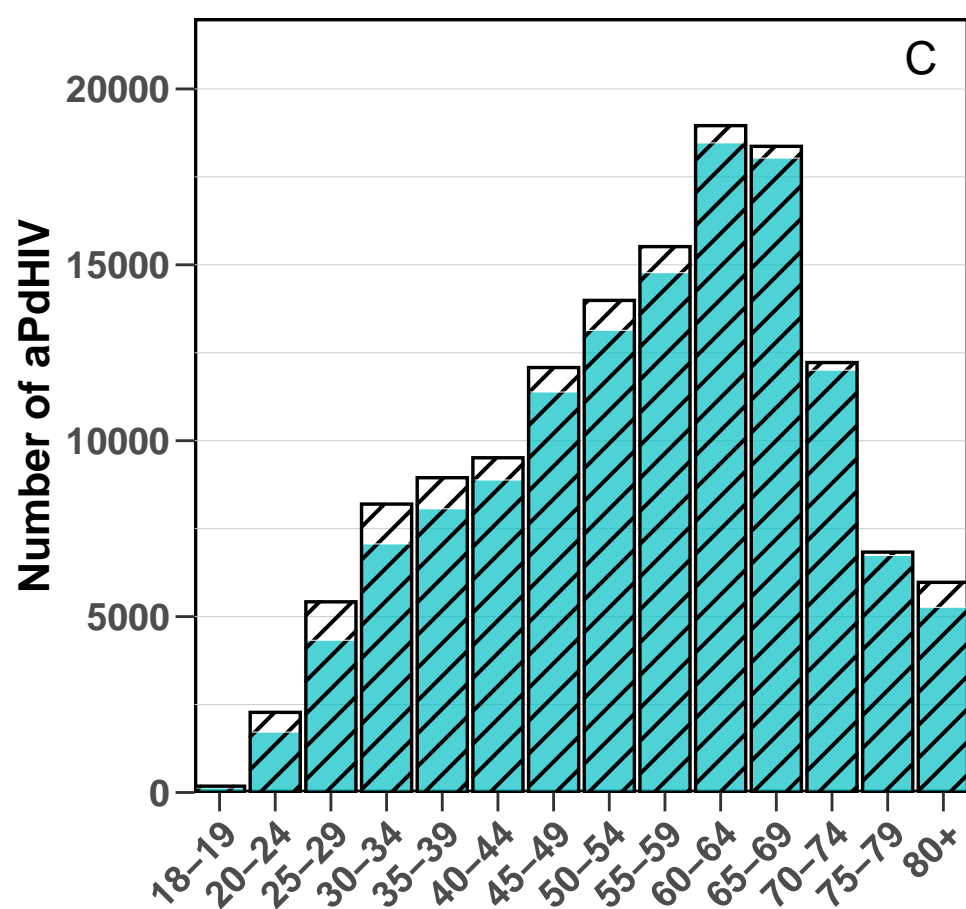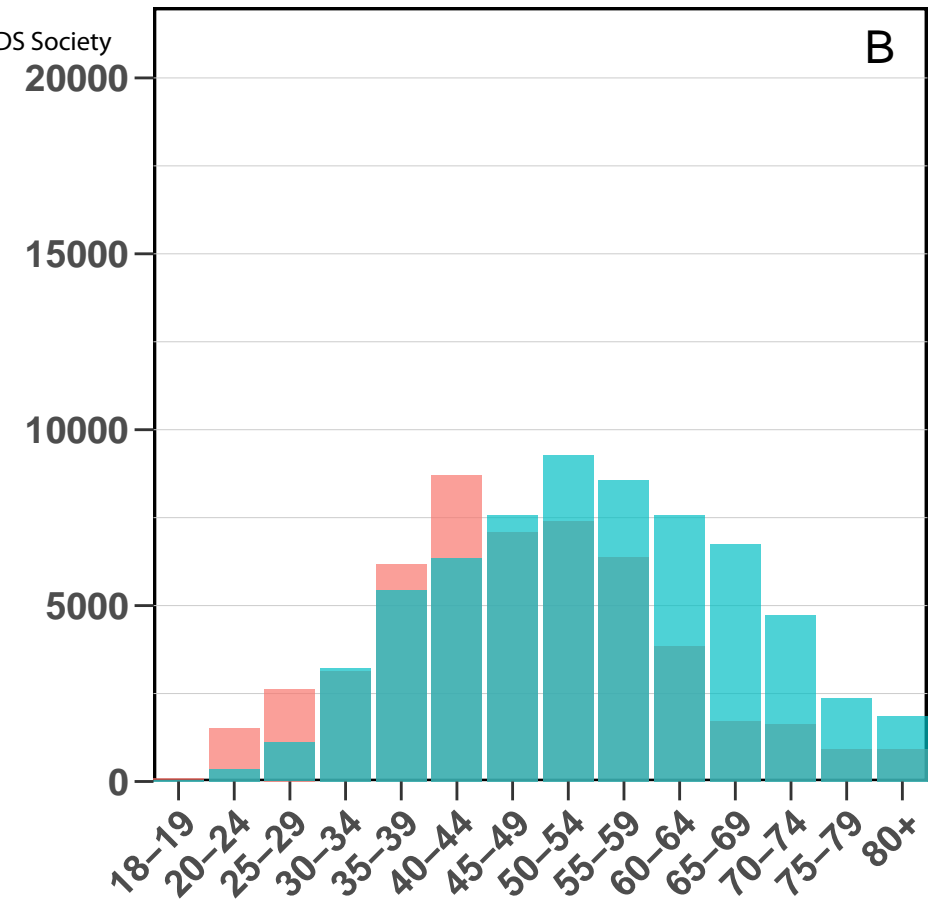