



**HAL**  
open science

## **Viral rebound on antiretroviral therapy in France according to region of origin, sex, and HIV acquisition group. Results from the French Hospital Database on HIV (ANRS CO4-FHDH)**

S Abgrall, H Selinger-Leneman, E Lanoy, A Becker, S Matheron, P de Truchis, J Pavie, A Canestri, M Khuong, D Rey, et al.

### ► To cite this version:

S Abgrall, H Selinger-Leneman, E Lanoy, A Becker, S Matheron, et al.. Viral rebound on antiretroviral therapy in France according to region of origin, sex, and HIV acquisition group. Results from the French Hospital Database on HIV (ANRS CO4-FHDH). HIV Medicine, 2024, Online ahead of print. 10.1111/hiv.13729 . hal-04837197

**HAL Id: hal-04837197**

**<https://hal.science/hal-04837197v1>**

Submitted on 13 Dec 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.



L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

## ORIGINAL ARTICLE

# Viral rebound on antiretroviral therapy in France according to region of origin, sex, and HIV acquisition group. Results from the French Hospital Database on HIV (ANRS CO4-FHDH)

S. Abgrall<sup>1</sup>  | H. Selinger-Leneman<sup>2</sup> | E. Lanoy<sup>2</sup> | A. Becker<sup>3</sup> | S. Matheron<sup>4</sup> | P. de Truchis<sup>5</sup> | J. Pavie<sup>6</sup> | A. Canestri<sup>7</sup> | M. A. Khuong<sup>8</sup> | D. Rey<sup>9</sup> | F. Caby<sup>2,10</sup> | P. Tattevin<sup>11</sup> | R. Palich<sup>12</sup> | S. Grabar<sup>13</sup>  | on behalf of ANRS CO4-FHDH

<sup>1</sup>AP-HP, Hôpital Bécclère, Service de Médecine Interne, Clamart, and Université Paris-Saclay, CESP INSERM U1018, Le Kremlin-Bicêtre, France

<sup>2</sup>Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France

<sup>3</sup>Hospices Civils de Lyon, Hôpital de la Croix-Rousse, Lyon, France

<sup>4</sup>AP-HP, Hôpital Bichat-Claude Bernard, GHU Paris Nord, Paris, France

<sup>5</sup>AP-HP Hôpital Raymond Poincaré, Université Paris-Saclay, Garches, France

<sup>6</sup>AP-HP, Hôtel-Dieu, Paris, France

<sup>7</sup>AP-HP, Hôpital Pitié-Salpêtrière, Paris, France

<sup>8</sup>Hôpital Delafontaine, Saint-Denis, France

<sup>9</sup>Strasbourg University Hospital, Strasbourg, France

<sup>10</sup>Hôpital Victor Dupouy, Argenteuil, France

<sup>11</sup>Pontchaillou University Hospital, Rennes, France

<sup>12</sup>Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, and AP-HP, Hôpital Pitié-Salpêtrière, Paris, France

<sup>13</sup>Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, AP-HP, Hôpital St Antoine, Paris, France

## Correspondence

S. Abgrall, Hôpital Bécclère, 157 rue de la Porte de Trivaux, 92 140 Clamart, France.

Email: [sophie.abgrall@aphp.fr](mailto:sophie.abgrall@aphp.fr)

## Funding information

ANRS-MIE; Institut National de la Santé et de la Recherche Médicale; Sorbonne Université; the French Ministry of Health

## Abstract

**Background:** Assessing the potential increased risk of viral rebound (VR) in migrants requires adequate control for sex and acquisition risk groups.

**Methods:** People living with HIV1, enrolled in the ANRS CO4-French Hospital Database on HIV, who achieved virological suppression with antiretroviral therapy (ART) initiated between 2006 and 2016 were included. We first compared the risk of VR, with loss to follow-up and death considered as competing events, across origin among the HIV acquisition groups, then across acquisition groups among the different origins, and finally across modality of a variable combining sex, acquisition group, and origin. Models were adjusted for clinical and biological confounding factors.

Part of this work was presented at the Afraviv conference, 8–11 November 2020.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2024 The Author(s). *HIV Medicine* published by John Wiley & Sons Ltd on behalf of British HIV Association.

**Results:** We included 21 571 French natives (FRA), 10 148 migrants from sub-Saharan Africa (SSA), 1137 migrants from the non-French West Indies (NFWI), and 4205 other migrants (OTHER). The 5-year probability of VR was 19% (95% confidence interval [CI] 19–20) overall, 15% in FRA, 21% in OTHER, 26% in SSA, and 34% in NFWI ( $p < 0.0001$ ). It was 14% in men who have sex with men (MSM), 23% in heterosexual men, and 23% in women ( $p < 0.0001$ ). After adjustment, all acquisition groups had a higher risk of VR than MSM from FRA, with men and women from NFWI having the highest risk (adjusted hazard ratio [aHR] 2.46; 95% CI 2.12–2.86 and aHR 2.59; 95% CI 2.20–3.04, respectively). Within each acquisition group, all groups of origin had a higher risk of VR than FRA. Within each region of origin, except the NFWI, heterosexual men had a higher risk of VR than MSM.

**Conclusions:** After accounting for sex and acquisition group, migration, especially from NFWI, remains prognostic of VR.

#### KEYWORDS

geographical origin, heterosexual, HIV, migrant, virological rebound

## INTRODUCTION

Achievement of the 95:95:95 Joint United Nations Programme on HIV/AIDS (UNAIDS) target for 2030 is conditioned by sustained viral suppression on antiretroviral therapy (ART) in all population groups living with HIV. However, although access to HIV care and treatment is universal in most European countries, disparities remain in virological outcomes to ART between individuals. Several studies have suggested that, after the initial response to ART, rates of virological suppression are lower in migrants than in the native population [1, 2]. Geographical disparities have also been described among migrants, with male migrants from sub-Saharan Africa (SSA) and Caribbean women presenting a particularly higher risk of virological failure on ART [3–5]. In these studies, the native group included heterosexual people living with HIV and men who have sex with men (MSM). Other studies have suggested that viral suppression on ART does not differ due to ethnicity, either among heterosexual people living with HIV (i.e., when men and women are analysed together) or MSM [6, 7]. However, in a previous study, we also analysed HIV acquisition groups and showed that, in France, native women but not migrant women, had a lower likelihood of viral suppression on ART than did native MSM [4]. We also found that heterosexual men, either migrants or non-migrants, had a lower likelihood of virological success on ART than native MSM [4]. We thus concluded that socioeconomic factors, sex-based differences in motivation, and/or lifestyle factors must be considered in HIV care.

