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Birth country influences the choice of antiretroviral therapy in HIV-infected individuals: experience from a French HIV centre

Romain Palich, Rachid Agher, Dimoke Wetshikoy, Lise Cuzin, Sophie Seang, Cathia Soulie, Roland Tubiana, Marc-Antoine Valantin, Luminita Schneider, Valérie Pourcher, et al.

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1 **Title**

2 **Birth country influences the choice of antiretroviral therapy in HIV-infected**
3 **individuals: experience from a French HIV centre**

4

5 **Running title**

6 Antiretroviral therapy according to geographic origin

7

8 **Authors**

9 Romain Palich, MD, PhD,¹ Rachid Agher,¹ Dimoke J. Wetshikoy, MSc,² Lise Cuzin, MD,³
10 Sophie Seang, MD,¹ Cathia Soulie, PhD,⁴ Roland Tubiana, MD,¹ Marc-Antoine Valantin, MD,¹
11 Luminita Schneider, MD,¹ Valérie Pourcher, MD, PhD,¹ Anne-Geneviève Marcelin, PharmD,
12 PhD,⁴ Lambert Assoumou, PhD,² Christine Katlama, MD, PhD¹

13

14 **Affiliations**

- 15 1. Sorbonne University, Infectious Diseases department, Pitié-Salpêtrière Hospital, AP-
16 HP, Pierre Louis Epidemiology and Public Health Institute (iPLESP), INSERM 1136,
17 Paris, France
- 18 2. Sorbonne University, Pierre Louis Epidemiology and Public Health Institute (iPLESP),
19 INSERM 1136, Paris, France
- 20 3. Martinique University Hospital, Infectious and Tropical diseases, Fort-De-France, FWI;
21 CERPOP, INSERM UMR1295, Paul Sabatier University, Toulouse, France
- 22 4. Sorbonne University, Virology department, Pitié-Salpêtrière Hospital, AP-HP, Pierre
23 Louis Epidemiology and Public Health Institute (iPLESP), INSERM 1136, Paris,
24 France

25

26 **Corresponding author**

27 Romain Palich, MD, PhD

28 Service de Maladies Infectieuses et Tropicales, hôpital Pitié-Salpêtrière, 47-83 boulevard de

29 l'hôpital, 75013 Paris, France

30 Tel: +33.1.42.16.01.71, fax: +33.1.42.16.04.45

31 Email: romain.palich@aphp.fr

32

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43 **ABSTRACT**

44 **Objectives:** To assess whether antiretroviral therapy (ART) prescriptions differ between naive
45 and virally suppressed HIV patients born in France (PBFs) and in Sub-Saharan Africa
46 (PBSSAs).

47 **Setting:** Observational single-centre study.

48 **Methods:** We included all PBFs and PBSSAs entered into care at Pitié-Salpêtrière Hospital,
49 Paris, France, from 01/01/2000 to 31/12/2018, with plasma HIV-RNA >200 copies/mL. We first
50 compared the initial ART in naive PBFs and PBSSAs. Second, we compared the last prescribed
51 ART (including drug-reduced ART: daily 2-drug regimens, daily 1-drug regimens and
52 intermittent 3-drug regimens) in virally suppressed PBFs and PBSSAs, by focusing on patients
53 in care in 2018 with HIV-RNA <50 copies for at least 24 months. A uni- and multivariable
54 logistic regression model was used to assess the impact of geographical origin on ART
55 prescriptions.

56 **Results:** A total of 1,944 naive patients were included (915 PBSSAs and 1,029 PBFs). PBSSAs
57 were more frequently women, hepatitis B coinfecting, with a lower pretherapeutic CD4 T-cell
58 count, and most had tuberculosis at HIV diagnosis. After adjustment for confounders, PBSSAs
59 were more likely to receive a first-line protease inhibitor-based regimen (OR 1.61, 95%CI 1.31-
60 1.98), and less likely to receive an integrase inhibitor-based regimen (OR 0.61, 95%CI 0.42-
61 0.88). Out of the 968 virally suppressed patients (431 PBSSAs and 537 PBFs), PBSSAs were
62 less likely to receive drug-reduced ART, including two-drug regimens and intermittent three-
63 drug regimens (OR 0.48, 95%CI 0.36-0.65).

64 **Conclusions:** Differences in ART prescriptions between PBSSAs and PBFs were not only
65 explained by different clinical and virological situations. Personal motivations of doctors in
66 choosing ART according to country of birth need to be explored.

