

# Roll-out of HIV pre-exposure prophylaxis use in France: A nationwide observational study from 2016 to 2021



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## Summary

**Background** Oral HIV pre-exposure prophylaxis (PrEP) has been available and fully reimbursed for people at high risk of sexually acquired HIV infection in France since January 2016. Its dissemination has been widely promoted to reduce HIV incidence in high-risk populations. This study aimed to assess the roll-out of PrEP use in France from its implementation until mid-2021.

**Methods** Using the French National Health Data System (SNDS) covering 99% of people residing in France, all PrEP users defined as individuals aged 15 years or older who received at least one dispensing of PrEP between 1 January 2016 and 30 June 2021 were identified. PrEP users number and their socio-demographic and PrEP use characteristics were assessed over time.

**Findings** As of 30 June 2021, a total of 42 159 individuals had initiated PrEP in France. Monthly PrEP initiations increased steadily up to 1027 in February 2020, and then slowed down sharply from the onset of the COVID-19 epidemic until a recovery in the first half of 2021. PrEP users were overwhelmingly men (97.5%, 41 126/42 159), aged 36 years on average, living in a large metropolitan area (73.8%, 31 096/42 159), and among whom a minority (7.0%, 2966/42 159) were socio-economically disadvantaged. Throughout the study period, 80.90% of users renewed PrEP from one semester to another, suggesting a good level of maintenance among those engaged in treatment. Nevertheless, for 20.1% (7148/35 549) of new PrEP users no prescription renewal was recorded in the first six months after initiation, suggesting a substantial proportion of early treatment discontinuation. Private practitioners accounted for a minority (21.3%, 77 885/366 399) of PrEP renewal prescriptions.

**Interpretation** PrEP roll-out has been markedly impacted by the COVID-19 pandemic in France. Although PrEP deployment has been substantial among men who have sex with men, further action is needed to expand access to PrEP to all other population groups who could benefit from it and to promote adherence to treatment.

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**Keywords:** HIV infection; Pre-exposure prophylaxis (PrEP); Tenofovir disoproxil fumarate; Emtricitabine; HIV prevention; Men who have sex with men (MSM); Pharmacoepidemiology

## Introduction

Human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) using the fixed-dose combination of oral tenofovir disoproxil fumarate and emtricitabine (TDF-FTC), has been shown to be a highly effective individual protection strategy for HIV-negative people in randomized control trials<sup>1,2</sup> and real-life<sup>3,4</sup> studies, provided adherence is high.<sup>5</sup> This oral combination of two

HIV reverse transcriptase inhibitors has been authorized for HIV PrEP in Europe since March 2017. In France, daily oral use of PrEP with TDF-FTC has had a pre-marketing approval since January 2016 and has been fully reimbursed since then for people at high risk of sexually acquired HIV infection (*i.e.* men or transgender people who have sex with men, persons who inject drugs, sex workers, people in vulnerable situations at risk of condomless sex in the context of high HIV prevalence or exposure<sup>6</sup>) as a complement to a comprehensive prevention strategy.<sup>7</sup> PrEP management includes quarterly HIV and STI screening and promotion of PrEP adherence and condom use.<sup>6</sup> The recommended regimen is either continuous with daily dosing, or on-

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### Research in context

#### *Evidence before this study*

HIV pre-exposure prophylaxis (PrEP) with tenofovir disoproxil fumarate and emtricitabine (TDF-FTC) has been available and fully reimbursed for people at high risk of sexually acquired HIV infection in France since January 2016. Its dissemination and appropriate use, strongly encouraged in France, are expected to reduce HIV incidence in high-risk populations. Large-scale, real-life data are essential to assess the roll-out of PrEP dissemination and its uptake by different subgroups of the concerned population in routine clinical practice. Such data are needed to guide policies ensuring accessibility to and efficiency of this highly effective prevention tool to all those for whom it might be beneficial.

#### *Added value of this study*

Using comprehensive data of the French National Health Data System (SNDS) which covers 99% of people residing in France, we identified all PrEP users between 1 January 2016 and 30 June 2021. As of 30 June 2021, a total of 42 159 individuals had initiated PrEP in France. After a continuously increasing trend in PrEP initiations until February 2020, a marked slowdown occurred with the onset of the COVID-19 pandemic in 2020. A recovery was observed in the first half of 2021. PrEP users were overwhelmingly socio-economically advantaged men living in a large metropolitan area, suggesting that PrEP use has mostly remained limited to men who have sex with men. Although our data suggest a good overall level of maintenance among those engaged in treatment, 20.1% of new PrEP users had no renewal prescription in the first six months after initiation, suggesting a substantial proportion of early treatment discontinuation. Private practitioners accounted for a minority of PrEP prescriptions.

