

Missed opportunities of HIV pre-exposure prophylaxis in France: a retrospective analysis in the French DAT'AIDS cohort

C. Lions, O. Cabras, L. Cotte, T. Huleux, A. Gagneux-Brugnon, A. Makinson, A. Cabié, B. Bonnet, C. Duvivier, L. Hocqueloux, et al.

► **To cite this version:**

C. Lions, O. Cabras, L. Cotte, T. Huleux, A. Gagneux-Brugnon, et al.. Missed opportunities of HIV pre-exposure prophylaxis in France: a retrospective analysis in the French DAT'AIDS cohort. BMC Infectious Diseases, BioMed Central, 2019, 19 (1), 10.1186/s12879-019-3915-5 . hal-02202222

HAL Id: hal-02202222

<https://hal-amu.archives-ouvertes.fr/hal-02202222>

Submitted on 22 May 2020

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.



RESEARCH ARTICLE

Open Access



Missed opportunities of HIV pre-exposure prophylaxis in France: a retrospective analysis in the French DAT'AIDS cohort

C. Lions¹, O. Cabras², L. Cotte³, T. Huleux⁴, A. Gagneux-Brugnon⁵, A. Makinson^{6,7}, A. Cabié⁸, B. Bonnet⁹, C. Duvivier^{10,11,12,13}, L. Hocqueloux¹⁴, E. Cua¹⁵, A. Cheret¹⁶, L. Hustache-Mathieu¹⁷, V. Obry-Roguet¹, C. Jacomet¹⁸, I. Poizot-Martin^{1,19,20*}  and the DAT'AIDS STUDY GROUP

Abstract

Background: HIV pre-exposure prophylaxis (PrEP) was implemented in France in November 2015 based on individual-level risk factors for HIV infection. We evaluated the proportion of missed opportunities for PrEP among newly HIV-diagnosed people entering the Dat'AIDS cohort in 2016.

Methods: Multicenter retrospective analysis in 15 French HIV clinical centers of patients with a new diagnosis of HIV infection. Among them we differentiated patients according to the estimated date of infection: those occurring in the PrEP area (a previous negative HIV test in the last 12 months or those with an incomplete HIV-1 western blot (WB) with no HIV-1 anti-Pol-antibody at time of HIV diagnosis) and those in the pre-PrEP area (older infections). Epidemiological, biological and clinical data at HIV diagnosis were collected. Clinicians retrospectively identified potential eligibility for PrEP based on individual-level risk factors for HIV infection among those infected in the PrEP area.

Results: Among 966 patients with a new HIV diagnosis, 225 (23.3%) were infected in the PrEP area and 121 (53.8%) had complete data allowing evaluation of PrEP eligibility. Among them, 110 (91%) would have been eligible for PrEP, median age 31 years, with 68 (75.6%) born in France and 10 (11.1%) in Central/West Africa, with more than one previous STI in 19 (15.7%). The main eligibility criteria for PrEP were being a man who had sex with men or transgender 91 (82.7%) with at least one of the following criteria: unprotected anal sex with ≥ 2 partners in the last 6 months: 67 (60.9%); bacterial sexually transmitted infection in the last 12 months: 33 (30%); Use of psychoactive substances in a sexual context (chemsex): 16 (14.5%). PrEP was indicated for other HIV risk factors in 25 (22.7%).

Conclusion: With 91% (110/121) of patients infected in the PrEP area eligible for PrEP, this study highlights the high potential of PrEP in avoiding new infection in France but also shows a persistent delay in HIV testing. Thus, an important limit on PrEP implementation in France could be insufficient screening and care access.