67 INTRODUCTION

68 Antiretroviral therapy (ART) is universally recommended for people living with HIV today
69 worldwide, regardless of their immunological and virological situation. In high-income
70 countries, many therapeutic options are available for both naive and virally suppressed patients,
71 and individualization of ART should be the rule, according to each situation. Although integrase
72 inhibitors (INSTI)-based regimens have become preferred options in most guidelines for naive
73 patients since the mid-2010s,^{1,2} non-nucleoside reverse transcriptase inhibitor (NNRTI)- and
74 protease inhibitor (PI)-based regimens were for a long time the only ones available, and are still
75 today therapeutic alternatives. Drug-reduced ART strategies have increasingly become the
76 preferred option for optimizing ART in pretreated patients with prolonged control of viral
77 replication, when standard triple therapy is no longer necessary.³ These drug-reduced strategies
78 include single and two-drug therapies (reduction in the number of drugs) as well as intermittent
79 regimens, given 4 to 5 days a week (reduction in the number of days taken).

80 In France, in 2018, 56% of new HIV diagnoses concerned people born abroad, including 66%
81 from Sub-Saharan Africa.⁴ It has been estimated that almost half of patients originating from
82 Sub-Saharan Africa, including a large majority of women, acquired HIV after migrating to
83 France.⁵ In-depth analysis of biographical narratives show a high level of socio-economic
84 insecurity in this population.^{6,7} It should be noted that in France, health insurance is free of
85 charge, including for undocumented individuals. Therefore, incomes of people living with HIV
86 do not affect the choice of treatment.

87 Many papers have reported that migrants living with HIV frequently have poor HIV clinical
88 outcomes in comparison with native-born persons.⁸ These outcomes included higher frequency
89 of AIDS status and lower CD4 T-cell count at entry into HIV care⁹⁻¹³ as well as higher risk of
90 loss to follow-up (LFU),¹⁴⁻¹⁷ poor ART adherence, and a high risk of virological failure once
91 in care.¹⁸⁻²⁴ These poor results could be mainly due to socio-economic barriers, including

92 difficulties with administrative procedures, finding a job and housing, as well as difficulties in
93 understanding the health care system. To our knowledge, there is very little data on the
94 differences in ART received by HIV migrants and native-born persons.

95 We assumed there could be differences in terms of prescriptions between migrant and native-
96 born patients. These prescription differences could be integrated into sub-standard care, which
97 is why we conducted this study. At our French HIV centre, we aimed to compare ART
98 prescribed for HIV-1-patients born in France (PBFs) and those born in Sub-Saharan Africa
99 (PBSSAs) at two distinct times: i) at ART initiation and ii) in the context of sustained viral
100 suppression.

101

102 **MATERIAL AND METHODS**

103 *Study population*

104 For this observational single-centre study, we selected all PBFs and PBSSAs newly entered
105 into care at Pitié-Salpêtrière Hospital, Paris, France, from 01/01/2000 to 31/12/2018, with
106 plasma HIV-RNA ≥ 200 copies/mL, defined as the “naive” group (Supplementary Figure).

107 We then selected all patients in care in our unit who had had at least one clinical visit in 2018,
108 and with all plasma HIV-RNA < 50 copies/mL in the last 24 months, defined as the “virally
109 suppressed” group (Supplementary Figure). In order to ensure at least 24 months on ART, we
110 excluded for analysis patients who initiated ART after 01/01/2017.

111

112 *Data collection*

113 All clinical, therapeutic, immunological and virological data were prospectively collected by
114 HIV physicians as part of routine follow-up using the *Nadis*[®] database, prior to ART initiation
115 and at each routine visit until 31/12/2018. Clinical data included gender, age, birth country, risk
116 factor for HIV transmission, year of HIV diagnosis, CDC stage at diagnosis, and time between

117 entry into care and ART initiation. Therapeutic data included number and class of antiretrovirals
118 with daily or intermittent prescription. Immunological data included pretherapeutic CD4 T-cell
119 count, CD4 T-cell nadir, last CD4 T-cell count and last CD4/CD8 ratio. Virological data
120 included pretherapeutic HIV-RNA value and HIV-RNA value at each routine visit. We also
121 collected the status of the last HIV referring doctor for each patient (full-time or part-time
122 consulting physician).

123

124 *Statistics*

125 The first part of the analysis was conducted in order to compare the therapeutic classes included
126 in first-line ART prescribed in naive PBFs and PBSSAs, and involved all patients matching the
127 inclusion criteria. The second part of the analysis was conducted in order to compare the
128 proportion of drug-reduced ART strategies, in virally suppressed PBFs and PBSSAs.

