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

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| Abstract: | <p>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.</p> <p>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.</p> |

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| | <p>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.</p> <p>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.</p> |
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1 **Projection of age of individuals living with HIV and time since ART**
2 **initiation in 2030: estimates for France**

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30

For Review Only

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.

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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

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.

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 CERES (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.

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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

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 $\sim 83,400$ individuals ($\sim 28\%$ women) aged ≥ 60
236 and $\sim 33,100$ individuals aged ≥ 70 ($\sim 27\%$ women); in comparison, in 2018, it was
237 respectively 35,715 ($\sim 25\%$ women) and 12,582 ($\sim 27\%$ 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 <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.

261 Discussion

262 We projected that by 2030, the HIV epidemic in France would be growing, most likely by
263 more than 20%, and **ageing**, with a doubling of the proportion of individuals aged ≥ 60 and
264 ≥ 70 . More than two-third of aPLdHIV would be aged ≥ 50 , $\sim 50\%$ aged ≥ 60 , and $\sim 20\%$
265 aged ≥ 70 . Interestingly, whatever the scenario considered for the epidemic dynamics over
266 2019-2030, we estimated that $\sim 83,000$ individuals will be aged ≥ 60 in 2030, including
267 $\sim 33,000$ aged ≥ 70 . Our results are in line with studies forecasting the age structure of HIV
268 population in other high-income countries [10,11,13,14,16]. It was estimated that the
269 proportion of PLHIV on ART aged ≥ 50 would be 73% in 2030 in the Netherlands [13] and
270 54% in the United States (US) [16], and $\sim 75\%$ in 2035 in the US and in Italy [14]. Bretaña
271 et al. [10] performed projections for Australia, considering three scenarios for the future
272 number of newly diagnosed cases over 2018-2027. **They highlighted that, whatever the**
273 **scenario, the age distribution of PLHIV would have its highest peak in the 55-59 age group**
274 **in 2027, which aligns with our findings of highest peak in the 60-64 age group for men,**
275 **50-54 for women.**

276
277 In addition, our study predicts that in 2030, in France, there will be more than 38,000
278 individuals who would have started ART more than 30 years ago (i.e. before 2000), with
279 most of them being aged ≥ 60 (85%, $\sim 33,000$), 37% aged ≥ 70 ($\sim 14,000$) and 8% aged ≥ 80
280 ($\sim 3,000$). These individuals were thus exposed to the first generation of nucleoside
281 reverse transcriptase inhibitors (AZT, D4T) and protease inhibitors, which have been
282 associated with **body morphology changes** and cardiovascular diseases [24,25]. In
283 addition, ART duration and time living with diagnosed HIV infection have been associated
284 with increased risk of multimorbidity [7,9], but also with psychological morbidity and
285 lower quality of life [26,27], which should be considered as part as integrated HIV care.

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.

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367

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383

384

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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 C04-FHDH) who had at least one follow-up clinical visit between January 1, 2017 and December 31, 2019. *Values for the general population were obtained from the Human Mortality Database (<https://www.mortality.org>)

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

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

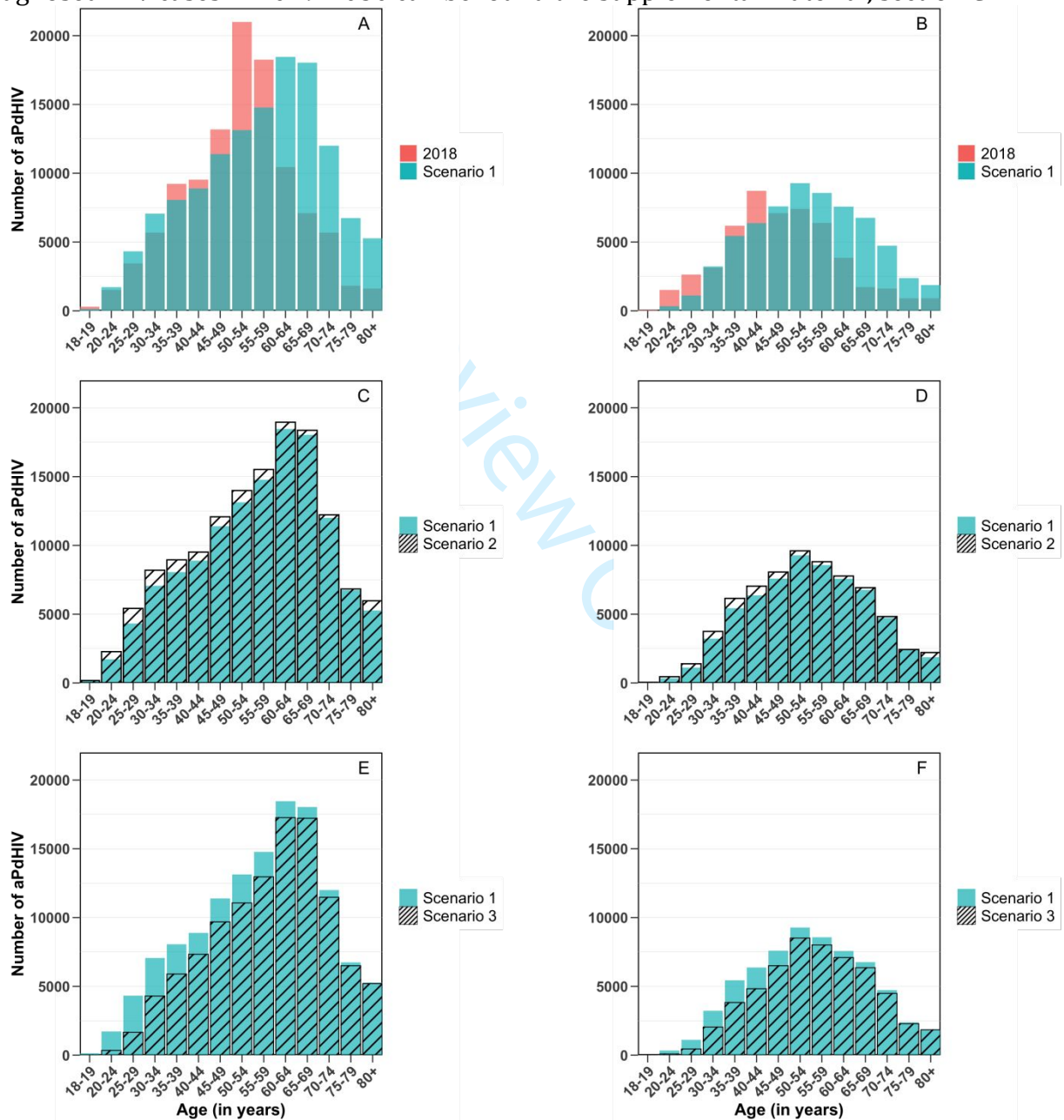
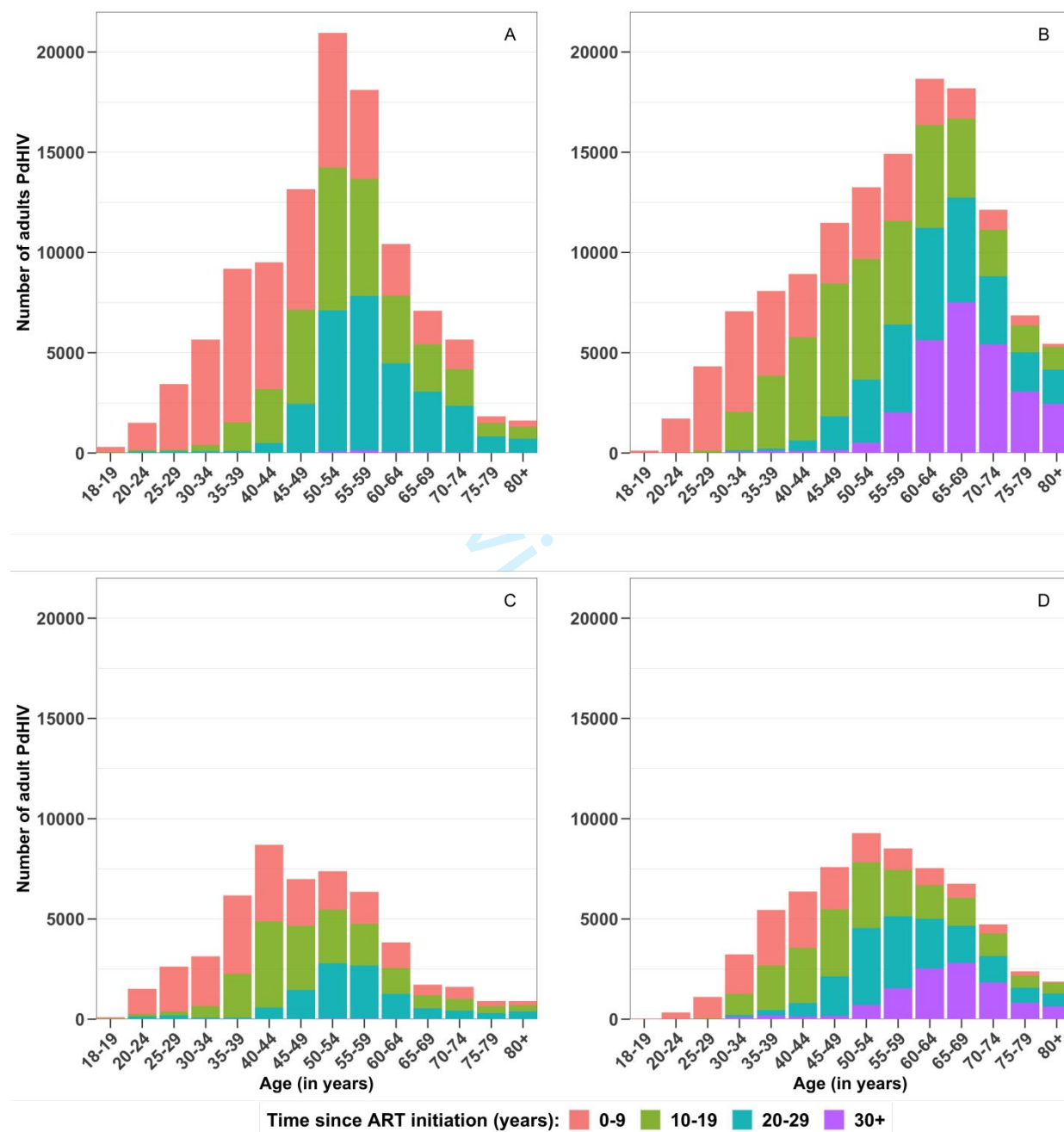