Keywords: Pre-exposure prophylaxis, PrEP, HIV, Missed opportunities, HIV testing

* Correspondence: isabelle.poizot@ap-hm.fr

¹APHM Hôpital Sainte-Marguerite, Service d'Immuno-hématologie clinique, Aix-Marseille University, Marseille, France

¹⁹Aix-Marseille Univ, INSERM, IRD, SESSTIM, APMH Sainte-Marguerite, Clinical Immuno-Hematological Unit Marseille, Aix Marseille Univ, Marseille, France

Full list of author information is available at the end of the article



Background

The HIV epidemic remains active in France, as evidenced by approximately 6000 new HIV infectionsThe development of a concentrated diagnosed yearly since 2011 [1, 2] despite a favorable cascade of care [3]. The dynamic of the epidemic is mainly driven by men who have sex with men (MSM) (44% of new HIV diagnosis) but also by the migrant women's population (23%), mainly from sub-Saharan African countries [1]. Several actions have been taken to curb the dynamics of the epidemic across the territory, of whom pre-exposure prophylaxis treatment (PrEP) with 300 mg daily tenofovir (TDF) co-formulated with 200 mg emtricitabine (FTC). HIV pre-exposure prophylaxis is an effective tool in preventing HIV infection among high-risk men who have sex with men. Indeed, a PrEP uptake at 25% of a high-risk population of MSM, without any additional preventative strategies could prevent 30.7% of infections [4]. PrEP was first evaluated in France with the ANRS Ipergay trial who was initiated in July 2014 among 6 clinical centers in France. Then, PrEP was implemented since November 25, 2015, first as part of a Temporary Recommendation for Use (TRU) [5] based on individual-level risk factors for HIV infection, followed by a marketing authorization extension without advance fees for the patient in February 2017 [6].

French guidelines assist clinicians in the evaluation of patients who are seeking PrEP, in commencing and monitoring patients on PrEP including PrEP dosing schedules, management of side-effects and toxicity, use of PrEP in pregnancy and in chronic hepatitis B infection and how to cease PrEP. Daily PrEP can be used continuously or for shorter periods of time, or on demand [7]. According to French guidelines, two negative HIV tests performed 4 weeks apart without HIV risk behavior during these 4 weeks are required [8] in order to avoid PrEP initiation during the HIV seroconversion period.

However, since the introduction of this preventive tool in France, new HIV infections are still occurring [9]. It is still too early at that time to quantify the impact of PrEP on the number of new infections, and to date, no data are available on the proportion of newly HIV-infected people who would have been potential candidates for PrEP in France. We report here the results of a retrospective study evaluating the proportion of missed opportunities for PrEP among newly HIV-infected people during the year 2016.

Methods

This multicenter retrospective analysis was performed in the French DatAIDS Cohort (NCT 02898987 ClinicalTrials.gov). This cohort represents a collaboration between 21 major French HIV clinical centers using a common electronic medical record (NADIS®) [10] for the follow-up of HIV infected adults coinfecting or not with hepatitis B virus (HBV) and hepatitis C virus (HCV), among which data

from 59,829 patients were collected during the year 2016. For this retrospective study, 15 centers accepted to participate. The data collection has been approved by the French National Commission on Informatics and Liberty (CNIL 2001/762876; MR 003: 2044467 v.0), and all patients signed an informed consent before being included in this database. Patient-related data are recorded during medical encounters in a structured database, allowing for clinical, epidemiological or therapeutic studies. Data quality is ensured by automated checks during data capture, regular controls, annual assessments, and ad hoc processes before any scientific analysis is performed.

Data collection

Socio-demographic characteristics (age, sex, birth area, HIV transmission route), lifetime history of other sexually transmitted infections (STI) (e.g., syphilis, gonorrhoea, chlamydia) and biological data (HIV viral load, CDC stage, CD4 T cell count, hepatitis C, hepatitis B, hepatitis A and syphilis serology) were collected at the time of HIV diagnosis.

We also collected past HIV test and western blot (WB) at diagnosis. We differentiated patient according to estimate date of infection: before availability of PrEP or after. Then, among diagnosis occurring in 2016, we considered patients infected in the PrEP area, those with a previous negative HIV test realized in the last 12 months or those with an incomplete HIV-1 WB with no HIV-1 anti-Pol-antibody at time of HIV diagnosis (primary infection). Patients who did not presented these characteristics (older or indeterminate date of infection) were considered as infected in the pre-PrEP area.

For patients infected in the PrEP area, at each center, the referring clinician of each patient retrospectively identified eligibility for PrEP according to the individual-level risk factors for HIV infection as defined by TRU criteria (see Table 3 for TRU criteria).