129 Chi-square and Kruskal-Wallis tests were performed to investigate the differences between the
130 study variables. Uni- and multivariable logistic regressions were performed in order to assess
131 the impact of geographic origin on the prescription of ART, in terms of drug classes (nucleoside
132 reverse transcriptase inhibitors [NRTIs], NNRTIs, PIs, INSTIs) and type of ART (drug-reduced
133 ART, including single and two-drug therapies as well as intermittent triple-drug regimens,
134 defined as triple-drug regimens given 4 to 5 days a week), adjusted for potential confounders.
135 Multivariable logistic regressions, with backwise selection, first included all variables with an
136 odds ratio associated with a p-value <0.1 in the univariable analysis. Only the variables
137 significantly ($p<0.05$) were considered in the final models. In the “naive” group, potential
138 confounders included gender, age, HIV transmission risk factor, year of HIV diagnosis,
139 hepatitis B coinfection, CDC stage C, pretherapeutic CD4 T-cell count and plasma HIV-RNA,
140 time between entry into care and ART initiation and tuberculosis at HIV diagnosis. In the
141 “virally suppressed” group, they included gender, age, HIV transmission risk factor, year of

142 HIV diagnosis, hepatitis B coinfection, CDC stage C, CD4 T-cell nadir, zenith HIV-RNA, last
143 CD4 T-cell count and status of the referring doctor (i.e. full-time or part-time consulting
144 physician).

145 All analyses were conducted using IBM SPSS Statistics software (v. 25).

146

147 *Ethics*

148 Patients at Pitié-Salpêtrière Hospital are routinely followed using the *Nadis*[®] electronic medical
149 record system.²⁵ Data from *Nadis*[®] are collected prospectively after patients provide signed
150 consent (CNIL, French National Commission for Information Technology and Civil Liberties,
151 registration number 770134) permitting the use of data for research. All data were anonymized
152 before analysis. There were no additional biological samples used for this study.

153

154 **RESULTS**

155 *Antiretroviral therapy in naive patients*

156 Overall, 1,944 naive patients fulfilling the inclusion criteria were enrolled. This population
157 included 915 PBSSAs and 1,029 PBFs (Supplementary Figure). PBSSAs were most frequently
158 women (58% *versus* 11%, $p<0.001$), heterosexual (86% *versus* 26%, $p<0.001$) and were
159 younger (35 *versus* 37 years, $p<0.001$) in comparison with PBFs (Table 1). They had a lower
160 pretherapeutic CD4 T-cell count (231 *versus* 345 cells/mm³, $p<0.001$), with more frequent
161 AIDS status (22% *versus* 14%, $p<0.001$). Hepatitis B coinfection was also more frequent in
162 PBSSAs (9.9% *versus* 1.6%, $p<0.001$), as well as tuberculosis at time of HIV diagnosis (7.4%
163 *versus* 0.9%, $p<0.001$).

164 Naive PBSSAs received more PI-based regimens (58% *versus* 47%, $p<0.001$), less NNRTI-
165 based regimens (22% *versus* 26%, $p=0.026$), and fewer were on INSTI-based regimens (13%
166 *versus* 24%, $p<0.001$) compared to PBFs. After adjustment for confounders, geographic origin

167 remained a significant factor influencing ART prescription in naive patients (Tables 2 and 3).
168 In comparison to patients born in France, PBSSAs were more likely to receive a PI-based
169 combination (OR 1.61, 95%CI 1.31 to 1.98, $p<0.0001$) (Table 2) and less likely to receive an
170 INSTI-based combination (OR 0.57, 95%CI 0.4 to 0.84, $p=0.003$) (Table 3). Conversely, there
171 was no association between geographic origin and prescription of NRTIs or NNRTIs
172 (Supplementary Table 1).

173 In addition to country of birth, other factors were significantly associated with the prescription
174 of different antiretroviral classes at ART initiation, whether in PBSSAs or PBFs. The
175 probability of being prescribed a PI-based regimen was lower in patients who initiated ART
176 during the second study period (2013-2018) in comparison with the first study period (2000-
177 2006), and in those with tuberculosis at ART initiation; it was higher in the event of low CD4
178 T-cell count and high HIV-RNA at ART initiation. The probability of being prescribed an
179 INSTI-based regimen was much higher in the last study period and in the event of high HIV-
180 RNA at ART initiation. Lastly, the probability of being prescribed a NNRTI-based regimen
181 was higher in men, in the event of tuberculosis, low HIV-RNA and high CD4 T-cell count at
182 ART initiation.

183 In any of these analyses was interaction between gender and country of birth, and between
184 gender and age, significant.

185

186 *Antiretroviral therapy in virally suppressed patients*

187 968 patients were analyzed, including 431 PBSSAs and 537 PBFs (Supplementary Figure).
188 PBSSAs had been on ART for longer (11 *versus* 9 years, $p<0.001$), had a lower CD4 T-cell
189 count at time of analysis (588 *versus* 714 cells/mm³, $p<0.001$), and their referring doctor was
190 less frequently a “full-time physician” (52% *versus* 63%, $p<0.001$) in comparison with PBFs

191 (Table 4). The median duration of viral suppression was 76 months (IQR 53-107), with no
192 significant difference between PBSSAs and PBFs.