When considering virological outcome after initial virological success on ART, several studies have suggested

that viral rebound (VR) is more frequent both among non-white than white heterosexuals and among heterosexual men than women [6, 8]. We thus aimed to investigate, in a large hospital cohort (the ANRS CO4-French Hospital Database on HIV [FHDH]), the impact of migration status on risk of VR after undetectability on ART among different acquisition groups (i.e., MSM and heterosexual men and women), the impact of acquisition group on risk of VR among the different regions of origin, and the impact of a combined variable encompassing migration, acquisition group, and sex on risk of VR.

## METHODS

### Population

The data source was the ANRS CO4-FHDH, a large ongoing hospital cohort study of people with HIV receiving care in one of the 182 participating French hospitals [9] that have collected clinical, biological, and therapeutic data since 1989. All participants provided written informed consent for the use of their data for research purposes. The cohort was initially approved by the French data protection agency (Commission Nationale de l'Informatique et des Libertés [CNIL]) in 1991. The research authorisation was updated to comply with new regulations, including the General Data Protection Regulation. The ANRS CO4-FHDH cohort was approved by the CEREES (Comité d'Expertise pour les Recherches, les Études et les Évaluations dans le domaine de la Santé) in 2018, and as a hospital data warehouse authorized to conduct research by the CNIL in 2021.

For this study, we considered ART-naïve people living with HIV aged  $\geq 16$  years who initiated ART between the start of 2006 and the end of 2016. Individuals were excluded if their first ART regimen was prescribed for pregnancy before 2013. Transient ART was recommended for pregnant women with CD4 cell counts  $>350/\text{mm}^3$  until 2013, when national guidelines switched to universal recommendation of ART, regardless of the CD4 cell count [10]. Individuals infected via blood transfusion, mother-to-child transmission, or intravenous drug use were also excluded because of low numbers.

Individuals had to have at least one CD4 cell count and one plasma viral load (pVL) measurement 6 months before to 1 month after ART initiation. ART was defined as any combination of at least three antiretroviral drugs or dual therapy with a boosted protease inhibitor (PI) or an integrase strand transfer inhibitor combined with lamivudine or rilpivirine. We then selected individuals who achieved viral suppression, defined as two consecutive pVL values  $<50$  copies/mL, after ART initiation and who had one CD4 cell count measurement at the date of viral suppression and at least one available pVL afterwards. The date of viral suppression (baseline) was defined as the date of the second undetectable VL.

## Statistical analysis

The primary outcome criteria was VR after first viral suppression on ART. VR was defined as one pVL  $>1000$  copies/mL or two consecutive pVL values between 50 and 1000 copies/mL, according to current guidelines [11]. Persistent low-level viremia (51–199 copies/mL) and virological failure ( $\geq 200$  copies/mL on two or more successive determinations or a single VL  $\geq 1000$  copies/mL) are both associated with serious non-AIDS events [12], and low-level viraemia is associated with viral failure [13]. The time to VR was calculated from the date of first viral suppression to the date of the first pVL  $>1000$  copies/mL or the second of two consecutive pVLs between 50 and 1000 copies/mL.

Migrant status was based on the United Nations definition: ‘anyone born and having lived outside France and now residing in France, regardless of their nationality and the duration of their stay in France’ [14]. Regions of geographical origin were subdivided into the following four groups: France, including the French West Indies (FRA); SSA; the non-French West Indies (NFWI); and other regions (OTHER). Three HIV acquisition groups were considered: MSM, other men (othM), and women.

We used the chi-squared and Mann–Whitney *U* tests to compare demographic, immunovirological, and therapeutic characteristics at ART initiation across the four regions of origin and three HIV acquisition groups. To

further explore differences related to geographical origin, sex, and HIV acquisition group, an 11-category combined variable was created that included the following: MSM originating from FRA (MSM FRA), MSM originating from SSA (MSM SSA), MSM originating from other countries (MSM OTHER), heterosexual men originating from FRA (othM FRA), heterosexual men originating from SSA (othM SSA), men originating from NFWI (othM NFWI), heterosexual men originating from other countries (othM OTHER), women originating from FRA (women FRA), women originating from SSA (women SSA), women originating from NFWI (women NFWI), and women originating from other countries (women OTHER). Because of the low numbers, we pooled MSM and heterosexual men for the othM NFWI group.

The risk of VR after virological suppression was first compared across migrant status among the HIV acquisition groups, then across the HIV acquisition group among the migrant status, and then according to the 11-category combined variable. Loss to follow-up and death were considered as competing risks. Cumulative incidence functions were estimated and plotted. Fine and Grey multivariable regression analyses were used to estimate subdistribution hazard ratios [15]. Individuals were considered lost to follow-up if more than 18 months had elapsed between the individual's last medical visit and the last ANRS CO4-FHDH update. Individuals with neither VR nor a competing event were censored at the end of follow-up or, at most, at 31 December 2018.

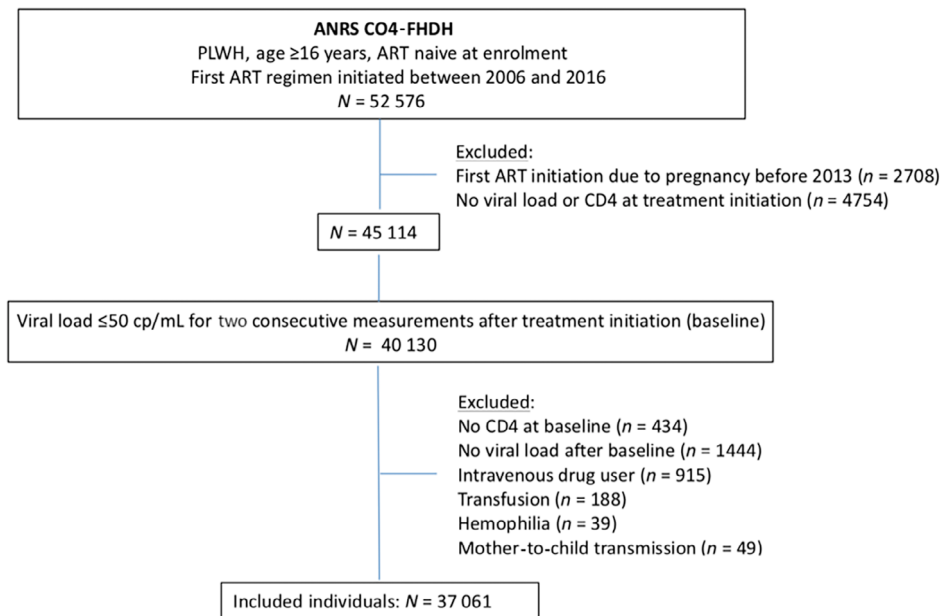
The subdistribution hazard ratios were adjusted for primary infection status at ANRS CO4-FHDH enrolment, type and calendar period of first-line ART, region of care (Paris area vs. other regions, including French West Indies), pVL and CD4 cell count at first ART, duration of ART before baseline, baseline age, preexisting AIDS status, preexisting hepatitis B or C infection, CD4 nadir, and CD4/CD8 ratio at baseline. The hepatitis status at baseline was determined by the presence of hepatitis B virus antigen or anti-hepatitis C virus antibody.