#### *Implications of all the available evidence*

This comprehensive real-life study provides evidence of a major impact of the COVID-19 pandemic on PrEP roll-out in France, which deserves to be monitored in the longer term. It also highlights the need for additional measures to expand access to PrEP to all potential beneficiaries, including women, socio-economically disadvantaged people and those living in remote areas, as well as to improve adherence to treatment. Future studies are needed to assess the impact of the recent extension of PrEP initiation to all prescribers in France.

demand (only for men who have sex with men, MSM). PrEP prescriptions are made for a maximum duration of three months with monthly treatment dispensation. Until recently, PrEP initiation was reserved to physicians experienced in the management of HIV practicing in hospital or in sexual health centers.<sup>7</sup> Since June 2021, the initiation of PrEP has been extended to all prescribing physicians, including general practitioners (GPs), in

order to expand its use and diversify the profiles of beneficiaries.<sup>8</sup> Renewals can be made by any prescribing physician.

Strengthening HIV prevention is crucial in light of the continuing high incidence in European and other developed countries,<sup>9</sup> especially in the current context marked by the COVID-19 pandemic which has substantially weighted on access to preventive services including PrEP in France and other countries.<sup>10–13</sup> Large-scale, real-life data are essential to evaluate the roll-out of PrEP dissemination and its uptake by different subgroups of the affected population in routine clinical practice. Such data are needed to guide policies ensuring accessibility to and efficiency of this highly effective prevention tool to all those for whom it might be beneficial. This nationwide study aimed to assess the roll-out of PrEP use in France from its implementation up to mid-2021, using comprehensive data of the French National Health Data System (SNDS).

### Methods

#### Data sources

This study was conducted using comprehensive data of the French National Health Data System (*Système National des Données de Santé*, SNDS), which covers 99% of people residing in France (*i.e.* over 66 million inhabitants). The SNDS contains anonymised individual data on all reimbursed health expenditures, including prescribed drugs (coded according to the Anatomical Therapeutic Classification-ATC) and outpatient laboratory tests, and ambulatory health care recourses. Information on the medical indications for prescriptions is not available, but the existence of 100% coverage for care related to a serious and costly long-term illness (*e.g.* cancer, diabetes, HIV/AIDS etc.) is registered with the corresponding diagnosis coded according to the International Classification of Diseases, 10th Revision (ICD-10), as well as the date of the onset of the illness. The SNDS also contains socio-demographic data, such as age, sex, area of residence (postcode), and coverage by a complementary universal health insurance, CMU-C (system allowing free access to healthcare for people whose annual income is less than 50% of the poverty threshold). This information is linked to the national hospital database, which contains data on all stays in public and private hospitals (*i.e.* dates of entry and discharge, ICD-10 coded diagnoses, care and surgical procedures performed, costly drugs or medical devices provided). The SNDS has been described and used in multiple pharmacoepidemiological studies.<sup>4,14–18</sup> This study was approved by the French Data Protection Supervisory Authority (Commission Nationale de l'Informatique et des Libertés). No informed consent is required for studies based on the SNDS databases, as these data are anonymous.

### Identification of PrEP users during the study period

All individuals aged 15 years and older who received a first dispensing of TDF-FTC (ATC code J05AR03) for HIV PrEP between 1 January 2016 and 30 June 2021 (*i.e.* study period) were considered as ever PrEP users. PrEP dispensing was considered as an indicator of PrEP use independently of available data on sexual behaviour.

Each date of PrEP dispensing during the study period was registered. PrEP was considered as the indication of TDF-FTC prescription if TDF-FTC was dispensed alone (*i.e.* not combined with same-day dispensation of any other HIV antiretroviral drugs) to an HIV-uninfected individual. Previous HIV infection was identified by the presence of at least one of the following criteria at the date of dispensing TDF-FTC alone: (i) 100% healthcare coverage for a long-term illness with a diagnosis of HIV infection, (ii) at least one hospital stay in the last five years during which a primary diagnosis of HIV infection was recorded, (iii) at least one hospital stay in the previous year during which a secondary diagnosis of HIV infection was recorded, (iv) at least one reimbursement for a laboratory test specific of HIV infection monitoring, with the exception of HIV viral load testing for which at least three reimbursements were required, or (v) at least three outpatient or inpatient dispensations on different dates of an HIV antiretroviral drug (except TDF-FTC) within 12 months before and one month after the date of dispensation of TDF-FTC alone. The parameters used to exclude patients with HIV infection (*i.e.* ICD-10 codes related to HIV, ATC codes related to HIV antiretroviral drugs, laboratory tests specific to HIV monitoring) are detailed in Supplementary Material Table S1.

Among individuals identified as PrEP users, the first date of dispensing of TDF-FTC alone recorded during the study period was considered as the date of initiation. Subsequent PrEP dispensations were considered as treatment renewals.

### Outcomes studied

The following criteria were used to assess the number of PrEP users over the study period and their characteristics in terms of PrEP use characteristics and socio-demographic profile.