Statistics

We firstly compared patient's characteristics according to the estimated date of infection (PrEP area versus pre-PrEP area). Secondly, we compared patient's characteristics according to PrEP eligibility. Continuous and categorical variables were summarized as the median and interquartile range [IQR] or frequency and percentage, respectively. For these comparisons we used the non-parametric Mann-Whitney test for continuous variables and Chi² or Fisher's exact test for categorical data. All statistical analyses were performed using SAS software version 9.3 (SAS Institute Inc., Cary, North Carolina).

Results

In 2016, 966 patients were newly diagnosed as HIV seropositive in the 15 HIV clinical centers. Most of them were male ($N = 709$; 73.4%), HIV transmission route was MSM

for 46.7% ($N=449$) and heterosexual intercourse for 42.7% ($N=410$) (Table 1). This last category concerned mostly persons from sub-Saharan Africa ($N=177$; 43.0%) and especially women ($N=217$; 53.0%) (data not shown). Among the 966 patients, 225 patients fulfilled the criteria of infection occurring in the PrEP area, of whom 108 were in primary infection.

PrEP area vs pre-PrEP area infected patients

Compared to the patients infected in the PrEP area, those infected in the pre-PrEP area were significantly older and were more often women from west or central Africa and infected by heterosexual intercourse. The two groups also differed significantly according to CDC stage C with a higher percentage found in the pre-PrEP area group (16.1% vs. 0.50%, $p < 0.0001$), and positive syphilis serology at the time of HIV diagnosis, less often found in the pre-PrEP area group (20.4% vs. 34.7%, $p = 0.0004$). Median CD4 cell count/mm³ (347 [155–520] vs. 480 [334–635], $p < 0.0001$) and HIV viral load in log/ml (4.92 [4.05–5.60] vs. 5.50 [4.45–6.40], $p < .0001$) were significantly lower in the pre-PrEP area group. History of STI was available for 348 patients, and the percentage of those with a previous STI (chlamydia and the number of previous STIs) was significantly lower in those infected in the pre-PrEP area (Table 1).

Eligible for PrEP vs non-eligible among patients infected in the PrEP area

Among the 225 patients infected in the PrEP area, individual-level risk factors for HIV infection were available for 121 patients (53.7%), among which 110 (90.9%) patients would have been eligible for PrEP. The patients' characteristics are reported in Table 2. Patients with available data of individual-level risk factors for HIV infection were not different from those without these data ($n=104$; data not shown) except for age, with patients with available data being significantly younger than the others (31 [25–41] vs 36 [29–45] years; $p = 0.02$).

Among the 121 patients, the median [IQR] age was 31 years [25–44], without a significant difference according to PrEP eligibility (Table 2). The age distribution was also similar: 21.5% of patients were under 25 years old, 38.8% between 25 and 35, 17.4% between 35 and 45, 15.7% between 45 and 55 and 6.6% over 55 years. The birth area was France in 75% of cases and Central/West Africa in 11%, without a significant difference between the two groups. A history of STI was reported in 15.7% and was also similar between the groups. However, in the group of patients eligible for PrEP, there were significantly more MSM and more patients with positive syphilis serology at the time of HIV diagnosis.

Distribution of PrEP eligibility criteria among patients eligible for PrEP

The distribution of PrEP eligibility criteria are presented in Table 3. The most common situation was MSM who had condomless anal intercourse with at least two different men or transgender partners in the last 6 months. Among MSM, use of psychoactive drugs during sexual intercourse was reported in 14.5%. In 23% of cases, PrEP was indicated for other substantial risk factors for HIV (prostitution with unprotected sexual intercourse, vulnerability, physical factors increasing HIV risk transmission).

Discussion

With 225 infections occurring in the PrEP area and 741 in the pre-PrEP-area reported in 15 French major HIV clinical centers during the year 2016, this retrospective study highlights the high number of infections that could have been avoided with PrEP, estimated to be 91% among our population. Moreover, this study confirms the ongoing HIV epidemic in France that is driven mainly by recent infections among MSM. These results also stress the need to reinforce HIV screening strategies in order to decrease the number of missed opportunities and delay for HIV testing in all populations at risk.