Figure 2. Numbers and age distributions of adults aged ≥ 18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D) for scenario 1 (i.e. 30% decrease in newly diagnosed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



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

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30

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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.

For Review Only

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

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

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.

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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

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 $\sim 83,400$ individuals ($\sim 28\%$ women) aged ≥ 60
236 and $\sim 33,100$ individuals aged ≥ 70 ($\sim 27\%$ women); in comparison, in 2018, it was
237 respectively 35,715 ($\sim 25\%$ women) and 12,582 ($\sim 27\%$ 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 <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.

261 Discussion

262 We projected that by 2030, the HIV epidemic in France would be growing, most likely by
263 more than 20%, and ageing, with a doubling of the proportion of individuals aged ≥ 60 and
264 ≥ 70 . More than two-third of aPLdHIV would be aged ≥ 50 , $\sim 50\%$ aged ≥ 60 , and $\sim 20\%$
265 aged ≥ 70 . Interestingly, whatever the scenario considered for the epidemic dynamics over
266 2019-2030, we estimated that $\sim 83,000$ individuals will be aged ≥ 60 in 2030, including
267 $\sim 33,000$ aged ≥ 70 . Our results are in line with studies forecasting the age structure of HIV
268 population in other high-income countries [10,11,13,14,16]. It was estimated that the
269 proportion of PLHIV on ART aged ≥ 50 would be 73% in 2030 in the Netherlands [13] and
270 54% in the United States (US) [16], and $\sim 75\%$ in 2035 in the US and in Italy [14]. Bretaña
271 et al. [10] performed projections for Australia, considering three scenarios for the future
272 number of newly diagnosed cases over 2018-2027. They highlighted that, whatever the
273 scenario, the age distribution of PLHIV would have its highest peak in the 55-59 age group
274 in 2027, which aligns with our findings of highest peak in the 60-64 age group for men,
275 50-54 for women.

276
277 In addition, our study predicts that in 2030, in France, there will be more than 38,000
278 individuals who would have started ART more than 30 years ago (i.e. before 2000), with
279 most of them being aged ≥ 60 (85%, $\sim 33,000$), 37% aged ≥ 70 ($\sim 14,000$) and 8% aged ≥ 80
280 ($\sim 3,000$). These individuals were thus exposed to the first generation of nucleoside
281 reverse transcriptase inhibitors (AZT, D4T) and protease inhibitors, which have been
282 associated with body morphology changes and cardiovascular diseases [24,25]. In
283 addition, ART duration and time living with diagnosed HIV infection have been associated
284 with increased risk of multimorbidity [7,9], but also with psychological morbidity and
285 lower quality of life [26,27], which should be considered as part as integrated HIV care.

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.

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363 2020), and Janssen-Cilag (2020), outside the submitted work.

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

367

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378 licence has been applied by the authors to the present document and will be applied to all
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383

384

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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 C04-FHDH) who had at least one follow-up clinical visit between January 1, 2017 and December 31, 2019. *Values for the general population were obtained from the Human Mortality Database (<https://www.mortality.org>)

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

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

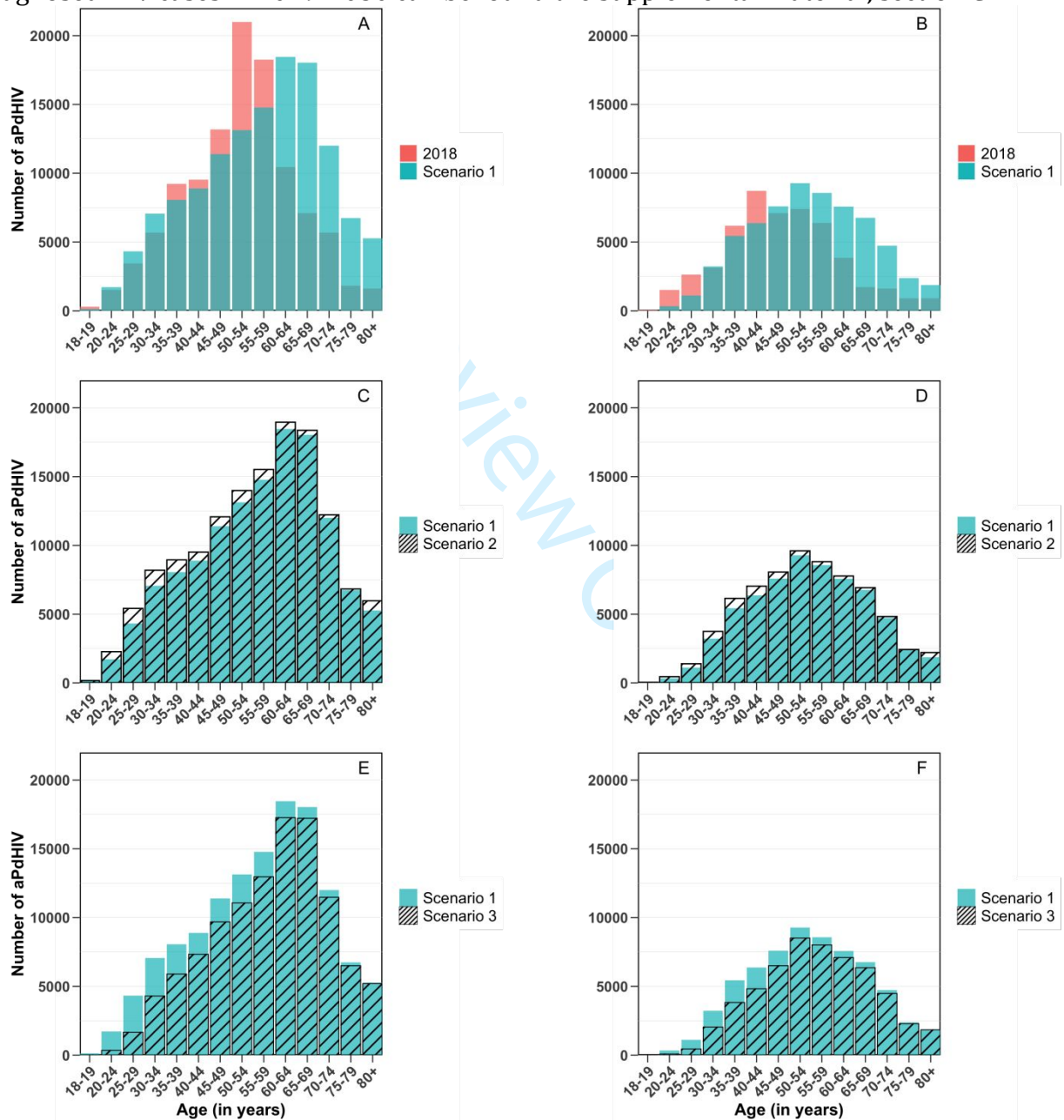
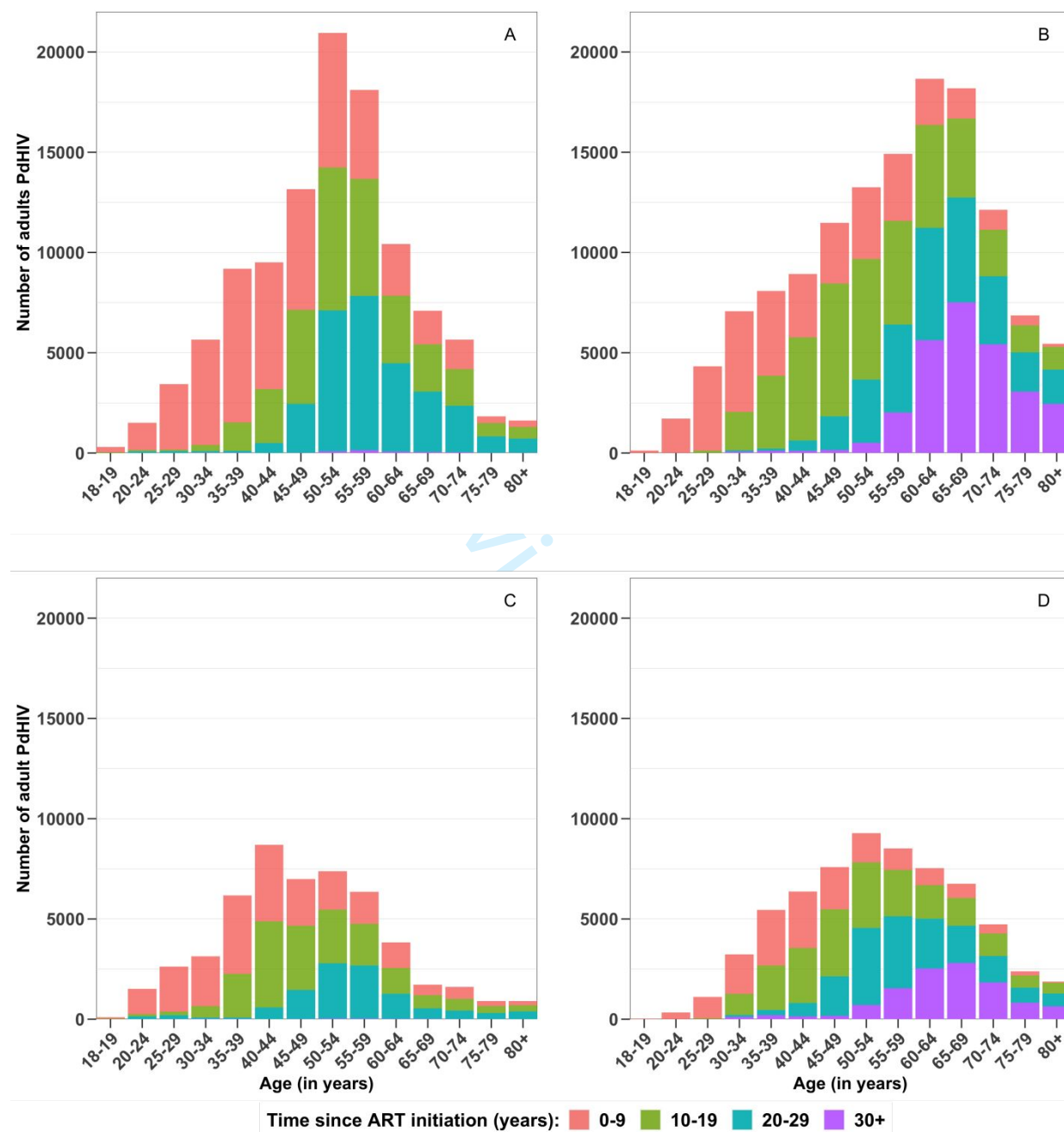