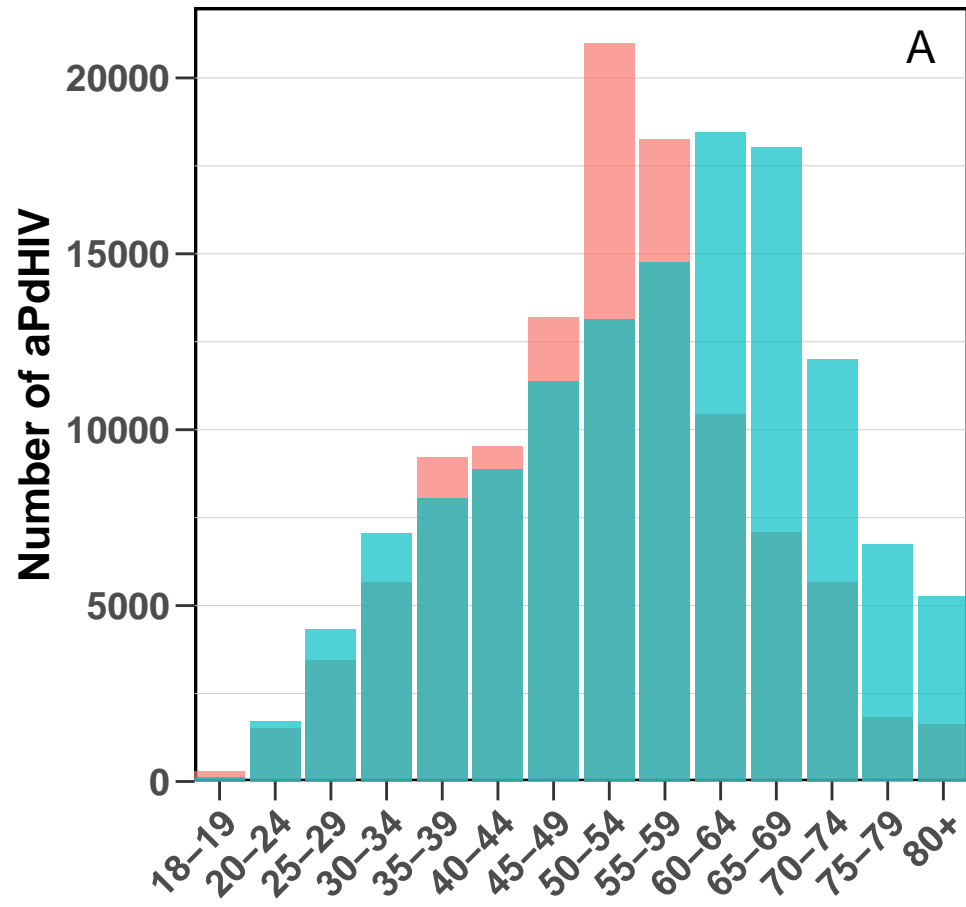