To our knowledge, only one previous study looked at missed opportunities for PrEP among new HIV diagnoses in South Carolina [11]. They found that African American/Black, women and younger people were more likely to have had health care visits prior to their HIV diagnosis, which was used as a proxy for a missed opportunity. However, they did not study missed opportunities with regard to risky practices and recommendations, and new diagnoses were approximated by CD4 count at diagnosis ≥ 500 cells/mm³. Therefore, our study is the first that evaluated missed opportunities of PrEP in a large cohort of newly HIV infected patients in France. However, to date, it is unknown how effective PrEP is on the dynamic of epidemic in the context of other implemented HIV prevention strategies, including condom use, seroadaptive practice, and treatment as prevention (TasP) [4]. Recently, Brown et al. reported a decrease by 32% in new HIV diagnoses among MSM at selected London sexual health clinics between October 2015 through September 2016. Although this decrease could be attributed to higher testing volumes and rapid initiation of treatment after diagnosis (TasP), these preliminary data suggest that a combination of PrEP and TasP could make elimination of HIV transmission achievable [12].

The development of a concentrated HIV epidemic among MSM has been observed in several countries on different continents, including Asia, Africa and South America [13–15]. In our study, among the 225 infections occurring in the PrEP area, 76% were MSM. If considering only the 121 patients with an infection occurring in

Table 1 Patients' characteristics at the time of HIV diagnosis according to the estimated date of infection (pre-PrEP area versus PrEP area)

Description N (%) or Median [IQR]	Pre-PrEP area infections N = 741	PrEP area infections N = 225	Total N = 966	p
Socio-demographic characteristics				
Age (years)	37 [29–47]	33 [26–44]	36 [29–46]	0.001
Sex				
Male	507 (68.42)	202 (89.78)	709 (73.40)	<.0001
Female	234 (31.58)	23 (10.22)	257 (26.60)	
Birth area				
West or central Africa	213 (34.98)	20 (11.30)	233 (29.64)	<.0001
France	238 (39.08)	128 (72.32)	366 (46.56)	
Other	158 (25.94)	29 (13.37)	187 (23.79)	
HIV transmission route				
MSM	281 (37.97)	168 (76.02)	449 (46.72)	<.0001
Heterosexual	365 (49.32)	45 (20.36)	410 (42.66)	
Other	94 (12.70)	8 (3.62)	102 (10.61)	
CDC Stage				
A	490 (78.03)	194 (96.04)	684 (82.41)	<.0001
B	37 (5.89)	7 (3.47)	44 (5.30)	
C	101 (16.08)	1 (0.50)	102 (12.29)	
Biological data at HIV-diagnosis				
HIV viral load (log cp/ml)	4.92 [4.05–5.60]	5.50 [4.45–6.40]	5.20 [4.30–6.00]	<.0001
CD4 (cell count/mm ³)	347 [155–520]	480 [334–635]	378 [202–555]	<.0001
CD4 (cell count /mm ³)				
≤200	205 (30.73)	14 (6.60)	219 (24.91)	<.0001
200–350	135 (20.24)	46 (21.70)	181 (20.59)	
350–500	145 (21.74)	59 (27.83)	204 (23.21)	
>500	182 (27.29)	93 (43.87)	275 (31.29)	
HCV antibodies				
Negative	565 (96.42)	189 (97.93)	754 (96.79)	0.30
Positive	21 (3.58)	4 (2.07)	25 (3.21)	
HBV AgHbs				
Negative	570 (95.80)	195 (98.98)	765 (96.59)	0.03
Positive	25 (4.20)	2 (1.02)	27 (3.41)	
HVA antibodies				
Negative	179 (37.45)	105 (63.25)	284 (44.10)	<.0001
Positive	299 (62.55)	61 (36.75)	360 (55.90)	
Syphilis serology				
Negative	340 (79.63)	98 (65.33)	438 (75.91)	0.0004
Positive	87 (20.37)	52 (34.67)	139 (24.09)	
History of other sexuality transmitted disease (STI): N = 348				
Syphilis				
No	177 (91.24)	110 (71.43)	287 (82.47)	<.0001
Yes	17 (8.76)	44 (28.57)	61 (17.53)	
Gonorrhoea				
No	187 (96.39)	134 (87.01)	321 (92.24)	0.001
Yes	7 (3.61)	20 (12.99)	27 (7.76)	