193 PBSSAs received more NRTI-based regimens (92% *versus* 88%, $p=0.043$), more PI-based
194 regimens (21% *versus* 10%, $p<0.001$), and less INSTI-based regimens (37% *versus* 48%,
195 $p=0.017$). They also received less drug-reduced ART (22% *versus* 40%, $p<0.001$), including
196 fewer two-drug therapies (15% *versus* 23%, $p=0.003$) and fewer intermittent therapies (4.6%
197 *versus* 14%, $p<0.001$). After adjustment for confounders, there was an independent impact of
198 geographic origin on ART prescription, in terms of type of antiretroviral strategy (drug-reduced
199 or not) (Table 5). Compared to PBFs, the probability of receiving drug-reduced ART was lower
200 in PBSSAs (OR 0.48, 95%CI 0.36-0.65, $p=0.0024$). This difference was significant for
201 intermittent ART (OR 0.33, 95%CI 0.19-0.55, $p<0.0001$), when studied separately
202 (Supplementary Table 2). Lastly, the probability of receiving a drug-reduced regimen was lower
203 in the event of prior AIDS status, and higher in patients whose doctor worked full time at the
204 hospital (OR 3.64, 95%CI 2.65 to 4.99, $p<0.001$).

205 In any of these analyses was interaction between gender and country of birth, and between
206 gender and age, significant.

207

208 **DISCUSSION**

209 Our work highlights significant discrepancies in ART prescriptions between PBFs and
210 PBSSAs, whether at initial ART prescription (naive patients), or in the context of sustained
211 viral suppression (pretreated patients). After adjustment for clinical and biological differences
212 between the two groups, discrepancies dependent on geographic origin remained. At ART
213 initiation, PBSSAs received significantly more PI-based regimens, and less INSTI-based
214 regimens. Among well-controlled patients with viral suppression for a median of over 6 years,
215 PBSSAs also received significantly less drug-reduced strategies.

216 In Western Europe today, migrants constitute a growing proportion of people living with HIV
217 treated in HIV centres, as illustrated by our study population in which ~50% of patients entered
218 into care between 2000 and 2018 were born in Sub-Saharan Africa. The proportion of HIV-
219 infected people born abroad is expected to increase sharply in Western European hospitals in
220 the future, due to population movements and lower new HIV diagnoses among native-born
221 individuals in high-income countries in the era of pre-exposure prophylaxis (PrEP).²⁶⁻²⁸ In this
222 context, it is particularly interesting to assess ART prescriptions with regard to geographic
223 origin. For this report, we chose to compare ART prescriptions between PBFs and PBSSAs, the
224 main migrant subpopulation in France.⁴

225 Many characteristics differentiate these two populations when entering care, with more
226 advanced disease observed in non-native patients, as highlighted in our study and others.⁹⁻¹³
227 However, after adjustment for confounders (i.e. comparable immunological and virological
228 situations), in PBSSAs, INSTIs were twice less likely to be prescribed and PIs 1.4 times more
229 likely to be prescribed compared to PBFs.

230 Several reasons could explain the preference for PI-based regimens in PBSSAs. One is the high
231 genetic barrier of PIs. In clinical practice, we frequently observe very precarious living
232 conditions in migrants, associated with difficulties in taking medication, which are in turn
233 associated with virological failure and treatment interruption. These empirical observations are
234 corroborated by several published data.¹⁴⁻²⁴ Favoring PIs has the advantage of reducing the risk
235 of emerging resistance in the event of poor compliance, due to the high genetic barrier of this
236 class. Conversely, this choice could have a negative impact because of the poorer overall
237 tolerance of PIs compared to INSTIs,^{29,30} which is potentially compounded by taking three
238 tablets instead of one (in France, no single tablet regimen including PIs is available).
239 Furthermore, second-generation INSTIs (dolutegravir and bictegravir) also have a high genetic
240 barrier, which was not the case with first-generation INSTIs (raltegravir and boosted

241 elvitegravir), and can therefore just as easily be used despite foreseeable compliance
242 difficulties. The study period may partly explain the lower prescription of INSTIs: raltegravir
243 was licensed in France in 2008, elvitegravir in 2013, dolutegravir in 2014, and bictegravir in
244 2018.

245 One other reason could be the occurrence of pregnancies or the desire to fall pregnant. This
246 factor could impact the choice of first-line ART, NRTIs + PIs being the standard treatment in
247 pregnant women in Europe during the study period. Pregnancies or the desire to fall pregnant
248 could be more prevalent in PBSSAs, due to the high proportion of women in this group.
249 However, adjustments for gender and age in multivariable analysis should limit this bias.