The number of PrEP users over time was assessed by (i) the number of individuals initiating PrEP each month during the study period (*or new users by month*) and (ii) the total number of PrEP users by semester (*or current PrEP users*), including for each semester both new users who initiated PrEP during the semester (*or new users in a given semester*) and individuals with at least one PrEP renewal dispensation during the semester (*or users in renewal in a given semester*). For each semester, PrEP continuation rate was calculated by dividing the number of users in renewal during the semester by the overall number of users on PrEP during the preceding

semester. Individuals who had initiated PrEP previously but without any PrEP renewal dispensation during a given semester were considered as discontinued users during that semester. During the subsequent semesters, discontinued users were either again considered as discontinued users in case they still did not have any PrEP renewal dispensation, or as users in renewal if they resumed PrEP.

Among individuals who initiated PrEP between 1 January 2016 and 31 December 2020, the number of PrEP renewals within the first six months following initiation was assessed by year of initiation. In France, a dispensation of PrEP usually corresponds to one box of 30 oral tablets, which covers one month of daily dosing. Thus, five renewals within six months of initiation theoretically cover (in addition to the initial prescription) the entire six-month period and may correspond to continuous use during this period. A lower number of renewals may reflect on demand-use or discontinuation of treatment. Characteristics of prescribers of PrEP renewals included their type of practice (hospital or private) and, for private practitioners only, their specialty (GP or specialist).

Socio-demographic characteristics of PrEP users included age, sex, CMU-C coverage, region of residence, and size of the urban area of residence at the time of PrEP initiation.

### Statistical analyses

For qualitative or ordinal variables (*i.e.* age, sex, CMU-C coverage, region of residence, size of the urban area of residence, number of renewals within six months of PrEP initiation, type of prescriber for PrEP renewals) the number and frequency of each modality were reported. When these variables were not binary the following categories were considered: (i)  $\leq 25$ , 26 to 35, 36 to 45, 46 to 55, 56 to 65,  $> 65$  years for age, (ii) Ile-de-France (*i.e.* Paris region), other region with high HIV incidence rate (*i.e.* Auvergne-Rhône-Alpes, Centre-Val de Loire, Grand Est, Nouvelle-Aquitaine, Occitanie, Provence-Alpes-Côte d'Azur, French overseas departments, for which  $\geq 50$  new HIV contaminations per million inhabitants had been recorded in 2018)<sup>19</sup> and other regions (*i.e.* Bourgogne-Franche-Comté, Bretagne, Corse, Hauts-de-France, Normandie, Pays de la Loire) for region of residence and, (iii)  $< 10\ 000$ , 10 000 to 49 000, 50 000 to 199 000 and  $\geq 200\ 000$  inhabitants for the size of the urban area of residence. Missing values, if any, were considered in a specific category. For quantitative variables, the mean and standard deviation, and the median and interquartile range were reported.

Statistical analyses were performed using SAS Enterprise Guide software, version 7.15.

### Role of funding sources

No funding or sponsorship was received for this study.

## Results

### Number of PrEP users over time

A total of 42 159 individuals initiated PrEP between 1 January 2016 and 30 June 2021. The monthly number of PrEP initiations steadily increased between the first half (H1) of 2016 (190 initiations per month on average) and the second half (H2) of 2019 (919 initiations per month on average). The increase continued in January and February 2020 (948 and 1027 initiations, respectively, *i.e.* 988 per month on average), until the beginning of the first wave of the COVID-19 pandemic in France in March 2020. During the first lockdown (17 March to 10 May 2020), the monthly number of PrEP initiations fell to 618 in March 2020 (*i.e.* a 37% decrease compared to the average of January and February 2020), 247 in April (-75%) and 474 in May (-52%). PrEP initiations resumed in June 2020 (914 initiations) and then stabilized at a level close to that observed before the start of the pandemic (966 initiations per month on average in H2 2020). In H1 2021, the number of PrEP initiations started to rise again, first moderately during the period from February to May, which was marked by the third wave of the COVID-19 pandemic (average of 1054 monthly initiations) and then more markedly in June (1466 initiations). (Figure 1 and Supplementary Material Table S2).

Each semester between H1 2016 and H2 2019, the current number of PrEP users steadily increased up to a total of 18 500, including 5513 new users (average increase between two semesters: +26%) and 12 987 users in renewal (+52%) during H2 2019 (Figure 2 and Supplementary Material Table S3). Subsequently, with the onset of the COVID-19 pandemic the number of new users decreased in H1 2020 (4228, *i.e.* -23% compared to H2 2019) before returning to pre-pandemic levels in H2 2020 (5798 *vs.* 5513 in H2 2019) and resuming an upward trend in H1 2021 (6610, *i.e.* +14% compared to H2 2020). The number of users in renewal continued to increase, but to a lesser extent than in the pre-pandemic period (15 486 in H1 2020, 17 561 in H2 2020 and 20 202 in H1 2021, *i.e.* +19%, +13% and +15%, respectively). Overall, 26 812 individuals used PrEP in H1 2021, representing 64% of the total 42 159 individuals who had initiated PrEP since H1 2016.