Figure 2. Numbers and age distributions of adults aged ≥ 18 years living with diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D) for scenario 1 (i.e. 30% decrease in newly diagnosed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



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.

44

45 **B. Extracting the date of ART initiation of individuals living with diagnosed HIV in**
46 **2018**

47 We used data from the EGB and the FHDH cohort to determine for each individual living with
48 diagnosed HIV in 2018 his/her date of ART initiation. These two data sources complement
49 each other as follows. On one hand, information on the date of ART initiation in EGB is not
50 complete (and less complete than in the FHDH cohort), since EGB was created in 2005, with
51 retrospective care consumption data from 2004 only, while FHDH data are available since
52 1985. On the other hand, as with any patient cohort, FHDH collects information on individuals
53 who are engaged in care but it loses track of patients who interrupt HIV care, whereas EGB
54 includes all patients, whether they are engaged in care or not.

55

56 Therefore, individuals living with diagnosed HIV in 2018 were split into two groups, according
57 to whether they were engaged in care in 2018 or not. For individuals who were engaged in
58 care in 2018, we extracted the date of ART initiation from FHDH, and defined five periods of
59 ART initiation (1985-1996, 1997-2005, 2006-2010, 2011-2016 and ≥ 2017). For individuals who
60 were not engaged in care in 2018, we extracted the date of ART initiation from EGB, and
61 defined only four periods of ART initiation, because of shorter data collection period (< 2006 ,
62 2006-2010, 2011-2016 and ≥ 2017). For both groups, we assumed that individuals who had
63 not initiated ART in 2018 would do so in 2019.

64 To identify the two groups (engaged in care in 2018 or not), we proceeded as follows. In a first
65 step, we applied the set of criteria described in section A over the years 2014-2018, and as a
66 second step, we applied the same set of criteria but only for the year 2018. Individuals identified
67 with the first step correspond to the whole population of individuals living with diagnosed HIV
68 in 2018 (engaged in care in 2018 or not) while individuals identified with the second step only
69 correspond to those engaged in care in 2018. Then, from individuals identified in the first step
70 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

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):

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

122 where $N_{a,t}^F$ 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:

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

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 :

$$141 \quad \delta_{a,t} = \rho_{a,t} \frac{D_{a,t}}{D_{a,t}^F} \quad (3)$$

142 where $D_{a,t}^F$ 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

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

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 (<i>t</i>) | Age group* (<i>a</i>) | 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.**

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

*five

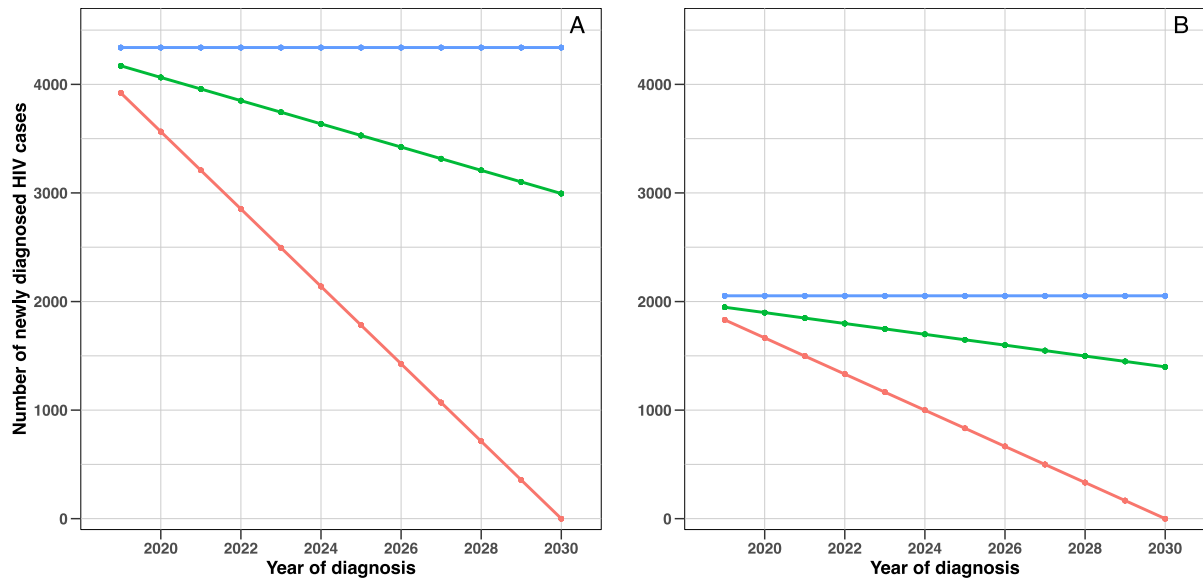
302 age groups (18-34, 35-54, 55-64, 65-74, 75+) to comply with available statistics from the
 303 French National Health Data System.

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

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).