All analyses were performed using SAS v9.4 software (SAS Institute, Inc., Cary, North Carolina, USA). A *p*-value  $<0.05$  was considered to denote statistical significance.

## RESULTS

### Population

Overall, 37 061 people living with HIV with virological suppression after ART initiation were included in the study (Figure 1), of whom 21 571 (58%) were born in France, 10 148 (27%) originated from SSA, 1137 (3%) from the NFWI, and 4205 (12%) from OTHER regions.



**FIGURE 1** Flowchart participant selection. ANRS CO4-FHDH, French Hospital Database on HIV-ANRS CO4; ART, antiretroviral treatment; PLWH, people living with HIV.

The characteristics are presented by sex, HIV acquisition group, and region of origin (Table 1). Most individuals were male (71%), 62% of these were MSM, who mostly originated from France or OTHER. The women mostly originated from SSA. The MSM HIV acquisition group and the FRA region of origin were the groups with the highest CD4 cell count at ART initiation. The heterosexual men HIV acquisition group and the NFWI region of origin had the lowest CD4 cell counts at ART initiation. Heterosexual men were older, had a lower CD4 nadir, and were more frequently diagnosed with AIDS before viral suppression than were MSM or women. People from the NFWI were older, had a lower CD4 nadir, and were more frequently diagnosed with AIDS than were people from OTHER. The ART consisted mostly of triple therapy with a PI and was initiated a median of 8 months (interquartile range 5–13) before viral suppression.

## Viral rebound

Overall, 7089 individuals presented with VR. The cumulative incidence of VR rose from 12% (95% confidence interval [CI] 11–12) at 2 years to 19% (95% CI 19–20) at 5 years after ART initiation (Table 2). The 5 year-probability of VR was 14% among MSM and 23% among other men and women. Regarding origin, the probability of VR was 15% among French natives, 21% among migrants from OTHER, 26% among migrants from SSA, and 34% among migrants from the NFWI. This gradient of increase

between the different groups of origin was similar for each acquisition risk group (Table 2, Figure 2).

After adjustment, in each HIV acquisition group, as compared with FRA, the risk of VR was approximately twice in the NFWI, 1.5-fold in the SSA, and 1.3-fold in the OTHER (Figure 3a). Within each geographical region of origin, except the NFWI, for which MSM and heterosexual men were combined, MSM had the lowest risk of VR, with an approximately 20% lower risk of VR than heterosexual men. For individuals from FRA, women had a 10% (95% CI –1–23) higher risk of VR than heterosexual men; and for individuals from SSA, women had a 6% (95% CI –2–13) lower risk of VR than heterosexual men. There were no differences in the risk of VR between women and heterosexual men in other origin groups (Figure 3b). The risk of VR according to the variable combining sex, HIV acquisition group, and geographical origin group is presented in Figure 3c. Overall, after adjustment, MSM born in France had a lower risk of VR than all other groups. Men from the NFWI and women from the NFWI had the highest risk of VR relative to MSM born in France (2.46; 95% CI 2.12–2.86 and 2.59; 95% CI 2.20–3.04, respectively) (Figure 3c).

Other risk factors for VR were HIV diagnosis not in the context of a primary HIV infection, the 2006–2008 period of ART initiation versus more recent periods, pVL >30 000 copies/mL versus ≤30 000 copies/mL, PI-containing ART and other ART versus ART containing non-nucleoside reverse transcriptase inhibitors or integrase strand transfer inhibitors, treatment duration before undetectability >12 months, age <40 years, AIDS

**TABLE 1** Characteristics of the patients according to sex and acquisition group and according to geographical origin group.

Characteristic	Sex and acquisition group				Geographical origin			
	Total	MSM	OthM	Women	FRA	SSA	NFWI	OTHER
<b>Total</b>	<b>N = 37 061</b>	<b>N = 16 271 (44%)</b>	<b>N = 10 153 (27%)</b>	<b>N = 10 637 (29%)</b>	<b>N = 21 571 (58%)</b>	<b>N = 10 148 (27%)</b>	<b>N = 1137 (3%)</b>	<b>N = 4205 (12%)</b>
At FHDH enrolment								
Geographical origin: <i>n (%)</i> *								
FRA	21 571 (58)	13 688 (84)	4692 (46)	3191 (30)				
SSA	10 148 (27)	457 (3)	3722 (37)	5969 (56)				
NFWI	1137 (3)	81 (1)	518 (5)	538 (5)				
OTHER	4205 (12)	2045 (12)	1221 (12)	939 (9)				
Acquisition groups: <i>n (%)</i> **								
MSM	16 271 (44)				13 688 (63)	457 (4)	81 (7)	2045 (49)
OthM	10 153 (27)				4692 (22)	3722 (37)	518 (46)	1221 (29)
Women	10 637 (29)				3191 (15)	5969 (59)	538 (47)	939 (22)
Primary HIV infection: <i>n (%)</i> ***	5929 (16)	4208 (26)	884 (9)	837 (8)	4694 (22)	594 (6)	53 (5)	588 (14)
At ART initiation								
Region of care (Paris area): <i>n (%)</i> ***	15 658 (42)	6214 (38)	4505 (44)	4939 (46)	6819 (32)	6369 (63)	261 (23)	2209 (53)
Initiation period: median (IQR)***	2011 (2009–2014)	2012 (2009–2014)	2011 (2009–2014)	2011 (2009–2014)	2011 (2009–2014)	2012 (2009–2014)	2012 (2008–2014)	2012 (2009–2015)
CD4 (cells/ $\mu$ L): median (IQR)***	312 (180–453)	360 (240–510)	255 (109–388)	289 (167–418)	339 (210–486)	269 (148–390)	261 (103–385)	299 (161–441)
pVL (cp/mL): median (IQR)****	56 519 (13440–188 000)	62 931 (17958–193 348)	75 000 (18020–247 000)	34 000 (6300–131 793)	63 218 (16657–204 900)	40 046 (9570–143 320)	43 120 (8318–158 489)	60 494 (15236–199 526)

(Continues)



TABLE 1 (Continued)