250 We decided to carry out the second part of the study in order to analyze prescriptions in patients
251 with optimal control of their viral replication. By definition, these patients with plasma HIV-
252 RNA <50 copies/mL for more than two years were ART-compliant. Once again, despite
253 adjustment for possible confounding factors, including characteristics at entry into care,
254 substantial differences in treatments remain between the two groups. PBSSAs received twice
255 less drug-reduced ART, including dual therapies and intermittent ART, and twice more NRTIs.
256 In the last years, numerous clinical trials have demonstrated the non-inferiority of drug-reduced
257 ART in comparison to standard triple regimens for maintaining viral suppression, including 2-
258 DR^{31,32} and intermittent 3-DR^{33,34}. We believe that these strategies should be offered to as many
259 patients as possible, provided the virological situation allows for it.³

260 One of the only reasons that could explain lower drug-reduced ART prescriptions in PBSSAs
261 would be the fear that they would have more resistance, assuming that the patients had had
262 more virological failures in the past. Unfortunately, we did not have data on resistance for the
263 included patients.

264 We believe, however, that PBSSAs do not receive the most innovative strategies as much as
265 PBFs, despite similar virological situations, and that they all pay the price for therapeutic

266 difficulties observed in only a small proportion of patients. This is evident when the analysis is
267 restricted to virally suppressed patients, who by definition have good adherence to ART.
268 Various papers have highlighted inequalities in treatment based on race, driven by implicit bias
269 among physicians.³⁵⁻³⁸ Several studies conducted in the US reported false beliefs about racial
270 differences, that could lead to different therapeutic attitudes based on skin color.³⁹⁻⁴¹ A recent
271 interventional study found that health care providers make clinical judgements about who is not
272 a good candidate for HIV pre-exposure prophylaxis (PrEP) based on unconscious and conscious
273 stereotypes and prejudices, quantified on a modern racism scale.⁴² These biases could be
274 maintained by lack of awareness during medical studies, race being a particularly divisive
275 subject in society at present.⁴³⁻⁴⁵ We assume that origin-related attitudes can partly explain the
276 lower prescription of drug-reduced ART in PBSSAs in our centre. We believe it is essential to
277 investigate this issue to correct these biases and improve practices.

278 Factors other than patients' geographical origin also influence prescriptions. We have shown
279 that the prescription of drug-reduced ART depends on the consulting physician's status at the
280 hospital. The prescription of drug-reduced ART was 3.7 times higher in patients who were
281 treated by full-time physicians, compared with those treated by part-time physicians. Our
282 premise is that greater experience is associated with greater confidence in ART, and greater
283 ease in proposing innovative strategies.

284 Our study has some limitations. On one hand, it was an observational single-centre study and
285 we cannot rule out that the findings would have been different in another centre. On the other
286 hand, the study period covers periods with very different prescribing practices, especially before
287 and after the introduction of INSTIs (schematically between 2000-2010 and 2010-2020). It is
288 also necessary to keep in mind that at the same time the concepts of equity, diversity and
289 inclusion have evolved considerably. We were as exhaustive as possible, including all available
290 variables in our models, but some potential confounding factors may be unexplored.

291 **In conclusion**, our results show large differences in terms of ART prescriptions according to
292 birth country – Sub-Saharan Africa or France –, not only at ART initiation but also after long-
293 term viral suppression, without clear clinical, virological or immunological justification. With
294 this work, we hope to encourage questioning of current practices, promoting more equity in
295 prescriptions according to geographical origin so as to offer all patients the best therapeutic
296 options.

297

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302

303 **TRANSPARENCY DECLARATION**

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308

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452

Table 1. Patient characteristics at ART initiation, according to birth country (N=1944).

	Patients born in Sub-Saharan Africa (PBSSA, n=915)	Patients born in France (PBF, n=1029)	p-value ^a
Gender, n(%)			<0.001
Male	381 (42)	913 (89)	
Female	534 (58)	116 (11)	
Age, years, median (IQR)	35 (28-42)	37 (30-45)	<0.001
Risk factor, n(%)			<0.001
MSM	30 (3.3)	685 (67)	
Heterosexual	787 (86)	264 (26)	
Other	98 (11)	80 (7.8)	
Year of HIV diagnosis, n(%)			<0.001
2000-2006	392 (43)	333 (32)	
2007-2012	291 (32)	412 (40)	
2013-2018	232 (25)	284 (28)	
HBV coinfection, n(%)	91 (9.9)	16 (1.6)	<0.001
CDC stage C, n(%)	200 (22)	140 (14)	<0.001
Pretherapeutic CD4 T-cell count, cells/mm ³ , median (IQR)	231 (124-351)	345 (206-497)	<0.001
<200/mm ³ , n(%)	380 (43)	248 (25)	<0.001
200-499/mm ³ , n(%)	434 (49)	521 (51)	
≥500/mm ³ , n(%)	76 (8.5)	241 (24)	
Pretherapeutic HIV-RNA, log ₁₀ cp/mL, median (IQR)	4.80 (4.13-5.31)	4.84 (4.34-5.36)	
<5 log ₁₀ cp/mL, n(%)	559 (61)	591 (57)	0.009
≥5 log ₁₀ cp/mL, n(%)	356 (39)	438 (43)	0.10
Tuberculosis at time of HIV diagnosis, n(%)	68 (7.4)	9 (0.9)	<0.001
Time between entry into care and ART initiation, months, median (IQR)	1.7 (0.7-7.2)	2.2 (0.6-18.8)	0.038
Drugs including in the first ART, n(%) ^b			
NRTI	899 (98)	1005 (98)	0.37
NNRTI	202 (22)	272 (26)	0.16
PI	534 (58)	486 (47)	0.003