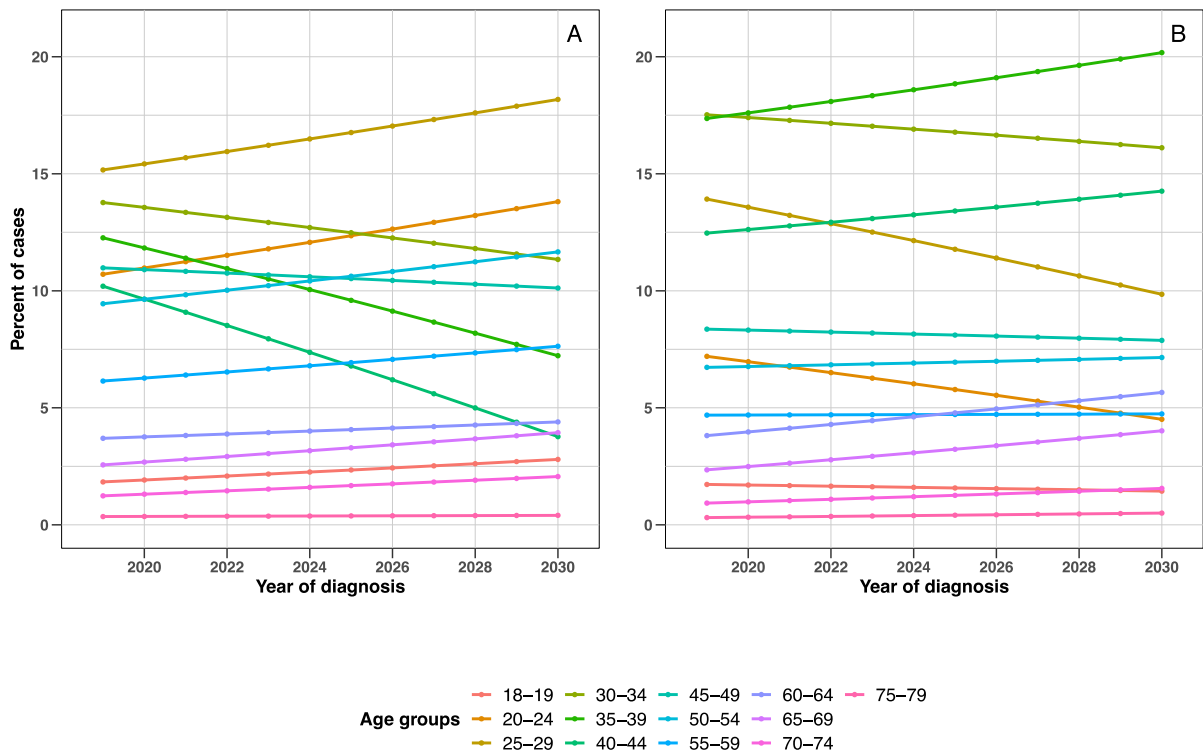


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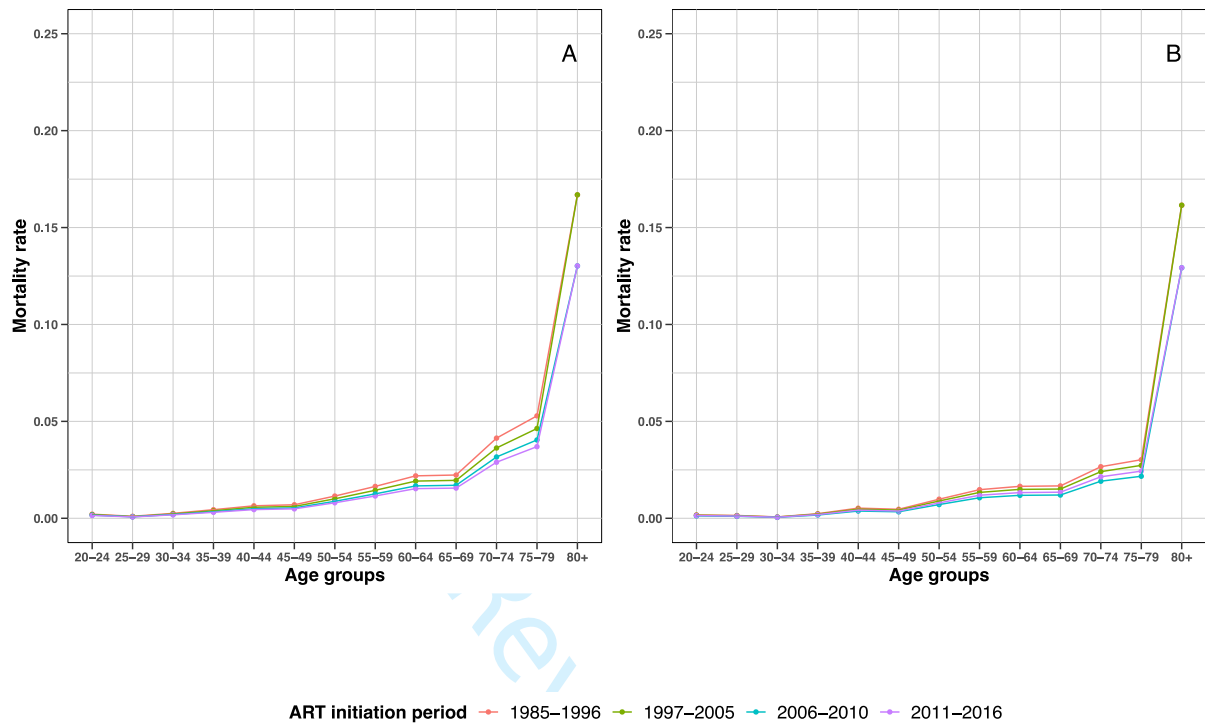
314 **Figure S2. Projected adult newly diagnosed HIV cases by age group at diagnosis over**
 315 **2019-2030 for men (A) and for women (B).**



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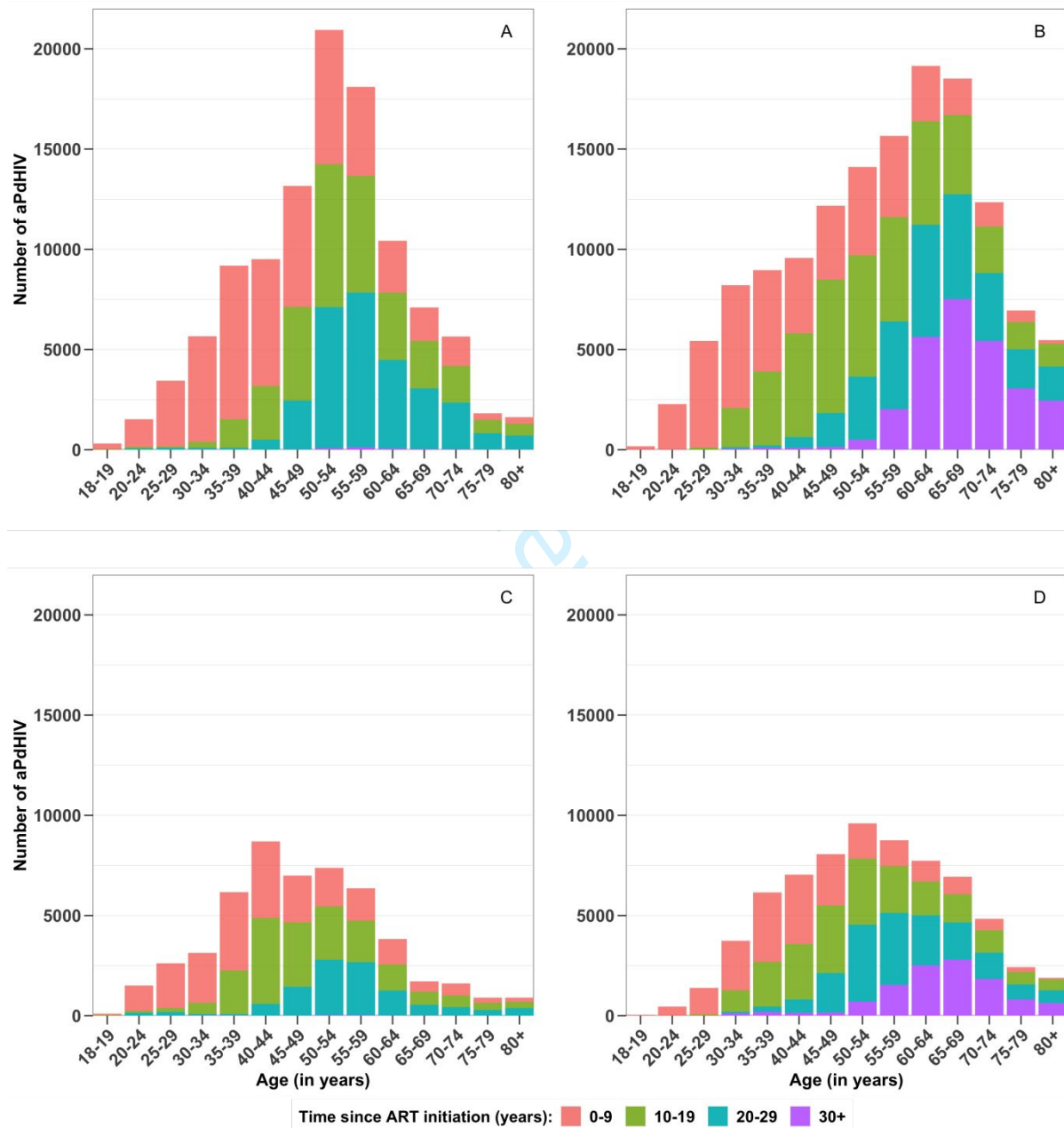
319 **Figure S3. Mortality rates of adults aged ≥ 20 years living with diagnosed HIV in**
 320 **2018, according to age and ART initiation period, for men (A) and women (B).**
 321