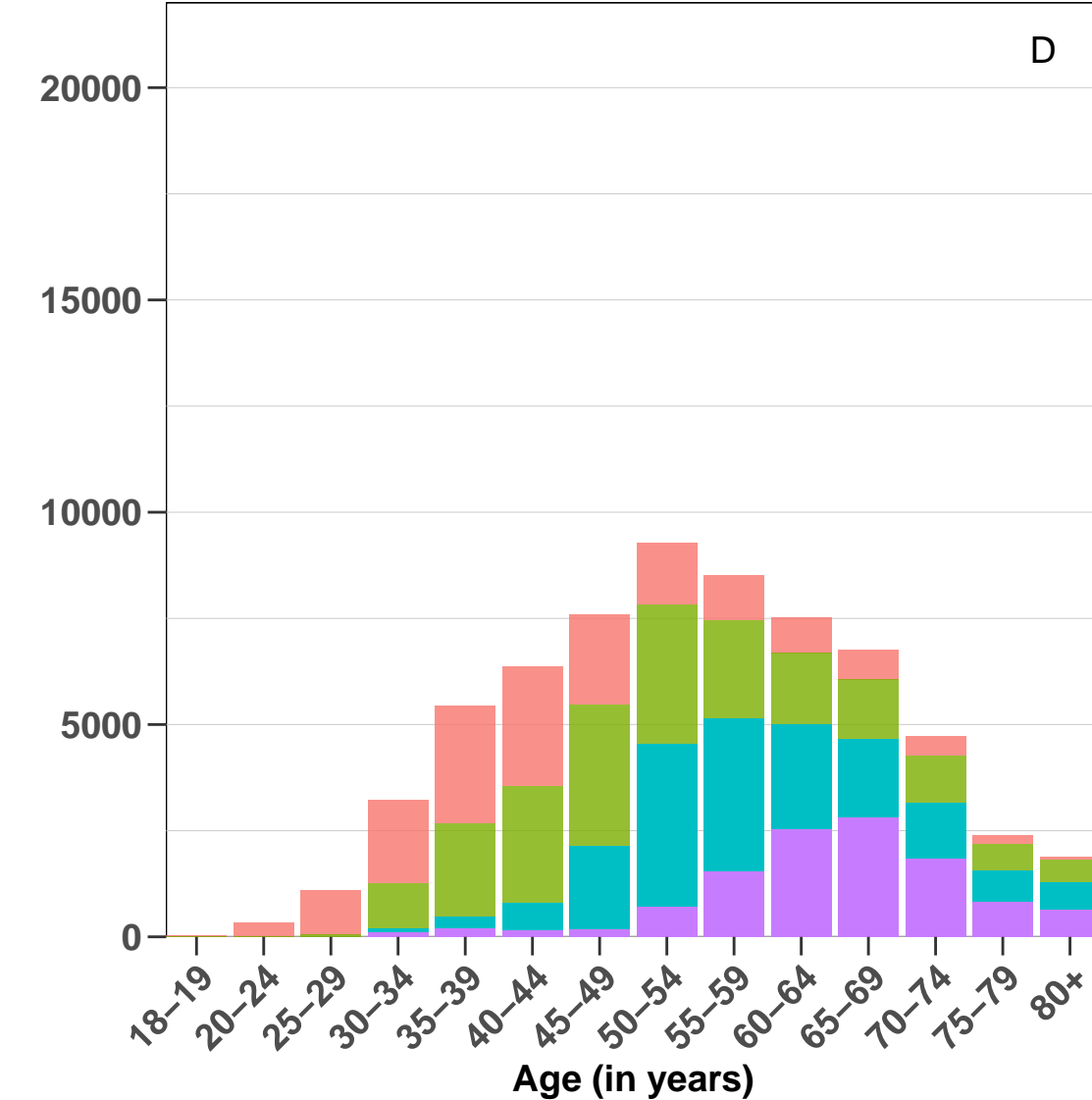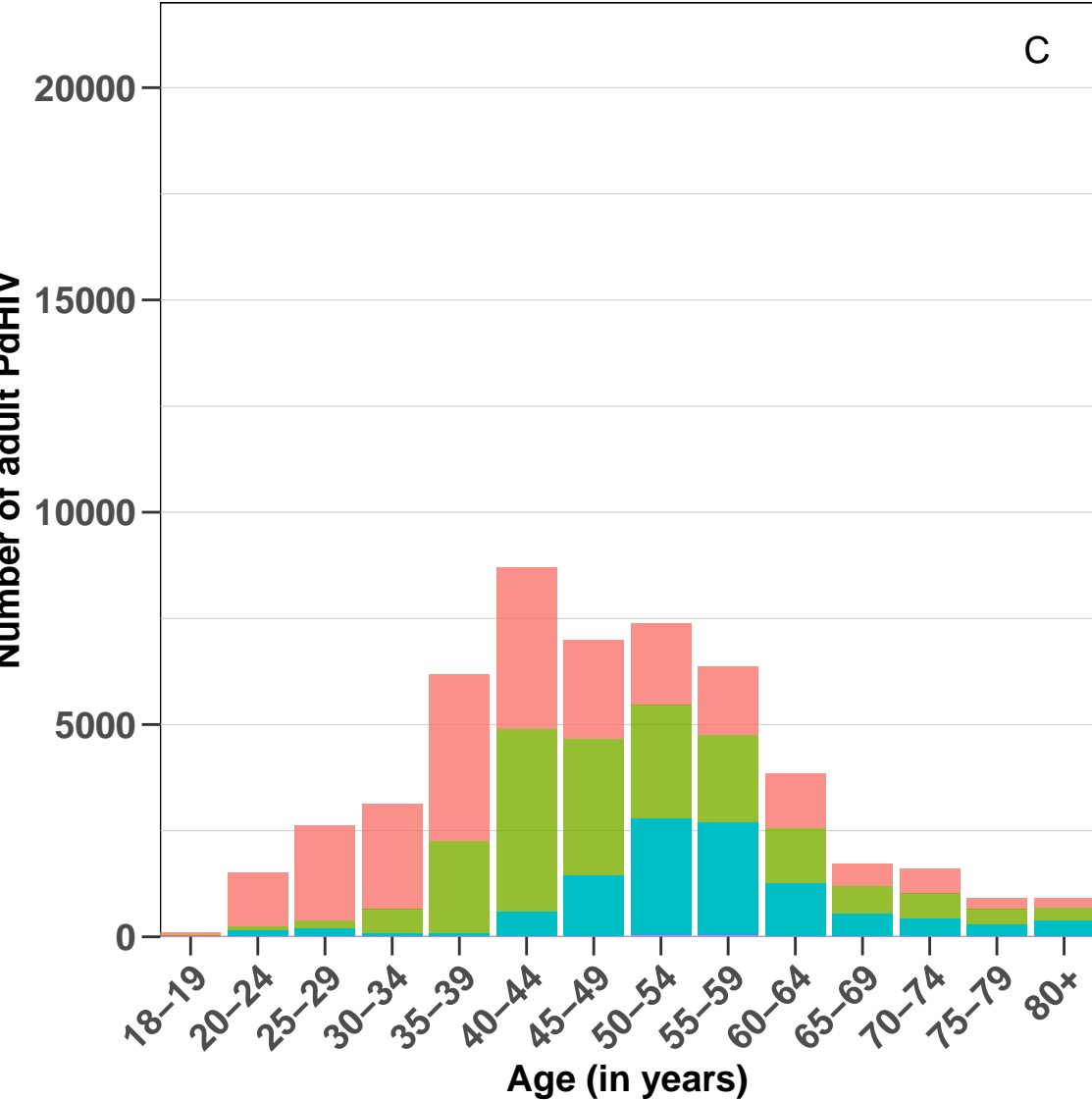