Characteristic	Sex and acquisition group				Geographical origin			
	Total N = 37 061	MSM N = 16 271 (44%)	OthM N = 10 153 (27%)	Women N = 10 637 (29%)	FRA N = 21 571 (58%)	SSA N = 10 148 (27%)	NFWI N = 1137 (3%)	OTHER N = 4205 (12%)
Type of ART: <i>n</i> (%)***								
Triple therapy with PI	19 335 (52)	7774 (48)	5407 (53)	6154 (58)	11 015 (51)	5696 (56)	590 (52)	2034 (48)
Triple therapy with NNRTI	10 561 (29)	4905 (30)	2886 (28)	2770 (26)	6123 (28)	2795 (27)	355 (31)	1288 (31)
Triple therapy with INSTI	5646 (15)	2872 (18)	1459 (15)	1315 (12)	3454 (16)	1291 (13)	165 (15)	736 (18)
Other cART	1519 (4)	720 (4)	401 (4)	398 (4)	979 (5)	366 (4)	27 (2)	147 (3)
CD4 nadir (cells/ $\mu$ L): median (IQR)***	279 (158–400)	323 (215–450)	226 (92–342)	258 (146–368)	304 (183–430)	240 (130–346)	226 (84–344)	265 (140–390)
At baseline (viral suppression)								
Age: median (IQR)***	40 (33–48)	39 (31–46)	44 (36–52)	38 (32–48)	41 (33–50)	38 (32–46)	43 (36–52)	39 (32–48)
AIDS: <i>n</i> (%)***	5768 (16)	1771 (11)	2300 (23)	1697 (16)	2955 (14)	1793 (18)	258 (23)	762 (18)
HBV or HCV: <i>n</i> (%)***	2785 (8)	906 (6)	1002 (10)	877 (8)	1138 (5)	1252 (12)	64 (6)	331 (8)
ART duration (months): median (IQR)***	8 (5–13)	8 (5–12)	9 (6–14)	8 (5–12)	8 (5–13)	8 (5–13)	8 (5–13)	8 (5–13)
CD4/CD8 ratio: median (IQR)***	0.61 (0.38–0.92)	0.67 (0.45–0.96)	0.50 (0.29–0.80)	0.61 (0.38–0.94)	0.66 (0.42–0.96)	0.66 (0.42–0.96)	0.48 (0.26–0.76)	0.59 (0.36–0.90)

Abbreviations: ART, antiretroviral therapy; cART, combined ART; FHDH, French Hospital Database on HIV; FRA, French natives; HBV, hepatitis B antigen; HCV, hepatitis C antibodies; INSTI, integrase inhibitor; IQR, interquartile range; MSM, men who have sex with men; NFWI, non-French West Indies; NNRTI, non-nucleoside reverse transcriptase inhibitor; OTHER, other regions of the world; OthM, other men; PI, protease inhibitor; SSA, sub-Saharan Africa.

\* $p < 0.0001$  for comparison according to sex and acquisition group. \*\* $p < 0.0001$  for comparison according to geographical origin. \*\*\* $p < 0.0001$  for both comparisons (comparison according to sex and acquisition group and comparison according to geographical origin). \*\*\*\* $p = 0.0006$  for comparison according to sex and acquisition group and  $p = 0.0155$  for comparison according to geographical origin.

**TABLE 2** Estimated cumulative incidence of viral rebound 2 and 5 years after viral suppression according to sex, acquisition, and geographical origin group.

Transmission group	Geographical origin	N	After 2 years % (95% CI)	After 5 years % (95% CI)
All		37 061	12 (11–12)	19 (19–20)
MSM		16 271	09 (08–09)	14 (14–15)
OthM		10 153	14 (13–15)	23 (22–24)
Women		10 637	15 (14–16)	23 (23–24)
	FRA	21 571	09 (09–10)	15 (15–16)
	SSA	10 148	16 (15–17)	26 (25–27)
	NFWI	1137	21 (19–24)	34 (31–37)
	Other	4205	13 (12–14)	21 (20–23)
MSM	FRA	13 688	08 (08–09)	14 (13–14)
	SSA	457	10 (07–13)	22 (17–26)
	Other	2045	11 (10–13)	18 (16–20)
OthM	FRA	4692	11 (10–12)	17 (16–19)
	SSAss	3722	16 (15–17)	28 (26–29)
	NFWI (men)	599	22 (19–26)	35 (31–40)
	Other	1221	15 (13–17)	25 (23–28)
Women	FRA	3191	12 (11–13)	18 (17–20)
	SSA	5969	16 (15–17)	26 (25–27)
	NFWI	538	20 (16–23)	32 (28–37)
	Other	939	15 (13–17)	22 (19–25)

Abbreviations: CI, confidence interval; FRA, French natives; MSM, men who have sex with men; NFWI, non-French West Indies; Other, other regions of the world; OthM, other men; SSA, sub-Saharan Africa.

status, CD4 nadir  $<100/\text{mm}^3$ , and  $\text{CD4}/\text{CD8} \leq 0.4$  (Table 3).