### Characteristics of PrEP users at the time of PrEP initiation

The socio-demographic characteristics of PrEP users at the time of treatment initiation are presented in Table 1. Throughout the study period, PrEP users were mainly men (97.5%), aged 36 years on average. A minority (7.0%) were covered by the CMU-C. The majority (73.8%) lived in a large urban area of more than 200 000 inhabitants, in the Paris region or in another region with high HIV incidence rate (44.4% and 40.1%

respectively). Individuals residing in French overseas departments (regions with the highest HIV incidence rates in France) accounted for only 1.3% of PrEP users. Details of the number of PrEP users by region and by year of initiation are presented in Supplementary Material Table S4.

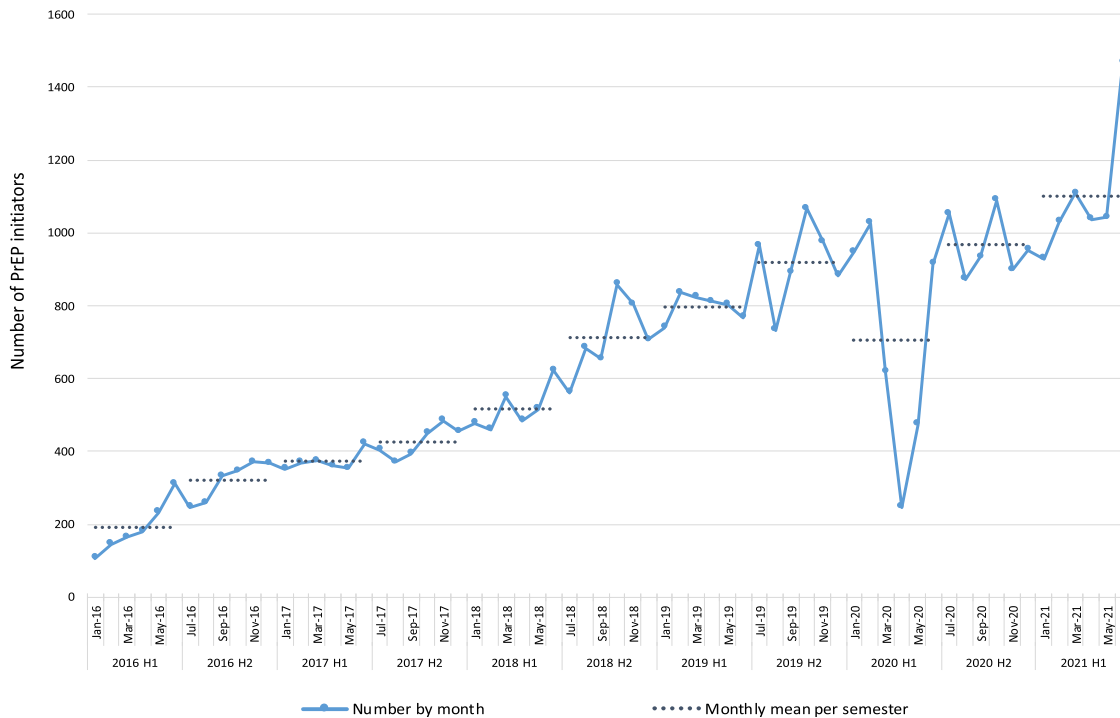
While the proportion of men remained fairly stable over time, the average age at PrEP initiation decreased, from 38 to 35 years between 2016 and H1 2021. The proportion of people aged 25 years or younger steadily increased from 9.1% in 2016 to 20.7% in H1 2021. CMU-C beneficiaries accounted for 8% of new PrEP users in H1 2021, a proportion slightly higher than in the previous years. The proportion of people living in large urban areas, especially Paris region, gradually decreased over time (from 80.8% in 2016 to 71.0% in H1 2021) in favour of other French regions.