Table 1 Patients' characteristics at the time of HIV diagnosis according to the estimated date of infection (pre-PrEP area versus PrEP area) (Continued)

Description N (%) or Median [IQR]	Pre-PrEP area infections N = 741	PrEP area infections N = 225	Total N = 966	p
Chlamydia				
No	191 (98.45)	141 (91.56)	332 (95.40)	0.002
Yes	3 (1.55)	13 (8.44)	16 (4.60)	
Number of STIs				
0	160 (82.47)	92 (59.74)	252 (72.41)	<.0001
1	29 (14.95)	40 (25.97)	69 (19.83)	
≥2	5 (2.58)	22 (14.29)	27 (7.76)	

the PrEP area and available information concerning PrEP eligibility, the estimated proportion of patients eligible for PrEP at the time of HIV infection was 91% and concerned mainly MSM.

Of note, use of psychoactive drugs during sexual intercourse was reported by 14.5% of the patients eligible for PrEP. A significant increase of psychoactive substances use in a sexual context (chemsex), and some measures of HIV-related behaviors (condomless sex with two or more partners in the past 3 months, self-reported bacterial STI diagnosis in the past year, Post-Exposure Prophylaxis use in the past year and HIV testing in the past 6 months) among HIV-negative MSM has been reported in the last few years [16]. Chemsex disclosure in sexual health settings was reported to be associated with a high level of HIV infection risk [17] and higher rates of STI diagnoses, including hepatitis C [18, 19], which concerned 2 patients in our study. Of note, for those patients who are going to initiate antiretroviral therapy, they should be advised of the high risk of potential drug-drug interactions between some recreational drugs and some antiretrovirals agents, with the major risk concerning ritonavir-boosting or cobicistat-boosting agents and some nonnucleoside reverse transcriptase inhibitors [20, 21]. Clinicians should evaluate the risk of such interactions before initiating HIV treatment and consider antiretroviral regimens with a lower risk of drug interactions [22].

Among eligible patients for PrEP, syphilis serology was positive at the time of HIV diagnosis in 39.4%, and a history of syphilis, gonorrhea, and chlamydia was present in 30.0, 12.7 and 10.0% of patients, respectively. Moreover, a history of two or more STIs affected 16.4% of these patients. High rates of STI have been reported among PrEP users, as well as high rates of condomless sex and increasing rates of STI over time [23, 24]. Recently, an increase in the rate of STI in PrEP users was reported in a study conducted in Montreal, Canada [25]. These data raised the discussion of how PrEP may impact STI control efforts. However, since we found more STIs in PrEP area HIV-infected patients, our data suggest that STIs should also be considered as a driver of HIV transmission risk

among MSM. Thus, as suggested by Scott et al., expanded PrEP implementation among high-risk MSM could promote better control of STIs through the systematic screening recommended before PrEP initiation and during the follow-up of PrEP users [26].

Before taking PrEP, users should also be tested for hepatitis B, to prevent reactivation or reinfection in case of PrEP interruption, even if this phenomenon seems to not be very common [27, 28]. Furthermore, for patients with negative HBV serology, HBV vaccination should be administered [7, 29]. In our study, chronic hepatitis B was diagnosed in two patients.

With 21% of patients under 25 years old and 7% over 55 diagnosed in the PrEP area, and with 22.7% of our patients presenting with high-risk situations for HIV infection other than MSM intercourse, our data highlight the need for diverse information campaign targets in order to optimize access to PrEP for different population groups. Indeed, PrEP may impact the HIV epidemic, but only if it reaches the at-risk population [30].

By July 2017, 5352 patients had initiated a tenofovir-emtricitabine treatment for PrEP in France [31]. Among them, they were mostly men, with a median age of 37 years, 9.2% were between 16 and 25 years, and 5% were over 55 years. The gap between availability and usage of PrEP by the population of concern is challenging and asks about obstacles of generalized use and ways for improving the spread of this preventative tool. To date, studies of factors influencing attitudes and behaviors towards PrEP have been established among high-risk populations but not among newly infected persons.