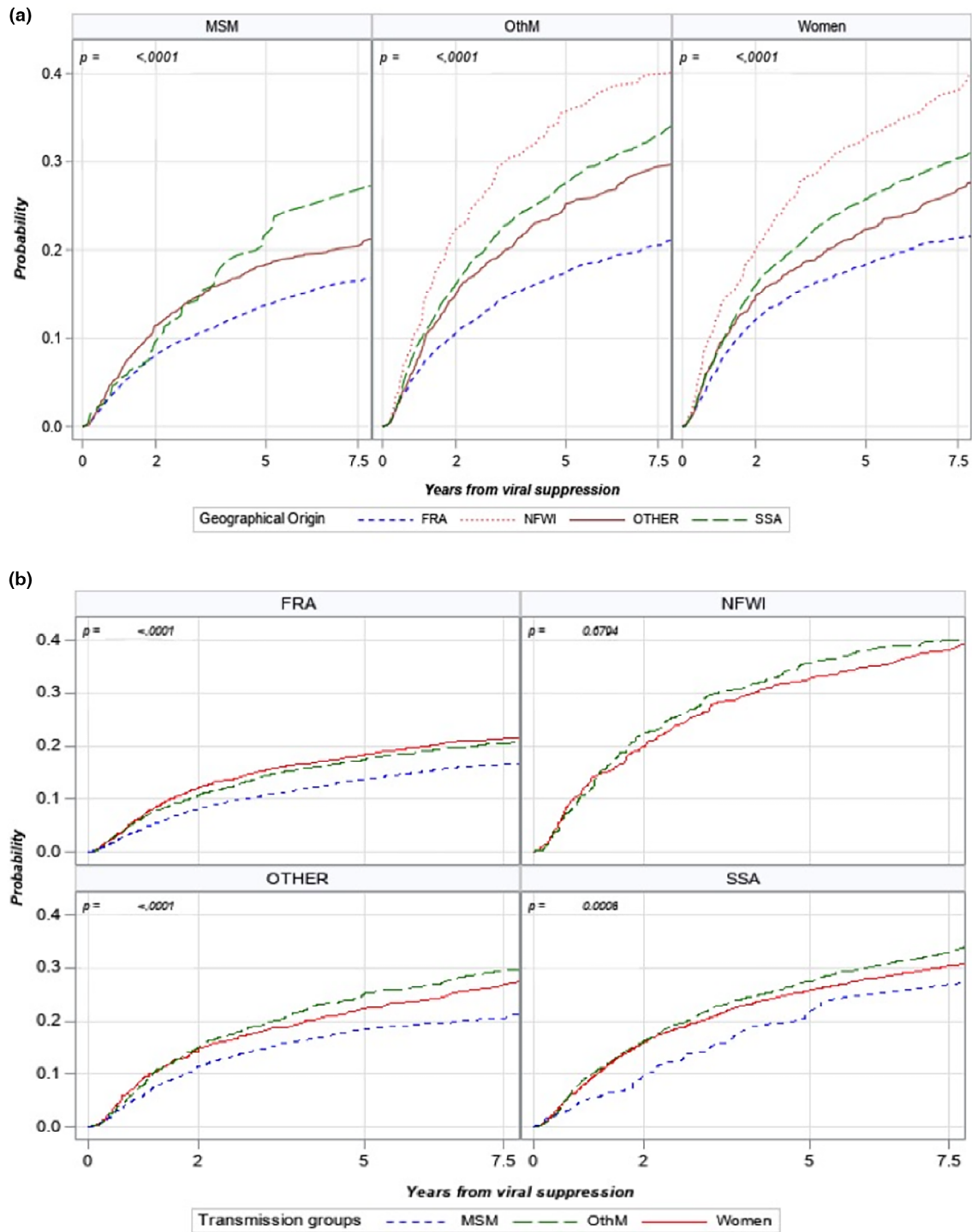
## DISCUSSION

Among individuals living in France achieving undetectability after ART initiation, 19% exhibited a VR within 5 years, but the VR reached 34% in migrants from NFWI. Despite free access to treatment in France, the long-term benefits from ART differed by HIV acquisition group or the migration status: the risk of VR was higher in migrants and in HIV acquisition groups other than MSM. After first undetectability on ART, all HIV acquisition groups had a higher risk of VR than MSM born in France, with men and women from the NFWI having the highest risk (almost 3-fold higher). Within each acquisition group, all groups of origin had a higher risk of VR than people born in France, with people from France having the lowest risk, those from OTHER and SSA having an intermediate risk, and those from the NFWI having the highest risk. Within the FRA, SSA, and OTHER origin group, MSM had a lower risk of VR than heterosexual men. For individuals from France, women

tended to have a higher risk of VR than heterosexual men, and for individuals from SSA, women tended to have a lower risk of VR than heterosexual men. There were no differences according to sex among heterosexual people from other countries and the NFWI.

The main strength of the ANRS CO4-FHDH prospective cohort is its large size and extended follow-up, which allowed us to compare different HIV risk groups, that is, according to sex, acquisition group, and region of origin. Our study had several limitations. No data on treatment adherence are available in the ANRS CO4-FHDH. We also had no data on travel abroad, which is more frequent for migrants than non-migrants and is associated with an increased risk of VR among migrants, at least partially due to lower adherence during trips [16, 17]. Loss to follow-up is generally associated with poorer adherence. Here, loss to follow-up before the last database update was considered as a competing risk. However, an interruption of follow-up of more than 18 months did not affect the results when added to the models (data not shown). Socio-economic factors and lifestyle factors, which could explain some differences between migrants and non-migrants [18, 19], are not recorded in the ANRS CO4-FHDH database. For example, individuals originating from SSA/the



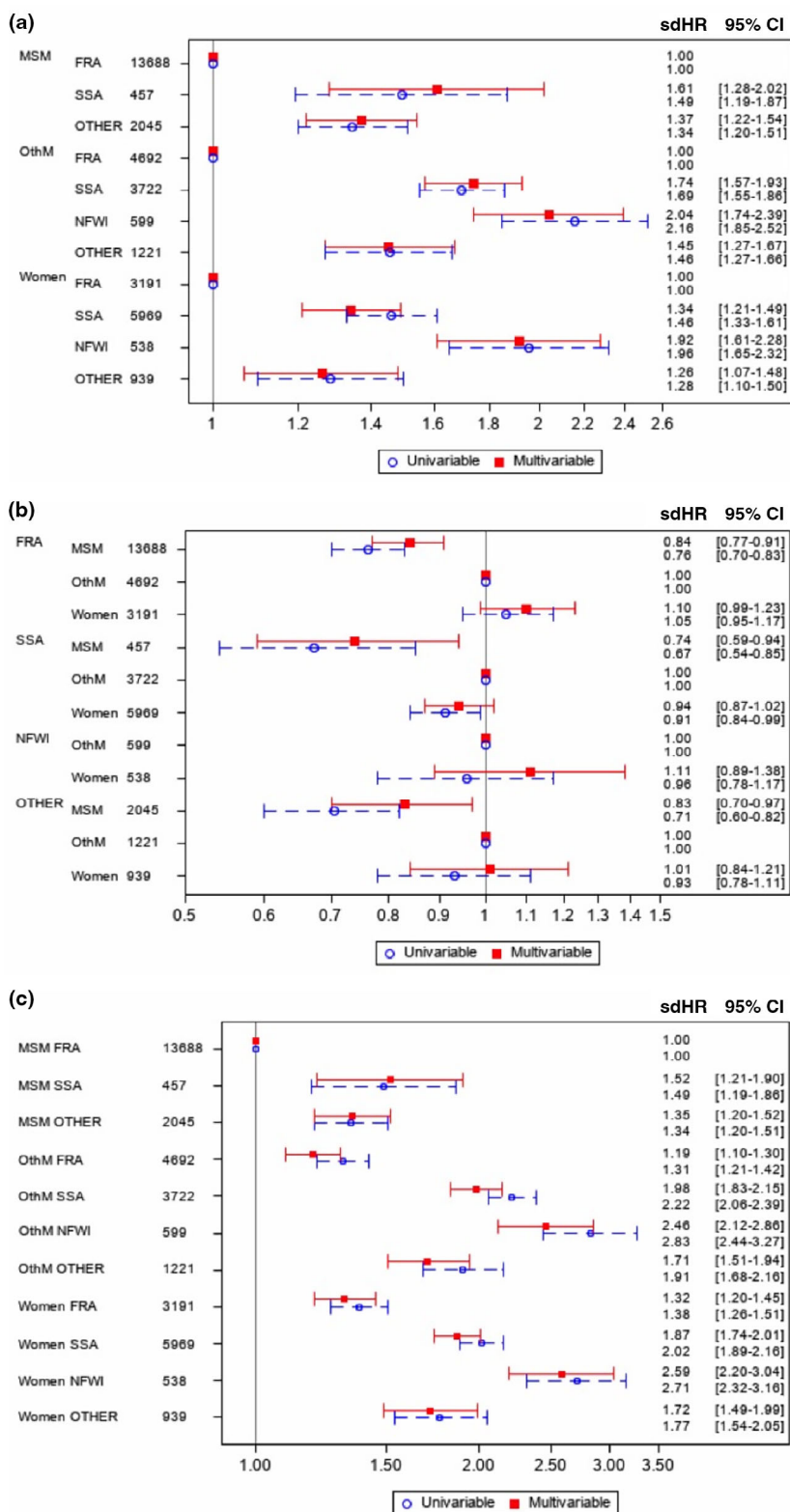


**FIGURE 2** Cumulative incident functions of viral rebound. (a) According to HIV sex acquisition group. (b) According to geographical region of origin. FRA, French natives; MSM, men who have sex with men; NFWI, non-French West Indies; OTHER, other regions of the world; OthM, other men; SSA, sub-saharan Africa.