### Characteristics of PrEP use

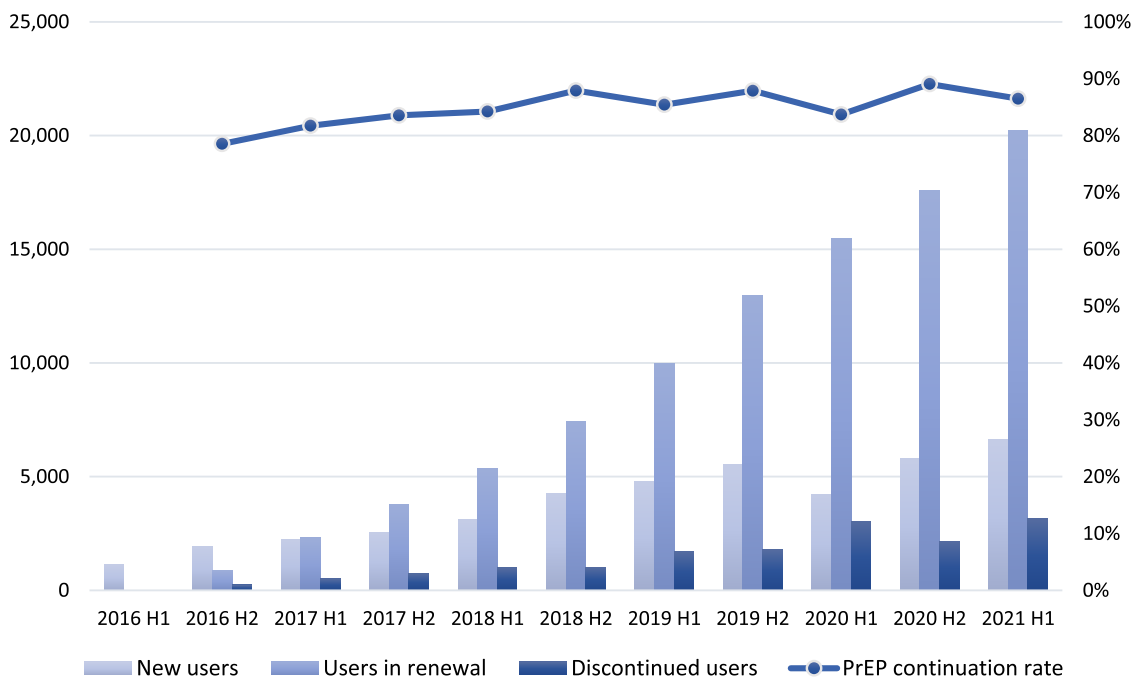
Each semester from H2 2016, users in renewal accounted for the large majority of people who had used PrEP in the preceding semester, resulting in a PrEP continuation rate from one semester to another consistently reaching 80 to 90% (mean: 84.9%) throughout the study period (Figure 2 and Supplementary Material Table S3). Among users in renewal, more than 90% each semester had received a PrEP dispensation during the preceding semester. Though, each semester a substantial proportion of individuals previously on PrEP did not receive any PrEP renewal during the semester and were thus considered as discontinued users during this semester. This proportion, which reached 12% each semester in average overall, tended to decrease over time, ranging from 21% in H2 2016 to 7% in H2 2020 (Figure 2 and Supplementary Material Table S3).

Among the 35 549 people who initiated PrEP between 1 January 2016 and 31 December 2020, the average number of PrEP renewals within the six months following initiation was 2.9. Overall, during the first six months of treatment 30.0% received at least five renewals (corresponding, including initial dispensing, to a continuous use), 23.9% received three to four renewals, 26.0% received one to two renewals and 20.1% did not receive any renewal (Table 2). The number of PrEP renewals within the six months following initiation remained stable for initiations between H1 2016 and H1 2019 (mean 3.0 renewals), but was lower when initiation took place in H2 2019 or in 2020 (mean 2.7 renewals). Among individuals who initiated PrEP in H2 2019 or in 2020, 28% had only one or two renewals and 23% had no renewal within the first six months of treatment, while these proportions reached 24% and 18%, respectively, among those who initiated PrEP between 2016 and H1 2019.

Between H1 2016 and H1 2021, a total of 413 425 PrEP renewals were recorded among the 42 159 PrEP



**Figure 1.** Number of PrEP initiations in France between 1 January 2016 and 30 June 2021, by month. The dotted lines indicate the average number of initiations per semester. Abbreviations: H1: first half of the concerned year; H2: second half of the concerned year.



**Figure 2.** Number of PrEP users and PrEP continuation rate in France between 1 January 2016 and 30 June 2021, by semester. The PrEP continuation rate for each semester was calculated by dividing the number of users in renewal during the semester by the overall number of users on PrEP during the preceding semester. Note: Discontinued users of PrEP in a given semester who resumed it in a later semester were considered users in renewal in that later semester. Abbreviations: H1: first half of the concerned year; H2: second half of the concerned year.