Factors associated with missed opportunities for PrEP can be of individual, social or structural kinds [32]. Major factors highlighted in the literature are mostly on the individual level and concern the intention to take PrEP but not use of PrEP. Moreover, the roles played by physicians, networks, communities and policies are also paramount for enhanced PrEP usage. The design of our study did not allow us to evaluate these factors, and further studies on the obstacles and facilitators of PrEP use are needed.

Table 2 Characteristics of patients infected during the PrEP area according to eligibility for PrEP

N (%) or Median [IQR]	Not eligible for PrEP (n = 11)	Eligible for PrEP. (n = 110)	PrEP area infection (n = 121)	p
Socio-demographic characteristics				
Age (years)	31 [29; 38]	31 [25; 44]	31 [25; 41]	0.74
<25 years	1 (9.09)	25 (22.73)	26 (21.49)	0.61
[25–35]	6 (54.55)	41 (37.27)	47 (38.84)	
[35–45[3 (27.27)	18 (16.36)	21 (17.36)	
[45–55[1 (9.09)	18 (16.36)	19 (15.70)	
≥55 years	0 (00)	8 (7.27)	8 (6.61)	
Sex				
Male	6 (54.55)	104 (94.55)	110 (90.91)	0.001 ^a
Female	5 (45.45)	6 (5.45)	11 (9.09)	
Birth area				
West or central Africa	1 (11.11)	9 (11.11)	10 (11.11)	0.85
France	6 (66.67)	62 (76.54)	68 (75.56)	
Other	2 (22.22)	10 (12.35)	12 (13.33)	
HIV transmission route				
MSM	4 (36.36)	91 (85.85)	95 (81.20)	0.001 ^a
Heterosexual	6 (54.55)	13 (12.26)	19 (16.24)	
Other	1 (9.09)	2 (1.89)	3 (2.56)	
Primary HIV infection				
No	6 (54.55)	53 (48.18)	59 (48.76)	0.76
Yes	5 (45.45)	57 (51.82)	62 (51.24)	
Biological data at HIV diagnosis				
HIV viral load (log/ml)	5.6 [4.7; 5.9]	5.4 [4.4; 6.4]	5.4 [4.3; 6.3]	0.64
CD4 (cell count /mm ³)	470 [340; 650]	478 [328; 635]	480 [340; 641]	0.46
CD4 (%)	19 [14–25]	26 [20–34]	25 [19–33]	0.05
HCV antibodies				
Negative	9 (100.00)	93 (97.89)	102 (98.08)	1 ^a
Positive	0 (0.00)	2 (2.11)	2 (1.92)	
HBV AgHbs				
Negative	9 (100.00)	93 (97.89)	102 (98.08)	1 ^a
Positive	0 (0.00)	2 (2.11)	2 (1.92)	
HAV antibodies				
Negative	6 (100.00)	51 (66.23)	57 (68.67)	0.17 ^a
Positive	0 (0.00)	26 (33.77)	26 (31.33)	
Syphilis serology				
Negative	7 (100.00)	40 (60.61)	47 (64.38)	0.05
Positive	0 (0.00)	26 (39.39)	26 (35.62)	
History of other sexuality transmitted diseases (STI)				
Syphilis				
No	10 (90.91)	77 (70.00)	87 (71.90)	0.18
Yes	1 (9.09)	33 (30.00)	34 (28.10)	
Gonorrhoea				
No	10 (90.91)	96 (87.27)	106 (87.60)	1 ^a
Yes	1 (9.09)	14 (12.73)	15 (12.40)	

Table 2 Characteristics of patients infected during the PrEP area according to eligibility for PrEP (Continued)

N (%) or Median [IQR]	Not eligible for PrEP (n = 11)	Eligible for PrEP. (n = 110)	PrEP area infection (n = 121)	p
Chlamydia				
No	11 (100.00)	99 (90.00)	110 (90.91)	0.60 ^a
Yes	0 (0.00)	11 (10.00)	11 (9.09)	
Number of STIs				
0	10 (90.91)	62 (56.36)	72 (59.50)	0.06 ^a
1	0 (0.00)	30 (27.27)	30 (24.79)	
≥2	1 (9.09)	18 (16.36)	19 (15.70)	

^aFisher's exact test**Table 3** Distribution of PrEP eligibility criteria as defined by Temporary Recommendation for Use (TRU) in France in 2016 [5] among the 110 patients eligible for PrEP*