NFWI have a lower prevalence of smoking and alcohol consumption than non-migrant individuals [20–22], and obesity is highly prevalent among migrant women from SSA [20, 23–25].

Our study shows that the risk of VR is higher in all migrant groups than in people born in France, regardless

of the HIV risk group, that is, MSM or heterosexual men or women. Previous European studies, which reported a higher risk of viral failure among migrants, did not differentiate migration status according to HIV acquisition groups [1, 2, 6] or did not differentiate region of origin [6]. We had the opportunity to assess differences among



**FIGURE 3** Subdistribution hazard ratio (sdHR) of viral rebound. (a) By geographical region of origin according to sex and acquisition group. (b) By acquisition group according to geographical region of origin. (c) Combined by geographical region of origin and sex and acquisition group. CI, confidence interval; FRA, French natives; MSM, men who have sex with men; NFWI, non-French West Indies; Other, other regions of the world; OthM, other men; SSA, sub-Saharan Africa.

TABLE 3 Risk of virological rebound. Subdistribution hazard ratio from univariable and multivariable Fine and Grey analyses.

Group	Subgroup	Univariable		Multivariable model	
		sdHR (95% CI)	p-value	sdHR (95% CI)	p-value
Sex, HIV acquisition, and geographical origin group			<0.0001		<0.0001
	MSM FRA	1		1	
	MSM SSA	1.49 (1.19–1.86)		1.52 (1.21–1.90)	
	MSM other	1.34 (1.20–1.51)		1.35 (1.20–1.52)	
	OthM FRA	1.31 (1.21–1.42)		1.19 (1.10–1.30)	
	OthM SSA	2.22 (2.06–2.39)		1.98 (1.83–2.15)	
	OthM NFWI <sup>a</sup>	2.83 (2.44–3.27)		2.46 (2.12–2.86)	
	OthM OTHER	1.91 (1.68–2.16)		1.71 (1.51–1.94)	
	Women FRA	1.38 (1.26–1.51)		1.32 (1.20–1.45)	
	Women SSA	2.02 (1.89–2.16)		1.87 (1.74–2.01)	
	Women NFWI	2.71 (2.32–3.16)		2.59 (2.20–3.04)	
	Women OTHER	1.77 (1.54–2.05)		1.72 (1.49–1.99)	
Primary HIV infection			<0.0001		0.04
	No	1		1	
	Yes	0.69 (0.64–0.74)		0.92 (0.86–0.99)	
At ART initiation					
Region of care			<0.0001		0.07
	Paris area	1		1	
	Other	0.89 (0.85–0.94)		1.05 (1.00–1.10)	
Period of ART initiation					
			<0.0001		<0.0001
	2006–2008	1		1	
	2009–2011	0.73 (0.69–0.78)		0.81 (0.76–0.85)	
	2012–2014	0.56 (0.53–0.60)		0.67 (0.62–0.71)	
	2015–2016	0.52 (0.48–0.57)		0.65 (0.59–0.73)	
Type of ART					
			<0.0001		<0.0001
	Triple therapy with PI	1		1	
	Triple therapy with NNRTI	0.70 (0.66–0.74)		0.78 (0.73–0.82)	
	Triple therapy with INI	0.62 (0.57–0.68)		0.88 (0.79–0.97)	
	Other cART	1.10 (0.98–1.22)		1.14 (1.02–1.27)	
pVL (cp/mL)					
			<0.0001		<0.0001
	≤500	0.73 (0.66–0.82)		0.74 (0.66–0.84)	
	>500–5000	0.73 (0.67–0.79)		0.79 (0.72–0.87)	
	>5000–30 000	0.72 (0.67–0.76)		0.80 (0.75–0.85)	
	>30 000	1		1	
CD4 (cells/μL)					
			<0.0001		0.07
	<100	1		1	
	100–199	0.90 (0.84–0.97)		1.23 (1.07–1.42)	
	200–349	0.68 (0.63–0.72)		1.17 (1.00–1.37)	
	350–499	0.53 (0.49–0.57)		1.19 (1.00–1.41)	
	≥500	0.43 (0.39–0.47)		1.15 (0.95–1.40)	

TABLE 3 (Continued)

Group	Subgroup	Univariable		Multivariable model	
		sdHR (95% CI)	p-value	sdHR (95% CI)	p-value
At baseline (viral suppression)					
Treatment duration (months)			<0.0001		<0.0001
	0–6	0.68 (0.64–0.72)		0.83 (0.77–0.89)	
	>6–12	0.72 (0.68–0.76)		0.81 (0.76–0.86)	
	>12	1		1	
Age			<0.0001		<0.0001
	16–29	1.04 (0.97–1.11)		1.22 (1.14–1.31)	
	30–39	1		1	
	40–49	0.91 (0.86–0.96)		0.88 (0.83–0.94)	
	≥50	0.92 (0.86–0.98)		0.88 (0.82–0.94)	
AIDS			<0.0001		<0.0001
	No	1		1	
	Yes	1.67 (1.58–1.77)		1.21 (1.13–1.30)	
HBV/HCV infection			<0.0001		0.08
	No	1		1	
	Yes	1.25 (1.15–1.35)		1.08 (0.99–1.17)	
CD4 nadir			<0.0001		<0.0001
	<100	1		1	
	100–199	0.84 (0.78–0.90)		0.82 (0.71–0.94)	
	200–345	0.63 (0.59–0.67)		0.78 (0.67–0.91)	
	350–499	0.47 (0.43–0.50)		0.71 (0.60–0.85)	
	≥500	0.39 (0.35–0.43)		0.71 (0.58–0.88)	
CD4/CD8			<0.0001		<0.0001
	0.0–0.4	1		1	
	>0.4–0.6	0.88 (0.82–0.96)		0.95 (0.89–1.02)	
	>0.6–0.8	0.71 (0.66–0.77)		0.86 (0.80–0.94)	
	>0.8	0.57 (0.53–0.61)		0.82 (0.76–0.89)	
	Missing	0.61 (0.54–0.68)		0.72 (0.65–0.79)	

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; FRA, French natives; HBV, hepatitis B antigen; HCV, hepatitis C antibodies; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; NFWI, non-French West Indies; NNRTI, non-nucleoside reverse transcriptase inhibitor; Other, other regions of the world; OthM, other men; PI, protease inhibitor; sdHR, subdistribution hazard ratio; SSA, sub-Saharan Africa.