INSTI	119 (13)	244 (24)	0.002
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a. Chi-2 test for categorical variables and Kruskal-Wallis test for continuous variables. b. Non-exclusive categories. NRTI: nucleoside reverse transcriptase inhibitor. NNRTI: non-nucleoside reverse transcriptase inhibitor. PI: protease inhibitor. INSTI: integrase stand transfer inhibitor.

Table 2. Factors impacting the choice of a PI-based regimen at ART initiation, uni- and multivariable regressions (N=1944).

		OR	CI95%	aOR	CI95%
Women		1.27	1.05-1.54	ns	
Age at HIV diagnosis	≥40 years	Ref.		ns	
	30-40 years	1.22	0.99-1.51		
	<30 years	1.15	0.91-1.44		
Born in Sub-Saharan Africa		1.57	1.31-1.87	1.61	1.31-1.98
Hepatitis B coinfection		1.55	1.04-2.32	ns	
Year of HIV diagnosis	2000-2006	Ref.		Ref.	
	2007-2012	1.03	0.83-1.27	1.06	0.84-1.33
	2013-2018	0.32	0.25-0.40	0.27	0.21-0.37
Time between HIV diagnosis and ART initiation	≥3 months	Ref.		Ref.	
	1-3 months	1.32	1.04-1.67	1.40	1.07-1.82
	<1 month	0.96	0.78-1.17	1.23	0.95-1.58
AIDS status		1.17	1.08-1.73	ns	
HIV transmission	MSM			ns	
	Heterosexual	1.45	1.19-1.75		
	Other	1.71	1.22-2.38		
Pretherapeutic CD4 T-cell count	<200	Ref.			
	200-500	0.49	0.40-0.61	0.57	0.45-0.72
	≥500	0.36	0.27-0.48	0.54	0.39-0.74
Pretherapeutic HIV-RNA	≥5 log ₁₀ copies/mL	1.70	1.41-2.04	1.67	1.36-2.07
Tuberculosis at HIV diagnosis		0.47	0.29-0.77	0.21	0.12-0.35

Table 3. Factors impacting the choice of an INSTI-based regimen at ART initiation, uni- and multivariable regressions (N=1944).

		OR	CI95%	aOR	CI95%
Women		0.61	0.47-0.79	ns	
Age at HIV diagnosis	≥40 years	Ref.		Ref.	
	30-40 years	0.56	0.43-0.73	0.68	0.50-0.93
	<30 years	0.65	0.49-0.88	0.75	0.53-1.07
Born in Sub-Saharan Africa		0.48	0.38-0.61	0.61	0.42-0.88
Hepatitis B coinfection		0.64	0.36-1.14	ns	
Year of HIV diagnosis	2000-2006	Ref.		Ref.	
	2007-2012	3.28	2.17-4.94	3.24	2.12-4.95
	2013-2018	17.5	11.9-25.9	21.5	13.8-33.5
Time between HIV diagnosis and ART initiation	≥3 months	Ref.		Ref.	
	1-3 months	0.96	0.68-1.36	0.49	0.32-0.74
	<1 month	2.57	1.98-3.30	0.70	0.5-0.98
AIDS status		1.08	0.81-1.46	1.51	1.05-2.18
HIV transmission	MSM	Ref.		Ref.	
	Heterosexual	0.46	0.36-0.59	0.57	0.38-0.85
	Other	0.43	0.27-0.68	0.48	0.27-0.84
Pretherapeutic CD4 T-cell count	<200	Ref.		ns	
	200-500	0.81	0.62-1.06		
	≥500	1.46	1.06-2.02		
Pretherapeutic HIV-RNA	≥5 log ₁₀ copies/mL	1.88	1.59-2.36	1.99	1.50-2.62
Tuberculosis at HIV diagnosis		0.72	0.37-1.37	ns	

Table 4. Characteristics of virally suppressed patients at time of analysis, according to birth country (N=968).