	TOTAL	BY YEAR					
	N = 42 159	2016 N = 3065	2017 N = 4791	2018 N = 7375	2019 N = 10 292	2020 N = 10 026	2021 H1 N = 6610
<b>Men, n (%):</b>	41 126 (97.5)	2965 (96.7)	4697 (98.0)	7205 (97.7)	10 043 (97.6)	9740 (97.1)	6476 (98.0)
<b>Age categories (years), n (%):</b>							
≤25	6881 (16.3)	280 (9.1)	562 (11.7)	1094 (14.8)	1664 (16.2)	1913 (19.1)	1368 (20.7)
26-35	15 523 (36.8)	1090 (35.6)	1726 (36.0)	2655 (36.0)	3740 (36.3)	3813 (38.0)	2499 (37.8)
36-45	10 648 (25.3)	992 (32.4)	1505 (31.4)	1965 (26.6)	2505 (24.3)	2284 (22.8)	1397 (21.1)
46-55	6673 (15.8)	553 (18.0)	780 (16.3)	1243 (16.9)	1705 (16.6)	1454 (14.5)	938 (14.2)
56-65	2003 (4.8)	129 (4.2)	185 (3.9)	344 (4.7)	551 (5.4)	461 (4.6)	333 (5.0)
>65	431 (1.0)	21 (0.7)	33 (0.7)	74 (1.0)	127 (1.2)	101 (1.0)	75 (1.1)
<b>Age (years):</b>							
Mean (SD)	36 (11)	38 (10)	37 (10)	37 (11)	37 (11)	36 (11)	35 (11)
Median (IQR)	34 (28-44)	37 (30-45)	36 (29-44)	35 (28-45)	35 (28-45)	33 (27-43)	33 (27-43)
<b>CMU-C, n (%)</b>	2966 (7.0)	209 (6.8)	319 (6.7)	477 (6.5)	705 (6.8)	725 (7.2)	531 (8.0)
<b>Region of residence, n (%):</b>							
Ile-de-France (Paris region)	18 721 (44.4)	1597 (52.1)	2207 (46.1)	3556 (48.2)	4437 (43.1)	4247 (42.4)	2677 (40.5)
Other regions with high HIV incidence <sup>a</sup>	16 919 (40.1)	1121 (36.6)	1888 (39.4)	2724 (36.9)	4223 (41.0)	4192 (41.8)	2771 (41.9)
Other regions <sup>b</sup>	6410 (15.2)	329 (10.7)	674 (14.1)	1071 (14.5)	1609 (15.6)	1572 (15.7)	1155 (17.5)
Missing information	109 (0.3)	18 (0.6)	22 (0.5)	24 (0.3)	23 (0.2)	15 (0.1)	7 (0.1)
<b>Size of the urban area of residence, number of inhabitants (%):</b>							
<10 000	4881 (11.6)	261 (8.5)	475 (9.9)	784 (10.6)	1290 (12.5)	1229 (12.3)	842 (12.7)
10 000 to 49 999	2098 (5.0)	100 (3.3)	269 (5.6)	308 (4.2)	542 (5.3)	510 (5.1)	369 (5.6)
50 000 to 199 999	3353 (8.0)	166 (5.4)	347 (7.2)	567 (7.7)	883 (8.6)	810 (8.1)	580 (8.8)
≥200 000	31 096 (73.8)	2477 (80.8)	3618 (75.5)	5585 (75.7)	7423 (72.1)	7302 (72.8)	4691 (71.0)
Missing information	731 (1.7)	61 (2.0)	82 (1.7)	131 (1.8)	154 (1.5)	175 (1.7)	128 (1.9)

**Table 1: Socio-demographic characteristics of PrEP users at the time of PrEP initiation, overall and by year.**

Abbreviations: CMU-C: complementary universal health coverage; SD: standard deviation; IQR: interquartile range; 2021 H1: first half of 2021.

<sup>a</sup> Auvergne-Rhône-Alpes, Centre-Val de Loire, Grand Est, Nouvelle-Aquitaine, Occitanie, Provence-Alpes-Côte d'Azur, French overseas departments, for which ≥50 new HIV contaminations per million inhabitants had been recorded in 2018.

<sup>b</sup> Bourgogne-Franche-Comté, Bretagne, Corse, Hauts-de-France, Normandie, Pays de la Loire.



TOTAL	BY SEMESTER OF PrEP INITIATION									
	2016 H1 N = 1142	2016 H2 N = 1923	2017 H1 N = 2232	2017 H2 N = 2559	2018 H1 N = 3108	2018 H2 N = 4267	2019 H1 N = 4779	2019 H2 N = 5513	2020 H1 N = 4228	2020 H2 N = 5798
<b>Number of PrEP renewals, n (%):</b>										
Mean (SD)	2.9 (2.1)	3.0 (2.1)	3.1 (2.1)	3.0 (2.1)	3.1 (2.1)	3.0 (2.2)	3.0 (2.2)	2.8 (2.1)	2.5 (2.1)	2.7 (2.2)
0	7148 (20.1)	349 (18.1)	381 (17.1)	468 (18.3)	506 (16.3)	803 (18.8)	915 (19.1)	1163 (21.1)	1051 (24.9)	1308 (22.6)
1 to 2	9235 (26.0)	271 (23.7)	548 (24.6)	625 (24.4)	762 (24.5)	1053 (24.7)	1142 (23.9)	1500 (27.2)	1275 (30.2)	1606 (27.7)
3 to 4	8503 (23.9)	326 (28.5)	586 (26.3)	620 (24.2)	787 (25.3)	992 (23.2)	1126 (23.6)	1362 (24.7)	958 (22.7)	1246 (21.5)
≥5	10 663 (30.0)	341 (32.3)	717 (32.1)	846 (33.1)	1053 (33.9)	1419 (33.3)	1596 (33.4)	1488 (27.0)	944 (22.3)	1638 (28.3)

**Table 2: Number of PrEP renewals within the 6 months following initiation, overall and by semester of PrEP initiation.**

Abbreviations: SD, standard deviation; H1, first half of the concerned year; H2, second half of the concerned year.