<sup>a</sup>OthM NFWI include MSM and heterosexual men originating from NFWI.

MSM or heterosexual men and women and showed that people from each origin group had a higher risk of VR than those native to France. Undocumented migrants are not included in the ANRS CO4-FHDH. In France, access to ART is universal and free for people living with HIV, regardless of their country of origin or health insurance. However, previous studies showed that differences in virological outcomes, either initial or sustained virological suppression, on ART are mainly driven by socioeconomic factors [2, 18, 26] and that differences according to migration status are largely explained by such factors [27]. A previous study suggested that Caribbean women but

not men have a higher virological failure rate than their French-native same-sex counterparts [5]. We show here that migrants from the NFWI, both men and women, have the highest risk of VR relative to native French heterosexual men or women. Differences in socioeconomic conditions, educational level, and fear of stigma with non-disclosure of HIV infection could explain these disparities, as was strongly suggested in a previous study on a smaller population [27].

The assessment of risk of VR among individuals from each country of origin allowed us to refine these results. Among people born in France, SSA, or OTHER

country, heterosexual men had a 20% (95% CI 10–30) to 35% (95% CI 6–69) higher risk of VR than MSM. Among heterosexual individuals, men from SSA tended to have a higher risk of VR, and those from France a lower risk, than women. A previous study suggested higher rates of VR among heterosexual men than women in the United Kingdom [8]. It was previously found that women from SSA had a better virological outcome on ART than men, either migrant or non-migrant, or women from France [4, 28].

Sex-specific data on the virological outcomes of individuals on ART are scarce, as are studies on minorities in HIV risk groups, such as MSM migrants. Our results suggest that migrants living with HIV in France, especially those from the NFWI, face significant barriers to maintaining viral suppression and remaining engaged in HIV care, regardless of their HIV risk group, and that heterosexual men experience worse outcomes than MSM regardless of their region of origin. As suboptimal adherence to treatment and disengagement from care are associated with HIV-related morbidity and mortality and acquisition, this is of concern.

We had the opportunity to assess other factors. ART containing PIs but not non-nucleoside reverse transcriptase inhibitors or integrase strand transfer inhibitors, and older periods when less well-tolerated ART was mainly prescribed, were predictive of VR, as previously shown [27, 29]. Higher pVL, lower CD4 nadir or CD4/CD8 ratio, and AIDS status were also associated with VR. This emphasizes the need for early HIV diagnosis and immediate treatment [13, 30]. The higher risk of secondary VR for higher viral load might be related to a higher HIV burden, which is less forgiving of a suboptimal regimen [29]. Previous studies have shown that younger age is independently associated with VR [13, 26, 27], with younger age being associated with non-adherence to ART [26].

Although progress has been made towards reaching the UNAIDS targets of ending the AIDS epidemic by 2030 and preventing new acquisition, there remain striking heterogeneities between HIV risk groups. Educational interventions culturally tailored to the migrant population would help to reduce the fear of stigmatization and improve their care seeking and adherence to ART. Political and public health decisions are also necessary to reduce the socioeconomic insecurity experienced by recent migrants, who are frequently undocumented and vulnerable to HIV infection.

#### AUTHOR CONTRIBUTIONS

Conceptualization: SA, HSL, SG. Methodology: SA, HSL, SG. Formal Analysis: SA, EL, HSL. Supervision: SA, SG. Analysis and interpretation of results: SA, HSL, EL, AB, SM, PdT, JP, AC, MAK, DR, FC, PT, RP, SG. Writing

original draft: SA, HSL. Review and editing: SA, HSL, EL, AB, SM, PdT, JP, AC, MAK, DR, FC, PT, RP, SG.

#### ACKNOWLEDGEMENTS

We are grateful to all ANRS CO4-FHDH participants and research assistants, without whom this work would not have been possible. Members of ANRS CO4-FHDH are listed at <https://anrs-co4.fhdh.fr/>.

#### FUNDING INFORMATION

The ANRS CO4-FHDH is supported by the ANRS-MIE (Agence Nationale de Recherche sur le Sida et les hépatites virales-Maladies Infectieuses Emergentes), Sorbonne University, INSERM (Institut National de la Santé et de la Recherche Médicale) and the French Ministry of Health. The funders had no role in the study design, data collection, data analysis and interpretation, or writing of the report.

#### CONFLICT OF INTEREST STATEMENT

In the past 3 years, FC was a member of the French Gilead HIV board and of the ViiV board. PT was a scientific advisor for Gilead and Pfizer. DR has received travel/accommodations/meeting expenses from MSD. MKJ has received travel/accommodations/meeting expenses from Gilead and MSD and was a member of the ViiV board and the MSD board. RP has received travel/accommodations/meeting expenses and advisory fees from Gilead, ViiV Healthcare and Merck France. The remaining authors have no funding or conflicts of interest to disclose.

#### ORCID

S. Abgrall  <https://orcid.org/0000-0002-7891-7594>

S. Grabar  <https://orcid.org/0000-0002-4816-4261>

#### REFERENCES

1. Dray-Spira R, Spire B, Heard I, Lert F, VESPA Study Group. Heterogeneous response to HAART across a diverse population of people living with HIV: results from the ANRS-EN12-VESPA study. *AIDS*. 2007;21(S1):S5-S12. doi:10.1097/01.aids.0000255079.39352.9b
2. Saracino A, Lorenzini P, Lo Caputo S, et al. Increased risk of virologic failure to the first antiretroviral regimen in HIV-infected migrants compared to natives: data from the ICONA cohort. *Clin Microbiol Infect*. 2016;22(288):e1-e8. doi:10.1016/j.cmi.2015.10.026
3. Monge S, Alejos B, Dronza F, et al. Inequalities in HIV disease management and progression in migrants from Latin America and sub-Saharan Africa living in Spain. *HIV Med*. 2013;14:273-283. doi:10.1111/hiv.12001
4. De Monteynard LA, Matheron S, Gilquin J, et al. Influence of geographic origin, sex and HIV transmission group on the outcome of first-line combined antiretroviral therapy in France. *AIDS*. 2016; 30(14):2235-2246. doi:10.1097/QAD.0000000000001193
5. Jarrin I, Monge S, Mocroft A, et al. Immunological and virological response to antiretroviral treatment in migrant and native