Men who have sex with men or transgender and at least one of these criteria	91 (82.7)
- Unprotected anal intercourse with at least two different partners in the last 6 months	67 (60.9)
- Incident of sexually transmitted infection (STI) in the last 12 months	33 (30.0)
- Several uses of Post-Exposure Prophylaxis in the last 12 months	1 (0.9)
- Use of psychoactive drugs during sexual intercourse	16 (14.5)
Other persons who are at substantial risk of HIV acquisition among whom PrEP can be considered case by case	25 (22.7)
- Person in situation of prostitution submitted to non-protected sexual intercourse	4 (3.6)
- Person in a situation of vulnerability exposed to non-protected sexual intercourse with a person belonging to a group with a high HIV prevalence:	13 (11.8)
✓ native of a high HIV prevalence area	8 (7.3)
✓ who has multiple sexual partners	4 (3.6)
✓ who injects drug	1 (0.9)
- Person who has non-protected sexual intercourse with persons with physical factors increasing HIV risk transmission to the exposed person (anal or genital ulceration, associated STI, bleeding)	3 (2.7)
- Other situations judged at high risk of HIV acquisition by sexual way:	5 (4.5)
✓ Migrant in precarious situation, probably exposed to non-consensual sex	1 (0.9)
✓ HIV seropositive partner not previously detected	1 (0.9)
✓ HIV seropositive regular partner (treated with no HIV viral load data)	1 (0.9)
✓ Untreated HIV seropositive partner	1 (0.9)
✓ MSM reports with excessive alcohol use during non-protected sexual intercourse	1 (0.9)

*several indications can be found for one patient

The proportion of MSM and west or central African women populations among those with new diagnoses observed in our study (40 and 15%, respectively) was consistent with those previously reported in France in 2015: 43% were MSM and 23% migrant women [1]. Among them, Pre-PrEP area infection that is a proxy of delay in HIV testing concerned 77% of our population, of whom 35% were born in west or central Africa, 31% with CD4 cell count less than 200/mm³ and 20% between 200 and 350/mm³. The delay in HIV diagnosis remains a persistent problem in France as in other countries [33, 34] leading to negative clinical, economic and public health implications. Late presentation is associated with increased patient morbidity and mortality and limits the effectiveness of all subsequent steps in the cascade of HIV care [35, 36]. We did not collect the conditions of HIV testing in our study, so we could not determine if the late diagnoses were due to low risk perception and/or lack of awareness about HIV. Whatever the reason, our results stress the need to reinforce HIV screening strategies in our country, taking into account specific populations more hidden and less engaged in concerned networks.

Limits

Our study had several limits. First, the study was retrospective and the selection criteria involved under-estimation of infection occurring during the PrEP area among new HIV diagnoses. Indeed, among the 741 patients considered infected during the pre-PrEP area, 198 patients did not have a serology in the last 12 months nor an incomplete WB so we could not exclude that these were infected in the PrEP area. However, in our study, the estimated proportion of infections occurring in the last 12 months was 23%, similar to the one-third of recent infections (in the 6 months) found in 2015 in France [1]. Second, we can also not exclude information biases because some physicians may have more often prospectively responded to the patient's eligibility for PrEP in cases of PrEP eligibility. Third, no behavioral data, like sexual practices, were collected and we cannot determine if some specific behavior are linked to the PrEP eligibility nor some specific practices.

Conclusion

This study highlights the high potential of PrEP in avoiding new infection in France, as 91% of patients infected in the PrEP area were eligible for. However, our results highlight a persistent delay in HIV testing in France as observed in other countries. PrEP could markedly decrease HIV infection if combined with a high diagnosis rate and viral suppression [37]. Thus, an important limit of PrEP implementation could be insufficient screening and care access. A prospective study on newly infected persons could allow to disentangle real obstacles of PrEP use in France and to optimize PrEP criteria.