	Patients born in Sub-Saharan Africa (PBSSA, n=431)	Patients born in France (PBF, n=537)	p-value^a
Gender, n(%)			<0.001
Male	162 (38)	467 (87)	
Female	269 (62)	70 (13)	
Age, years, median (IQR)	46 (41-52)	49 (42-56)	<0.001
Risk factor, n(%)			<0.001
MSM	11 (2.6)	360 (67)	
Heterosexual	378 (88)	149 (28)	
Other	42 (9.7)	28 (5.2)	
Year of HIV diagnosis, n(%)			<0.001
2000-2006	222 (51)	197 (37)	
2007-2012	145 (34)	239 (45)	
2013-2018	64 (15)	101 (18)	
HBV coinfection, n(%)	41 (9.5)	7 (1.3)	<0.001
CDC stage C, n(%)	89 (21)	71 (13)	0.002
CD4 T-cell nadir, cells/mm ³ , median (IQR)	194 (99-294)	289 (176-405)	<0.001
<200/mm ³ , n(%)	222 (51)	147 (27)	<0.001
200-499/mm ³ , n(%)	189 (44)	312 (58)	
≥500/mm ³ , n(%)	20 (4.6)	78 (15)	
Zenith HIV-RNA, log ₁₀ cp/mL, median (IQR)	4.67 (4.07-5.21)	4.78 (4.30-5.29)	0.008
<5 log ₁₀ cp/mL, n(%)	283 (66)	325 (61)	0.10
≥5 log ₁₀ cp/mL, n(%)	148 (34)	212 (39)	
ART duration, years, median (IQR)	11 (7-15)	9 (6-12)	<0.001
Last CD4 T-cell count, cells/mm ³ , median (IQR)	588 (442-743)	714 (560-911)	<0.001
Last CD4/CD8 ratio, median (IQR)	1.02 (0.71-1.40)	1.01 (0.77-1.38)	0.83
Duration of viral suppression, months, median (IQR)	76 (50-112)	76 (55-104)	0.68
Referring doctor, n(%)			<0.001
Full-time consultant	222 (52)	333 (63)	

Part-time consultant	208 (48)	197 (37)	
Drugs including in the last ART, n(%) ^b			
NRTI	396 (92)	472 (88)	0.043
NNRTI	174 (40)	216 (40)	0.96
PI	92 (21)	55 (10)	<0.001
INSTI	160 (37)	240 (48)	0.017
Kind of antiretroviral strategy, last ART, n(%)			
All drug-reduced ART	95 (22)	212 (40)	<0.001
Single-drug therapies	12 (2.8)	25 (4.7)	0.13
Two-drug therapies	64 (15)	121 (23)	0.003
Intermittent therapies	20 (4.6)	77 (14)	<0.001

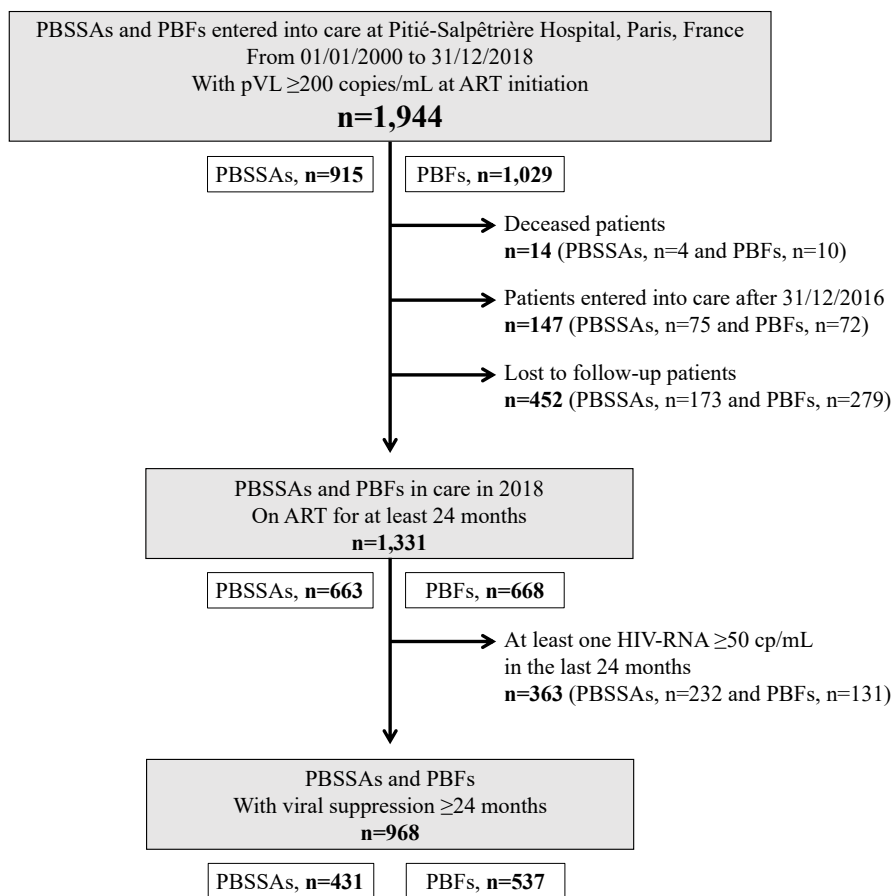
a. Chi-2 test for categorical variables and Kruskal-Wallis test for continuous variables. b. Non-exclusive categories. NRTI: nucleoside reverse transcriptase inhibitor. NNRTI: non-nucleoside reverse transcriptase inhibitor. PI: protease inhibitor. INSTI: integrase stand transfer inhibitor.