322

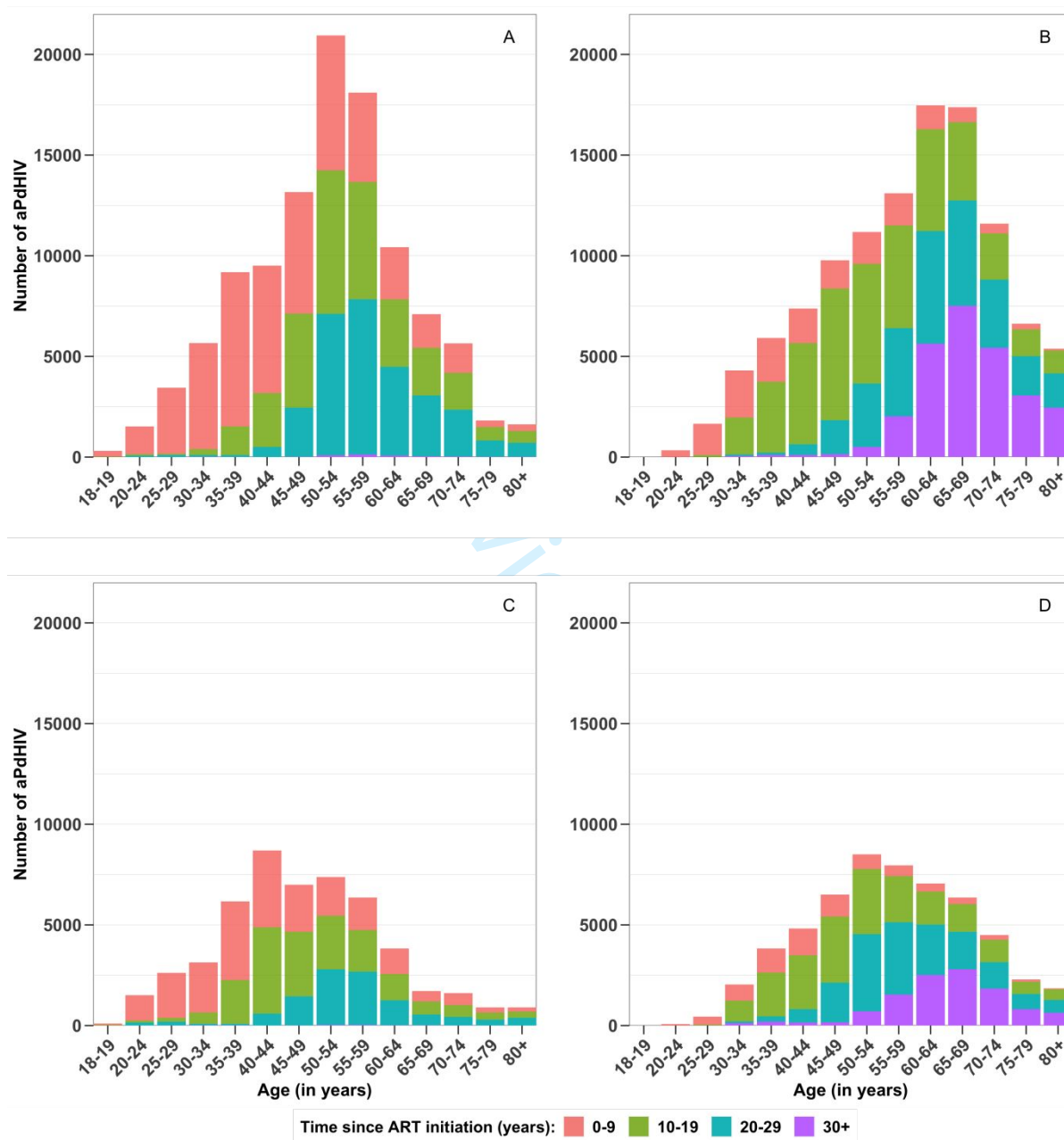
323

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).**
 329

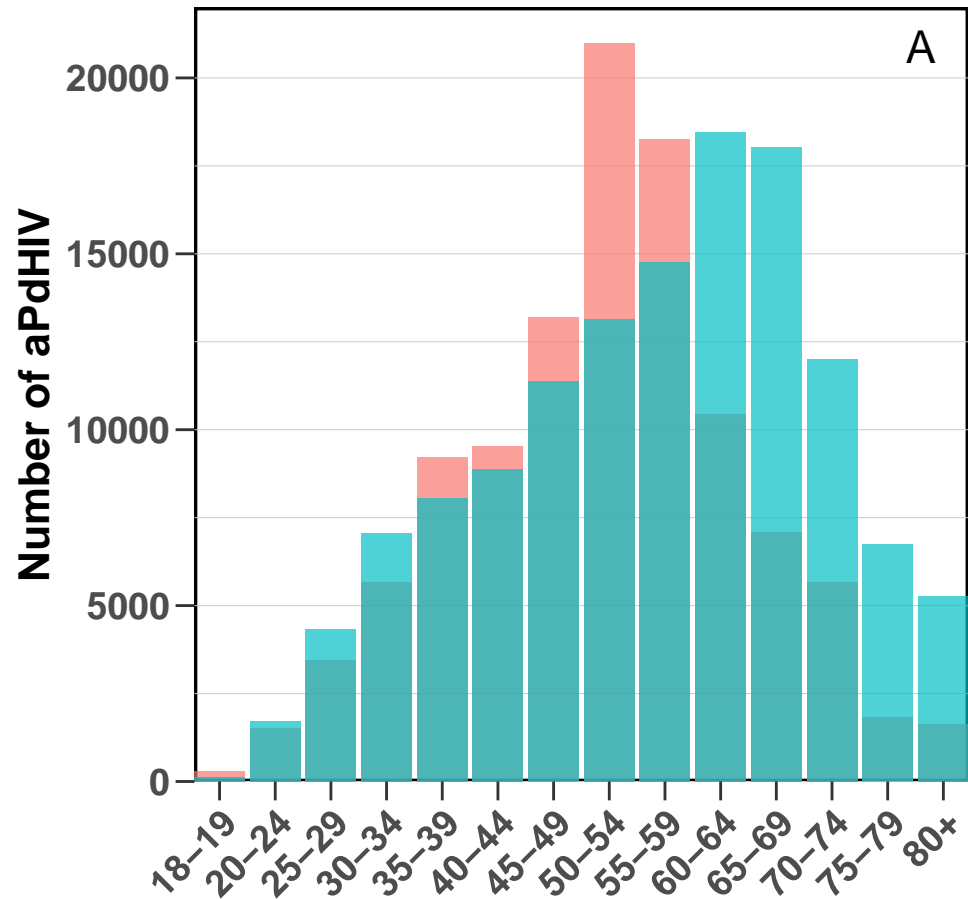


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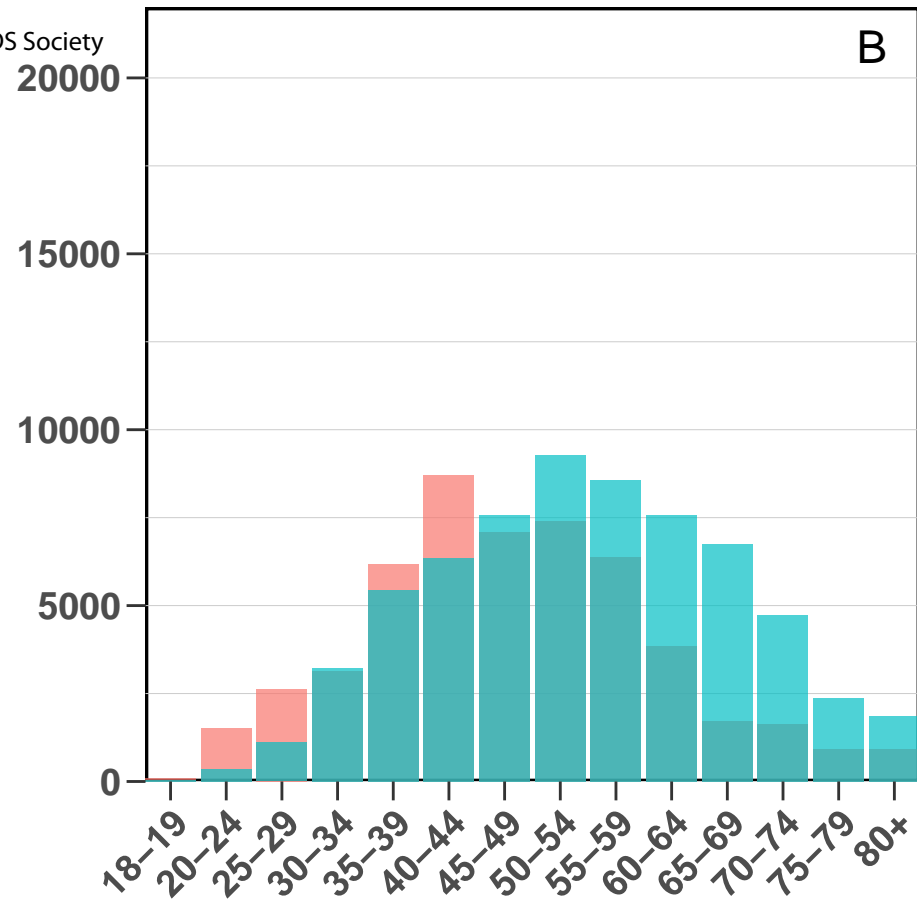
331 **Figure S5. Numbers and age distributions of adults aged ≥18 years living with**
 332 **diagnosed HIV (aPLdHIV) in 2018 and 2030, stratified by time since ART initiation (in**