- men and women in Western Europe; is benefit equal for all? *HIV Med.* 2018;19(1):42-48. doi:10.1111/hiv.12536
6. United Kingdom Collaborative HIV Cohort Study Group. Uptake and outcome of combination antiretroviral therapy in men who have sex with men according to ethnic group: the UK CHIC study. *J Acquir Immune Defic Syndr.* 2012;59(5):523-529. doi:10.1097/QAI.0b013e318245c9ca
  7. Dhairyawan R, Okhai H, Hill T, Sabin CA, UK Collaborative HIV Cohort (UK CHIC) Study. Differences in HIV clinical outcomes amongst heterosexuals in the United Kingdom by ethnicity. *AIDS.* 2021;35(11):1813-1821. doi:10.1097/QAD.0000000000002942
  8. Barber TJ, Geretti AM, Anderson J, et al. Outcomes in the first year after initiation of first-line HAART among heterosexual men and women in the UK CHIC study. *Antivir Ther.* 2011;16(6):805-814. doi:10.3851/IMP1818
  9. Mary-Krause M, Grabar S, Lievre L, et al. Cohort profile: French hospital database on HIV (FHDH-ANRS CO4). *Int J Epidemiol.* 2014;43:1425-1436. doi:10.1093/ije/dyu002
  10. Morlat P, Expert Group on HIV Infection. *Medical Care for People Infected with HIV.* Flammarion médecine-sciences; 2013. Accessed 03 Oct 2024. Available from [https://sante.gouv.fr/IMG/pdf/Rapport\\_Morlat\\_2013\\_Mise\\_en\\_ligne.pdf](https://sante.gouv.fr/IMG/pdf/Rapport_Morlat_2013_Mise_en_ligne.pdf)
  11. Rindi LV, Zaçe D, Compagno M, et al. Management of low-level HIV viremia during antiretroviral therapy: Delphi consensus statement and appraisal of the evidence. *Sex Transm Infect.* 2024;100(7):442-449. doi:10.1136/sextrans-2024-056198
  12. Ganesan A, Hsieh HC, Chu X, et al. Low level viremia is associated with serious non-AIDS events in people with HIV. *Open Forum Infect Dis.* 2024;11(4):ofae147. doi:10.1093/ofid/ofae147
  13. Antiretroviral Therapy Cohort Collaboration (ART-CC), Vandenhende MA, Ingle SM, et al. Impact of low-level viremia on clinical and virological outcomes in treated HIV-1 infected patients. *AIDS.* 2015;29:373-383. doi:10.1097/QAD.0000000000000544
  14. Thierry X. International migrations in Europe: towards harmonization of statistics. *INED Populat Soc.* 2008;442:1-4.
  15. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc.* 1999;94:496-509. doi:10.1080/01621459.1999.10474144
  16. Gebreselassie HM, Kraus D, Fux CA, et al. Ethnicity predicts viral rebound after travel to the tropics in HIV-infected travelers to the tropics in the Swiss HIV cohort study. *HIV Med.* 2017;18(8):564-572. doi:10.1111/hiv.12491
  17. Kankou JM, Bouchaud O, Lele N, et al. Factors associated with virological rebound in HIV-positive sub-Saharan migrants living in France after traveling back to their native country. *J Immigr Minor Health.* 2019;21:1342-1348. doi:10.1007/s10903-019-00864-y
  18. Gueler A, Schoeni-Affolter F, Moser A, et al. Neighbourhood socio-economic position, late presentation and outcomes in people living with HIV in Switzerland. *AIDS.* 2015;29:231-238. doi:10.1097/QAD.0000000000000524
  19. Gueler A, Moser A, Calmy A, et al. Life expectancy in HIV-positive persons in Switzerland: matched comparison with general population. *AIDS.* 2017;31(3):427-436. doi:10.1097/QAD.0000000000001335
  20. Agyemang C, Addo J, Bhopal R, Aikins A d G, Stronks K. Cardiovascular disease, diabetes and established risk factors among populations of sub-Saharan African descent in Europe: a literature review. *Glob Health.* 2009;5:7. doi:10.1186/1744-8603-5-7
  21. Lert F, Annequin M, Tron L, et al. et le groupe Vespa2. Situation socioéconomique des personnes vivant avec le VIH suivies à l'hôpital en France métropolitaine en 2011. Premiers résultats de l'enquête ANRSVespa2. *Bull Epidemiol Hebd.* 2013;26-27:293-299. Available at: [http://www.invs.sante.fr/beh/2013/27/2013\\_26-27\\_2.html](http://www.invs.sante.fr/beh/2013/27/2013_26-27_2.html). Accessed 24 May 2016.
  22. Lert F, Paye A, May T, et al. Caractéristiques sociales et comportementales des personnes séropositives pour le VIH décédées en 2010 en France métropolitaine: quelles implications pour la prise en charge? *Bull Epidemiol Hebd.* 2016;41-42:749-754.
  23. Pourcher G, Costagliola D, Martinez V. Obesity in HIV-infected patients in France: prevalence and surgical treatment options. *J Visc Surg.* 2015;152:33-37. doi:10.1016/j.jviscsurg.2014.12.001
  24. Sax PE, Erlandson KM, Lake JE, et al. Weight gain following initiation of antiretroviral therapy: risk factors in randomized comparative clinical trials. *Clin Infect Dis.* 2020;71:1379-1389. doi:10.1093/cid/ciz999
  25. Grabar S, Potard V, Piroth L, et al. Striking differences in weight gain after cART initiation depending on early or advanced presentation: results from the ANRS CO4 FHDH cohort. *J Antimicrob Chemother.* 2023;78(3):757-768. doi:10.1093/jac/dkac007
  26. Burch LS, Smith CJ, Anderson J, et al. Socioeconomic status and treatment outcomes for individuals with HIV on antiretroviral treatment in the UK: cross-sectional and longitudinal analyses. *Lancet Public Health.* 2016;1(1):e26-e36. doi:10.1016/S2468-2667(16)30002-0
  27. Abgrall S, Raho-Moussa M, Seng R, et al. Elevated risk of viral rebound on ART in migrants living in France: role of socioeconomic factors. *Antivir Ther.* 2019;24(7):541-552. doi:10.3851/IMP3339
  28. Novelli S, Delobel P, Bouchaud O, et al. Enhanced immunovirological response in women compared to men after antiretroviral therapy initiation during acute and early HIV-1 infection: results from a longitudinal study in the French ANRS Primo cohort. *J Int AIDS Soc.* 2020;23(4):e25485. doi:10.1002/jia2.25485
  29. Raffi F, Hanf M, Ferry T, et al. Impact of baseline plasma HIV-1 RNA and time to virological suppression on virological rebound according to first-line antiretroviral therapy. *J Antimicrob Chemother.* 2017;72:3425-3434. doi:10.1093/jac/dkx300
  30. The INSIGHT START Study Group, Lundgren JD, Babiker AG, et al. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *N Engl J Med.* 2015;373:795-807. doi:10.1056/NEJMoa1506816

**How to cite this article:** Abgrall S, Selinger-Leneman H, Lanoy E, et al. Viral rebound on antiretroviral therapy in France according to region of origin, sex, and HIV acquisition group. Results from the French Hospital Database on HIV (ANRS CO4-FHDH). *HIV Med.* 2024;1-13. doi:10.1111/hiv.13729