Note: a period of six months is taken into account when calculating the number of PrEP renewals for each initiator, starting from his/her own initiation date.

ever users. Renewals were mostly prescribed by non-private practitioners (78.7%). The proportion of PrEP renewals prescribed by a private prescriber increased over time, from 5.3% in 2016 to 27.3% in H1 2021. Private practitioners prescribing PrEP renewals were mostly GPs (84.2%) (Table 3).

### Discussion

Based on data of the French National Health Data System (SNDS), we showed that a total of 42 159 people aged 15 years and over initiated treatment with TDF-FTC for PrEP in France between 1 January 2016 and 30 June 2021. PrEP initiations increased steadily between the first half of 2016 and February 2020, until the onset of the first wave of the COVID-19 pandemic in March 2020. By then, PrEP initiations fell by up to 75%, probably as a result of a decreased accessibility to healthcare services, especially those offering PrEP, but also a lower level of exposure to sexual risk of HIV acquisition during lockdown.<sup>10,20–22</sup> PrEP initiations progressively resumed following the end of the first lockdown (from June 2020), but stagnated at the level observed before the start of the pandemic during the rest of year 2020. A trend toward a recovery in increase in PrEP initiations emerged from February 2021 and more particularly in June 2021, marked by the end of the third wave of the COVID-19 pandemic. This suggests that PrEP initiations during the second half of 2020 and the first half of 2021 were much less affected than during the first wave of the pandemic despite the continuation of some pandemic-related restrictions throughout these periods.

We found that in the first half of 2021, only about two thirds (64%) of individuals who had ever initiated PrEP since its implementation in 2016 were still using it. Our results suggest that after initiating PrEP, the vast majority of users (80.90%) renew their treatment from one semester to another, suggesting a good level of maintenance among those engaged in treatment. This level of PrEP maintenance improved over time since 2016. However, for 20% of new PrEP users no prescription renewal was recorded in the first six months after initiation, suggesting a substantial proportion of early treatment discontinuation. This phenomenon has even been more marked since the beginning of the COVID-19 pandemic. This could be explained by a reduction in the quantity of PrEP consumed due to the social distancing measures in place during the COVID-19 pandemic, particularly in case of intermittent (on-demand) PrEP use which is frequent in France (*i.e.* around 50% of PrEP users).<sup>23,24</sup> Both daily and on-demand PrEP have been shown to be highly effective in preventing HIV acquisition provided that adherence is good.<sup>25</sup> Promoting both modes of PrEP use and choosing appropriately according to individuals preferences and risk profile could improve adherence to treatment and allow access to this effective HIV prevention tool to a greater

	TOTAL N = 413 425	BY YEAR OF RENEWAL					
		2016 N = 72 16	2017 N = 30 343	2018 N = 60 141	2019 N = 104 283	2020 N = 130 377	2021 H1 N = 81 065
Non-private practitioner, n (%)	288 514 (78.7)	5930 (94.7)	23 313 (88.9)	43 997 (84.3)	73 586 (81.3)	89 464 (74.9)	52 224 (72.7)
Private practitioner, n (%):	77 885 (21.3)	330 (5.3)	2904 (11.1)	8185 (15.7)	16 966 (18.7)	29 916 (25.1)	19 584 (27.3)
General practitioner	65 549 (17.9)	209 (3.3)	2283 (8.7)	6799 (13.0)	14 027 (15.5)	25 525 (21.4)	16 706 (23.3)
Specialist	11 746 (3.2)	108 (1.7)	601 (2.3)	1290 (2.5)	2797 (3.1)	4198 (3.5)	2745 (3.8)
Missing information	590 (0.2)	13 (0.2)	20 (0.1)	96 (0.2)	142 (0.2)	193 (0.2)	133 (0.2)
Missing information, n	47 026	956	4126	7959	13 731	10 997	9257

**Table 3: Characteristics of prescribers of PrEP renewals, overall and by year of renewal.**

Abbreviation: 2021 H1: first half of 2021.