 333 **years): for men (A and B) and women (C and D) in 2018 (A and C) and in 2030 (B and D)**
 334 **under scenario 3 (i.e. epidemic elimination with zero new HIV cases in 2030).**
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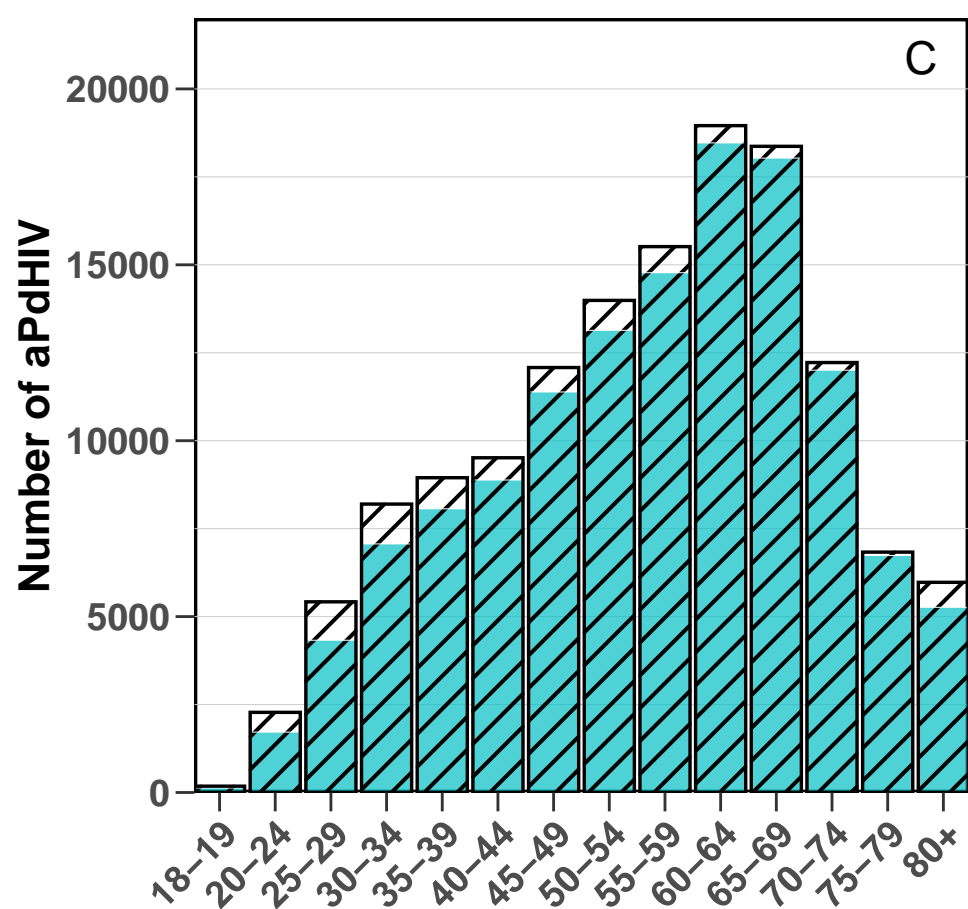
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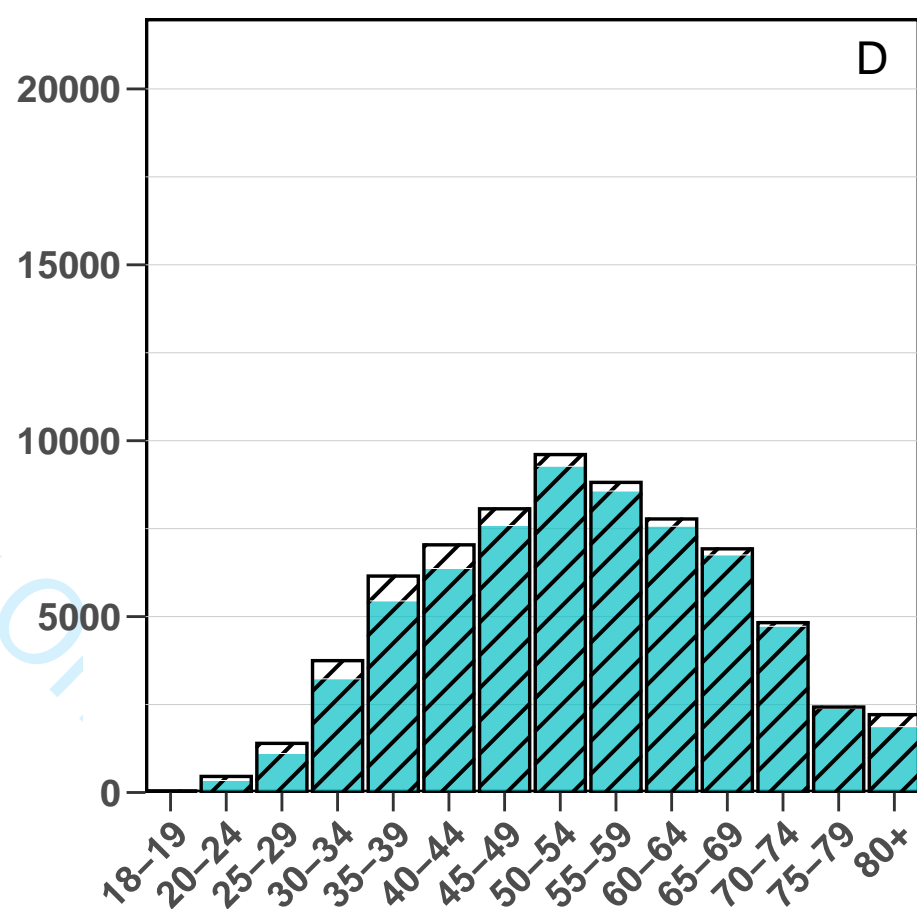
2018
Scenario 1