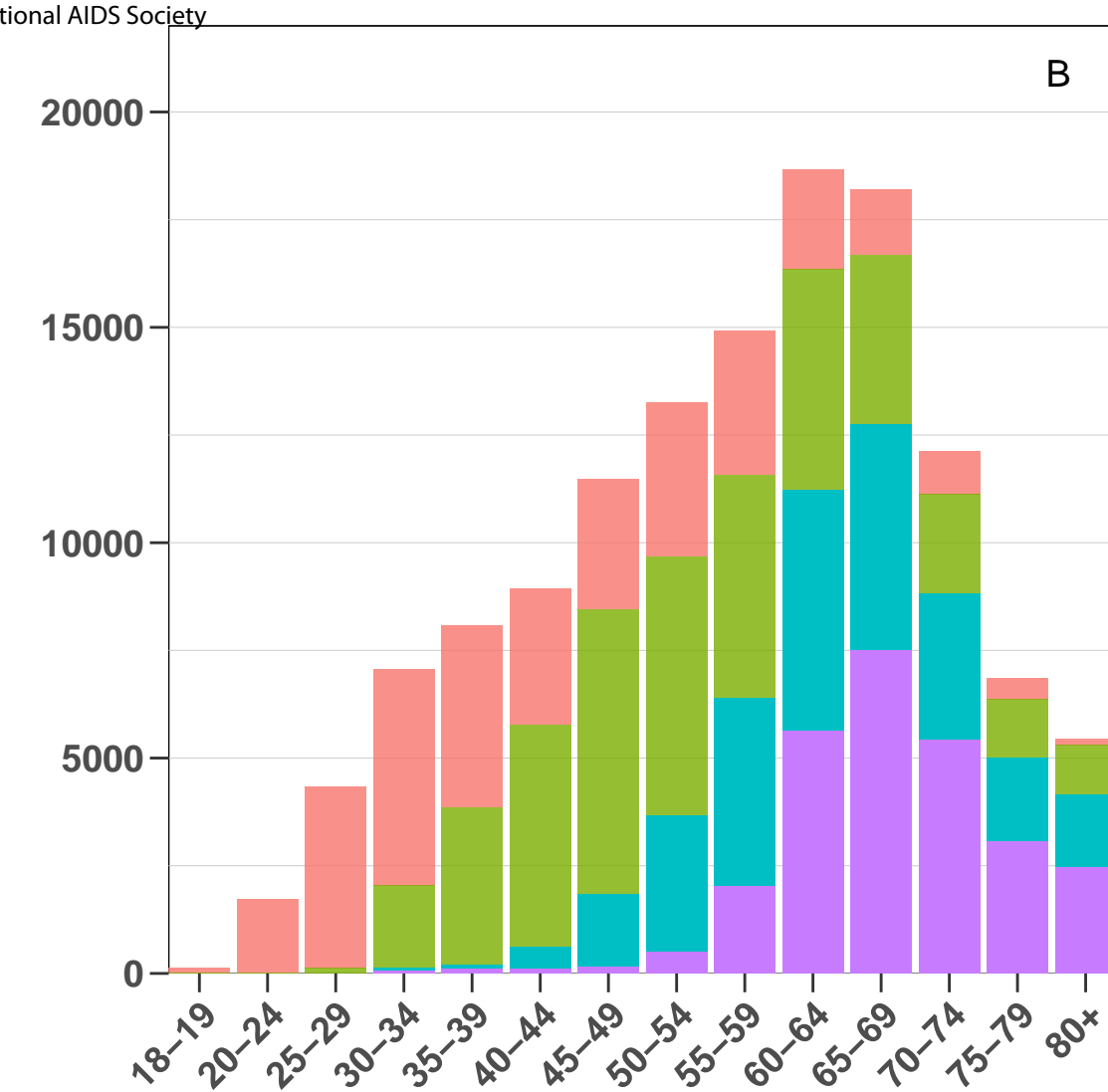
Time since ART initiation (years): ■ 0–9 ■ 10–19 ■ 20–29 ■ 30+