<sup>a</sup> Percentage of patients with no missing information regarding the type of prescriber renewing PrEP (i.e. private or not).

number of users. According to the ERAS COVID-19 survey, almost 60% of PrEP users had stopped PrEP and about 6% had switched from continuous to on-demand use during the first wave of COVID-19 pandemic in France.<sup>10</sup> PrEP discontinuation or switch from continuous to on-demand use during the pandemic has also been reported in other countries.<sup>26,27</sup>

These results confirm the major impact of the COVID-19 pandemic on PrEP use in France, as already reported for other health products<sup>17,18,28</sup> and in other countries.<sup>20,22,29,30</sup> In addition, they draw attention to the substantial frequency of early PrEP discontinuation. The negative impact of PrEP discontinuation on its real-life preventive effectiveness was demonstrated in a recent study conducted by our team.<sup>31</sup>

As of June 2021, in France PrEP users have been almost exclusively socio-economically advantaged men, aged 36 on average and living in Paris region or in other large metropolis. They are likely to be mainly MSM.<sup>23,32</sup> In metropolitan France, the regional distribution of PrEP initiations globally reflects that of new HIV diagnoses,<sup>19</sup> with almost half of initiations (45%) in Paris region. Although the proportion of PrEP users under 25 years of age, residing outside Paris region or large urban areas, and/or socio-economically disadvantaged level increased continuously over time, the use of PrEP has remained limited in certain population subgroups who could particularly benefit from it. In particular, women accounted for only 2.5% of PrEP users, highlighting the fact that PrEP is probably rarely offered in situations where women are at high risk of HIV acquisition (e.g., injecting drug use, sex workers, vulnerability to condomless sex in a context of high HIV prevalence or exposure). Furthermore, PrEP initiations in French overseas departments have remained scarce (1% of initiations), even though these departments account for the highest burden of new HIV diagnoses in France.<sup>33</sup> Until June 2021, PrEP renewals were generally carried out by non-private practitioners, although PrEP prescribing by private practitioners has increased over time. The extension of PrEP initial prescription to all prescribers since June 2021 in France is expected to further increase this trend.

This large real-life study provides a comprehensive overview of the roll-out of PrEP use since its approval in France, as well as its characteristics. To date, available data on PrEP use in real-life were restricted to specific subgroups in France.<sup>23,32,34</sup> Several representative studies on PrEP use and users characteristics were conducted in other countries<sup>35-40</sup> but did not cover the period of the COVID-19 pandemic which had a significant impact on access to prevention services, including PrEP.<sup>11-13</sup> Large scale, real-life studies assessing PrEP number of users and patterns of use, such the one presented here, are essential to guide health authorities in promoting the use of PrEP.



This study has some limitations inherent to the medico-administrative nature of the SNDS database. First, the SNDS does not make it possible to know whether a drug prescribed and dispensed was actually used. However, using the same database and the same definition of PrEP use, we previously found similar levels of PrEP effectiveness to those reported in randomized clinical trials,<sup>31</sup> which supports the validity of our definition of PrEP use. Second, because the SNDS does not contain information on medical indications nor on the results of biological tests, some misclassification cannot be excluded. Thus, some HIV-positive people may have been erroneously included among PrEP users. In addition, some HIV-uninfected individuals may have been inappropriately excluded, particularly if they had received antiretroviral therapy for post-exposure prophylaxis more than three times in the year before starting PrEP. However, such situations are probably infrequent. Third, in the absence of data on sexual behaviours in the SNDS database, interpretation of PrEP discontinuations figures is challenging due to the lack of information on the reasons of such discontinuations (*i.e.* decreased sexual risk exposure or suboptimal adherence). Nevertheless, using the same database we previously showed that treatment discontinuation was associated with a reduced level of PrEP effectiveness,<sup>31</sup> thus suggesting that discontinuations occurred despite persistent exposure to HIV risk. Fourth, the SNDS database does not allow to identify transgender people and contains non-exhaustive information for migrants with temporary visa, although this information would be interesting to characterise the PrEP user population more precisely. Finally, free dispensation of PrEP in sexual health centers is not systematically recorded in the SNDS claim database. However, evidence from the field suggests that such free dispensations are rare, suggesting that resulting underestimation is likely to be limited.

## Conclusion

This comprehensive real-life study provides evidence of a major impact of the COVID-19 pandemic on PrEP roll-out in France which deserves to be further monitored in the longer term. It also highlights the needs for further measures to expand access to PrEP to all potential beneficiaries, including women, socio-economically disadvantaged people and those living in remote areas, as well as to improve adherence to treatment. Future studies are needed to assess the impact of the recent extension of PrEP initiation to all prescribers in France.

## Contributors

*Concept and design:* Sophie Billioti de Gage and Rosemary Dray-Spira.

*Data extraction and collection:* David Desplas.

*Statistical analysis:* Sophie Billioti de Gage and David Desplas.

*Interpretation of the data:* Sophie Billioti de Gage and Rosemary Dray-Spira.

*Drafting of the manuscript:* Sophie Billioti de Gage.

*Critical revision of the manuscript for important intellectual content:* Sophie Billioti de Gage and Rosemary Dray-Spira.

*Supervision:* Rosemary Dray-Spira.

Underlying data has been verified by David Desplas and Sophie Billioti de Gage.

All authors had access to the data used in the present analyses and made the final decision to submit the manuscript for publication.

## Data sharing statement

David Desplas and Sophie Billioti de Gage have full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declaration of interests

No conflicting relationship exists for any author.

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## Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.lanepe.2022.100486](https://doi.org/10.1016/j.lanepe.2022.100486).

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