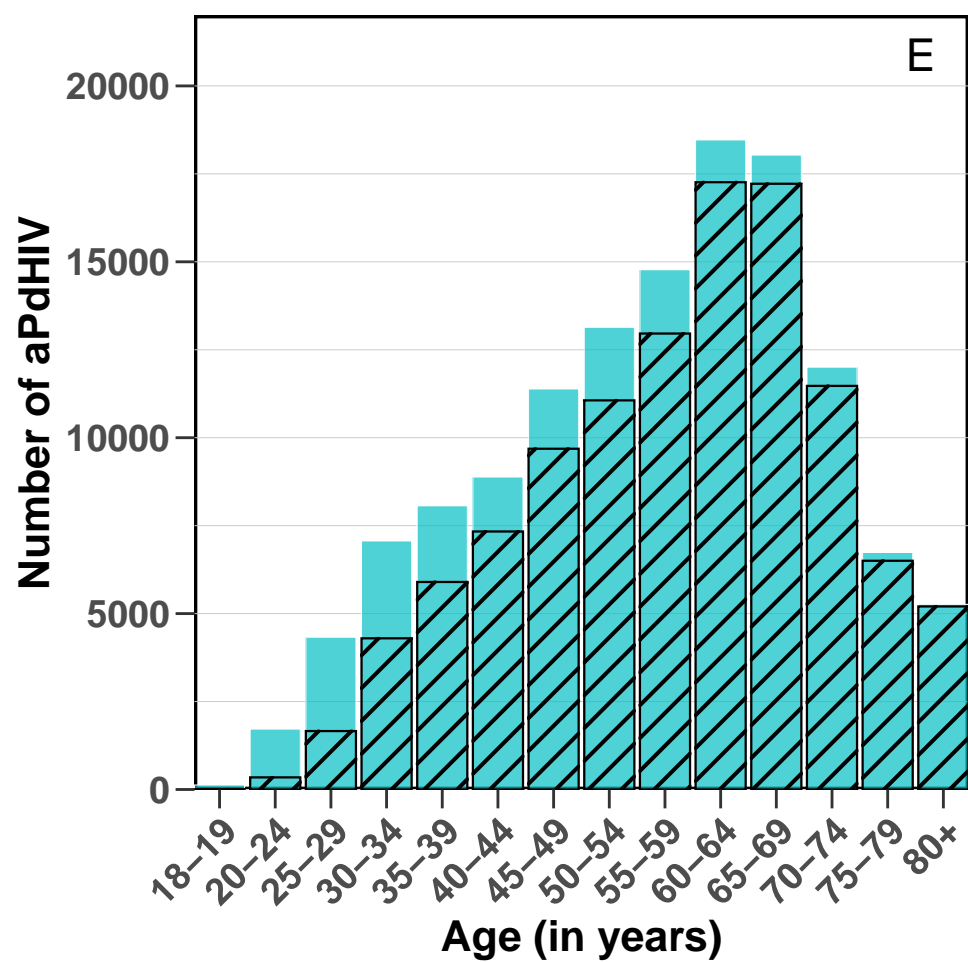
2018
Scenario 1



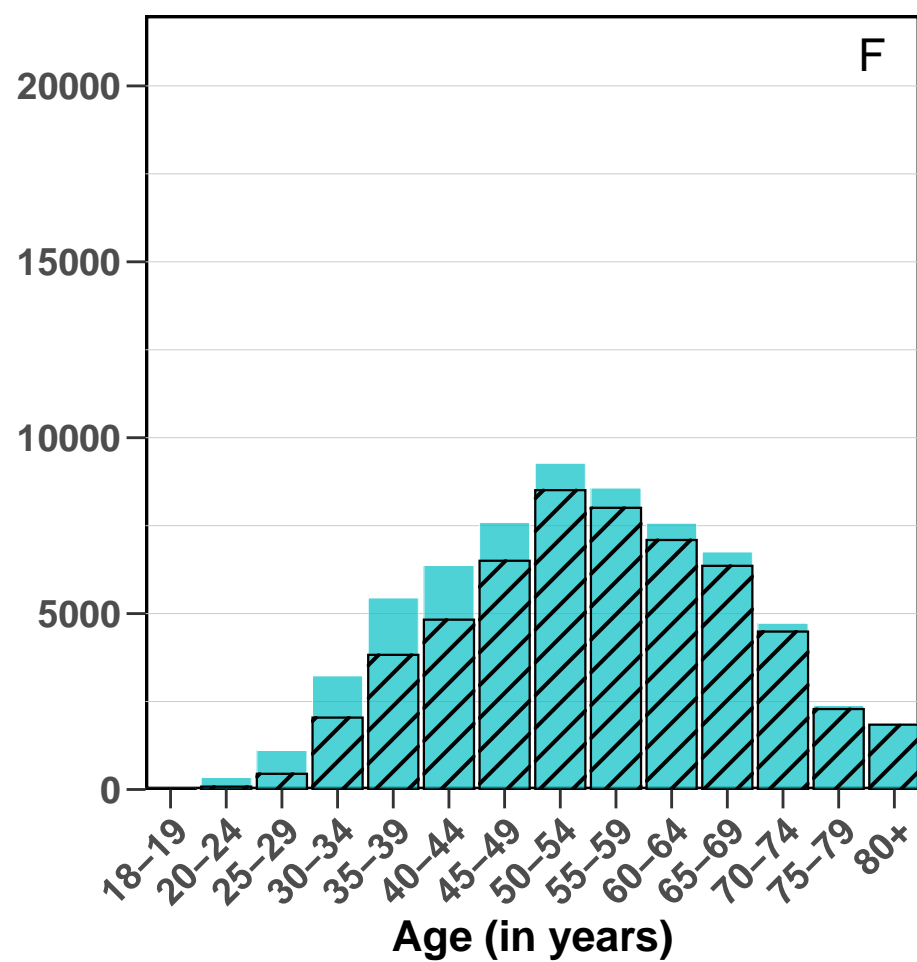
Scenario 1
Scenario 2



Scenario 1
Scenario 2

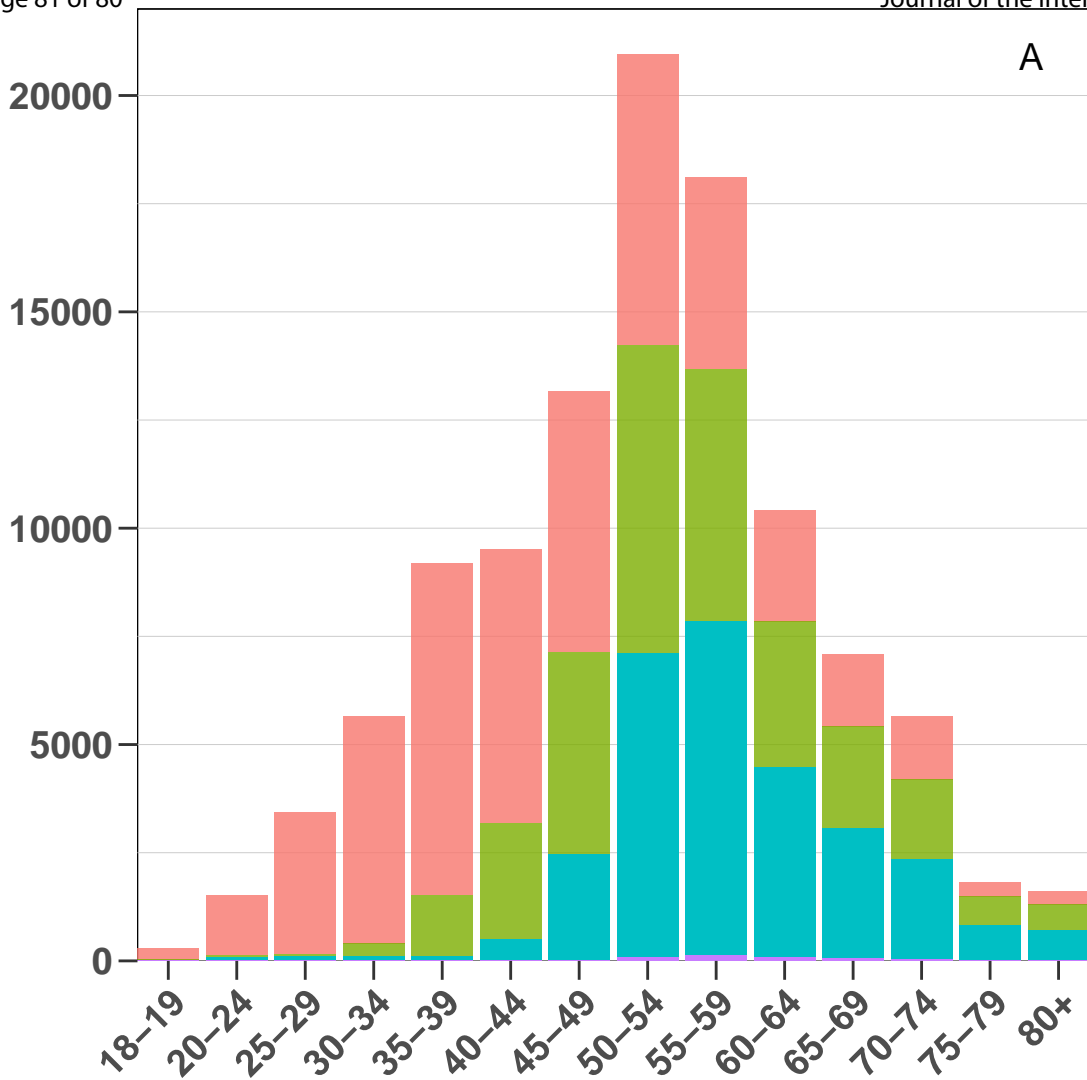


Scenario 1
Scenario 3

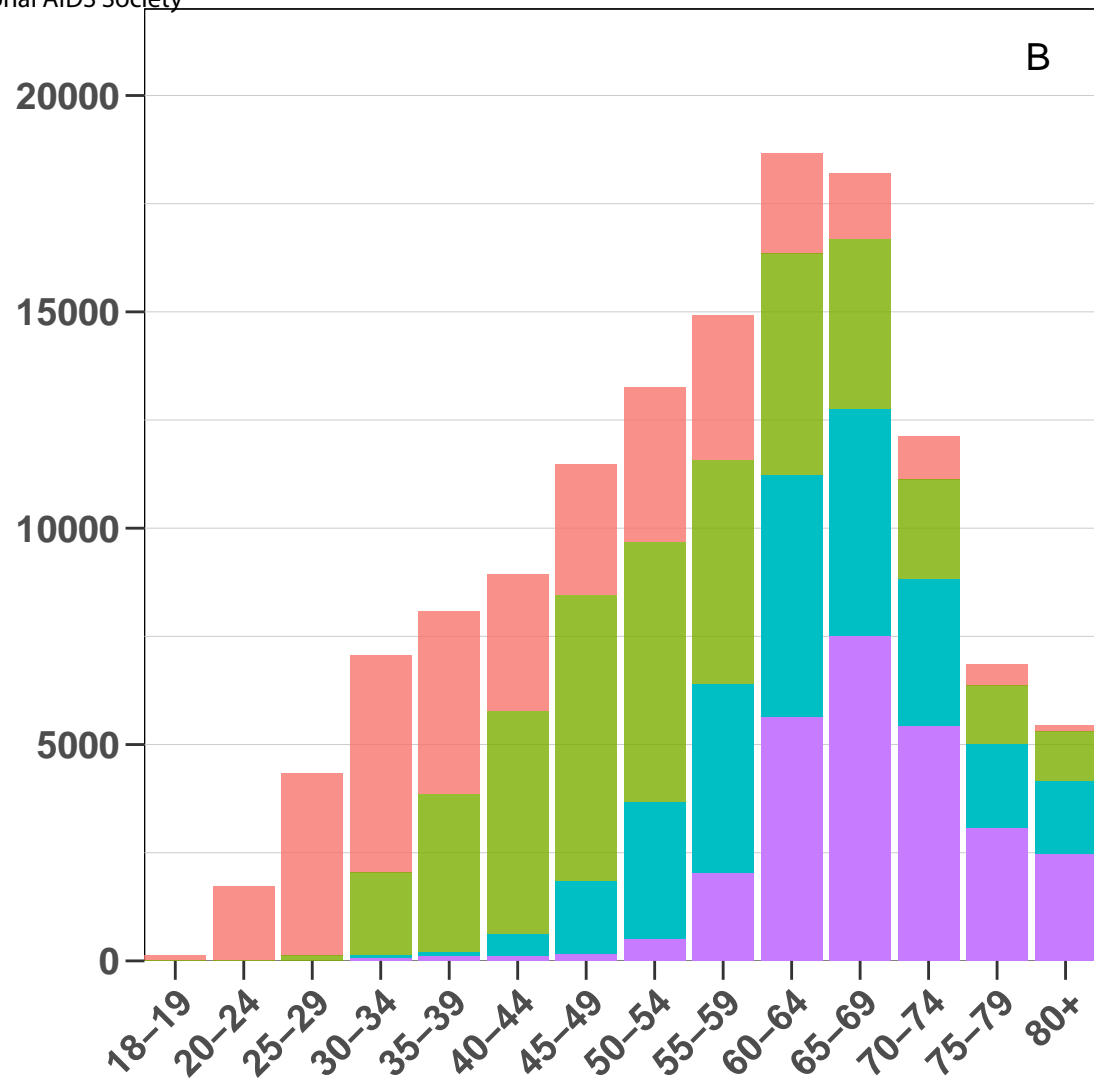