Table 5. Characteristics related with the choice of drug-reduced regimens in virally suppressed patients, uni- and multivariable logistic regressions (N=968).

		OR	CI95%	aOR	CI95%
Women		0.77	0.57-1.02	ns	
Age at HIV diagnosis	≥40 years	Ref.		ns	
	30-40 years	0.91	0.65-1.3		
	<30 years	1.26	0.88-1.8		
HIV Transmission	MSM	Ref.		ns	
	Heterosexual	0.54	0.4-0.72		
	Other	0.52	0.29-0.92		
Born in Sub-Saharan Africa		0.43	0.32-0.58	0.48	0.36-0.65
Year of HIV diagnosis	2000-2006	Ref.		ns	
	2007-2012	0.73	0.53-0.99		
	2013-2018	0.79	0.55-1.13		
Hepatitis B coinfection		0.48	0.23-1.01	ns	
AIDS status		0.48	0.32-0.73	0.51	0.33-0.78
CD4 T-cell nadir	≥500	Ref.		ns	
	200-499	0.76	0.49-1.19		
	<200	0.49	0.31-0.79		
Zenith CV	≥5log ₁₀ copies/mL	0.88	0.66-1.17	ns	
Last CD4 T-cell count	≥500	Ref.		ns	
	200-500	0.75	0.54-1.03		
	<200	0.49	0.14-1.78		
Full time hospital physician		3.79	2.77-5.17	3.64	2.65-4.99

Supplementary Material

Supplementary Figure. Study flow-chart.



Supplementary Table 1. Factors impacting the choice of an NNRTI-based regimen at ART initiation, uni- and multivariable regressions (N=1944).

		OR	CI95%	aOR	CI95%
Women		0.69	0.55-0.87	0.59	0.48-0.76
Age at HIV diagnosis	≥40 years	Ref.		ns	
	30-40 years	1.05	0.82-1.33		
	<30 years	0.82	0.62-1.08		
Born in Sub-Saharan Africa		0.78	0.64-0.97	ns	
Hepatitis B coinfection		0.70	0.42-1.15	ns	
Year of HIV diagnosis	2000-2006	Ref.		ns	
	2007-2012	1.00	9.79-1.27		
	2013-2018	0.75	0.58-0.99		
Time between HIV diagnosis and ART initiation	≥3 months	Ref.		Ref.	
	1-3 months	0.83	0.63-1.08	0.94	0.71-1.25
	<1 month	0.59	0.46-0.74	0.76	0.59-0.98
AIDS status		0.75	0.56-1.00	ns	
HIV transmission	MSM	Ref.		ns	
	Heterosexual	0.93	0.75-1.16		
	Other	0.79	0.53-1.18		
Pretherapeutic CD4 T-cell count	<200	Ref.		Ref.	
	200-500	2.22	1.72-2.86	1.94	1.46-2.57
	≥500	1.82	1.31-2.53	1.47	1.03-2.11
Pretherapeutic HIV-RNA	≥5 log ₁₀ copies/mL	0.48	0.38-0.59	0.49	0.38-0.63
Tuberculosis at HIV diagnosis		2.43	1.53-3.86	4.22	2.51-7.10

Supplementary Table 2. Characteristics related with the choice of intermittent regimens in virally suppressed patients, uni- and multivariable logistic regressions (N=968).

		OR	CI95%	aOR	CI95%
Women		0.39	0.11-0.18	NS	
Age at HIV diagnosis	≥40 years	Ref		NS	
	30-40 years	0.68	0.42-1.10		
	<30 years	0.57	0.32-1.02		
HIV Transmission	MSM	Ref		NS	
	Heterosexual	0.38	0.24-0.59		
	Other	0.33	0.11-0.93		
Born in Sub-Saharan Africa		0.29	0.17-0.48	0.33	0.19-0.55
Year of HIV diagnosis	2000-2006	Ref		NS	
	2007-2012	1.10	0.60-1.99		
	2013-2018	0.84	0.46-1.54		
Hepatitis B coinfection		0.80	0.28-2.3	NS	
AIDS status		0.42	0.20-0.89	NS	
CD4 T-cell nadir	≥500	Ref		NS	
	200-499	0.63	0.34-1.17		
	<200	0.51	0.26-0.98		
Zenith CV	≥5log ₁₀ copies/mL	1.27	0.82-1.94	NS	
Last CD4 T-cell count	≥500	Ref		NS	
	200-500	0.63	0.37-1.08		
	<200	NA			
Full time hospital physician		27.3	8.59-86.9	25.3	7.95-80.8