Scenario 1
Scenario 3

Number of adults PdHIV

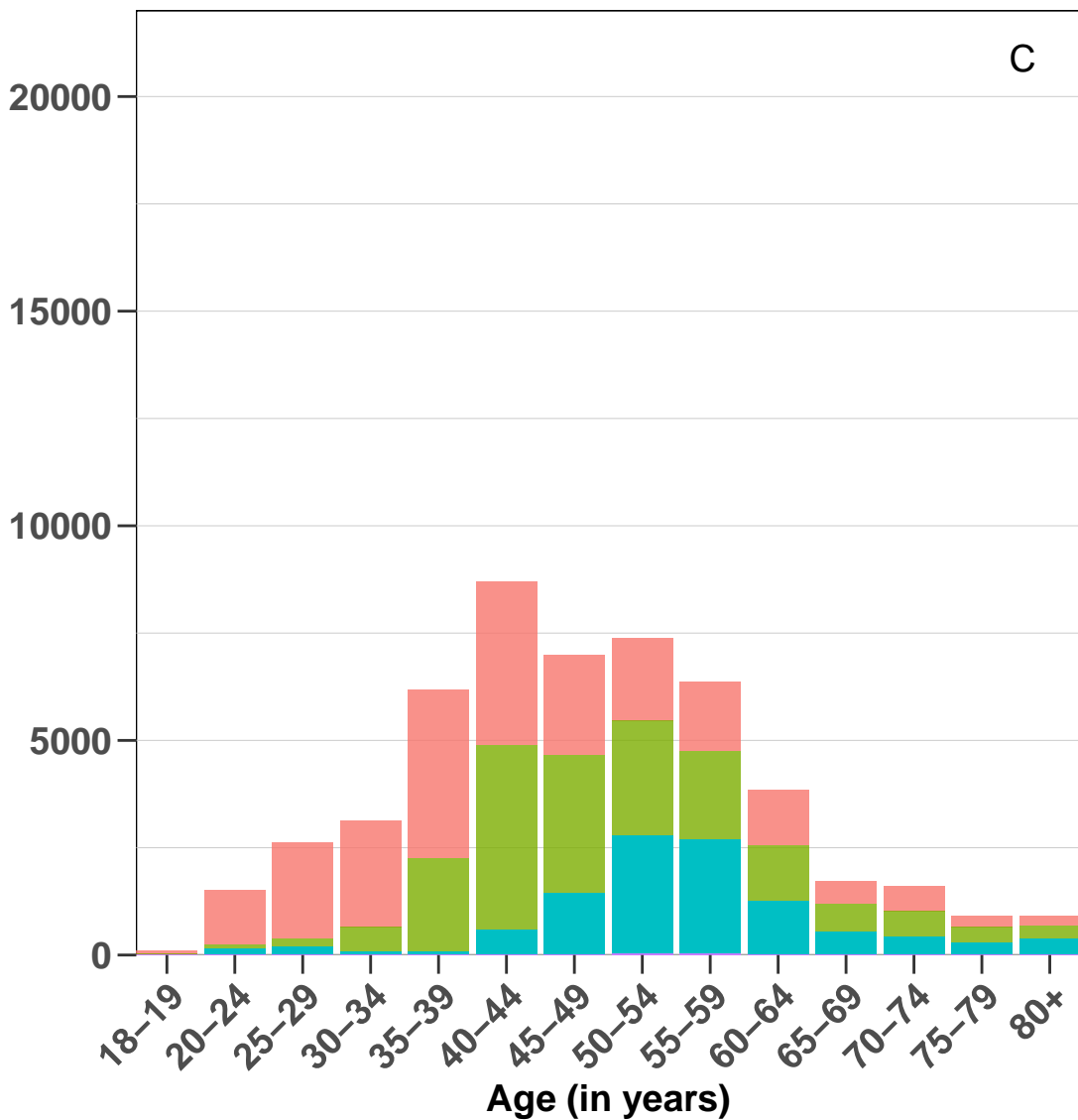


B

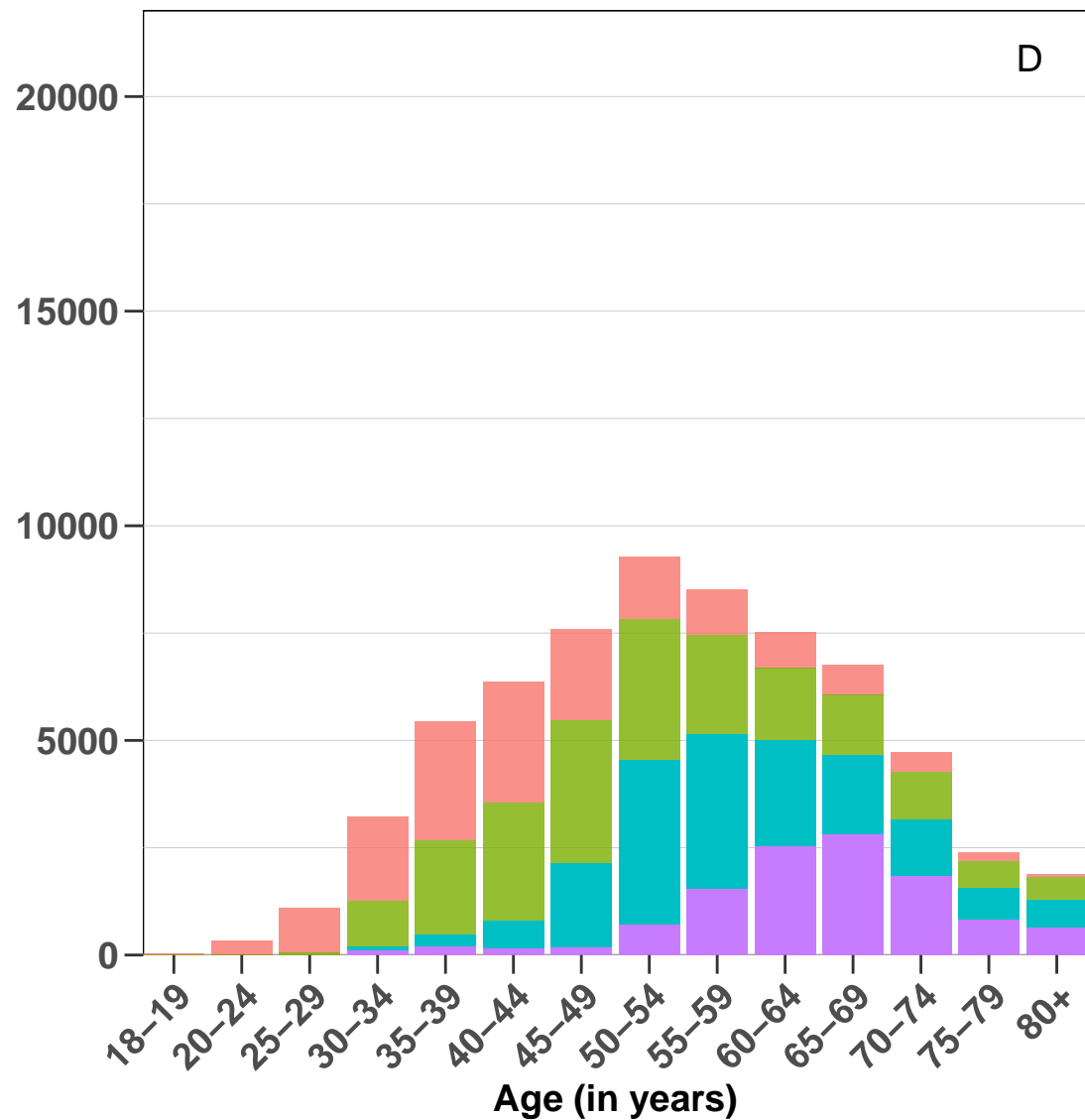


C

Number of adult PdHIV



D



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