Abbreviations

HBV: Hepatitis B virus; HCV: Hepatitis C virus; IQR: Interquartile range; MSM: Men who have sex with men (MSM); PrEP: Pre-exposure prophylaxis (PrEP); STI: Sexually transmitted infections; TasP: Treatment as prevention; TRU: Temporary Recommendation for Use (TRU); WB: Western blot

Acknowledgments

The DAT/AIDS Study group: Besançon: C. Drobacheff-Thiébaud, A. Foltzer, K. Bouiller, L. Hustache-Mathieu, C. Chirouze, Q. Lepiller, F. Bozon, O. Babre, P. Muret; Clermont-Ferrand: H. Laurichesse, O. Lesens, M. Vidal, N. Mrozek, C. Aumeran, O. Baud, V. Corbin, P. Letertre, S. Casanova, J. Prouteau, C. Jacomet; Guadeloupe: B. Hoen, I. Lamaury, I. Fabre, E. Curlier, R. Ouissa, K. Schepers, C. Herrmann-Storck, N. Dournon; La Roche sur Yon: D. Merrien, P. Perré, T. Guimard, O. Bollangier, S. Leautez, M. Morrier; Lyon: F. Ader, F. Biron, A. Boibieux, L. Cotte, T. Ferry, P. Mialhes, T. Perpoint, S. Roux, S. Degroodt, C. Brochier, F. Valour, C. Chidiac; Marseille (IHU): C. Dhiver, M. Saadia Mokhtari, A. Ménard, H. Tissot Dupont, C. Toméi, L. Meddeb, AY. Belkhir, I. Ravoux; Marseille Sainte-Marguerite: S. Bréigeon, O. Zaegel-Faucher, V. Obry-Roguet, H. Laroche, M. Orticoni, MJ. Soavi, P. Geneau de Lamarlière, E. Ressiot, MJ. Ducassou, I. Jaquet, S. Galie, A. Galinier, P. Martinet, M. Landon, AS. Ritleng, A. Ivanova, C. Debreux, C. Lions, I. Poizat-Martin; Martinique: S. Abel, L. Cuzin, Nguyen S. Pierre-François, J. Pasquier, M. Pircher, K. Rome, B. Rozé, A. Cabié; Montpellier: N. Atoui, V. Le Moing, A. Makinson, N. Meftah, C. Merle de Boever, B. Montes, A. Montoya Ferrer, J. Reynes; Nancy: M. André, L. Boyer, MP. Bouillon, M. Delestan, T. May; Nantes: C. Allavena, C. Bernaud, E. Billaud, C. Biron, B. Bonnet, S. Bouchez, D. Boutoille, C. Brunet-Cartier, C. Deschanvres, N. Hall, T. Jovelin, P. Morineau, V. Reliquet, H. Hue, S. Sécher, M. Cavellec, A. Soria, V. Ferré, E. André-Garnier, A. Rodallec, M. Lefebvre, O. Grossi, O. Aubry, F. Raffi; Nice: P. Pugliese, S. Breaud, C. Ceppi, J. Courjon, E. Cua, J. Cottalorda, P. Dellamonica, E. Demonchy, A. De Monte, J. Durant, C. Etienne, S. Ferrando, J. G. Fuzibet, R. Garraffo, A. Joulie, K. Risso, V. Mondain, A. Naqvi, N. Oran, I. Perbost, S. Pillet, B. Prouvost-Keller, C. Pradier, S. Wehrlen-Pugliese, V. Rio, E. Rosenthal, S. Sausse, G. Zouzou; Orléans: L. Hocqueloux, T. Prazuck, C. Gubavu, A. Sève, M. Niang, C. Boulard; Paris (Bicêtre): A. Cheret, C. Goujard, Y. Quertainmont, E. Teicher, N. Lerolle, D. Vittecoq, O. Deradji, F. Fourreau, C. Pallier, A. Barrail-Tran; Paris (Bichat): R. Landman, V. Joly, C. Rioux, S. Lariven, A. Gervais, F.X. Lescure, S. Matheron, F. Louni, C. Godard, Z. Julia, M. Chansombat, D. Rahli, C. Mackoumbou-Nkouka, C. Charpentier, D. Descamps, G. Peytavin, Y. Yazdanpanah, Paris (Necker- Pasteur): PH. Consigny, G. Cessot, P. Bossi, J. Goesch, J. Gilquin, G. Benabdelmoumen, F. Lanternier, C. Charlier, K. Amazough, B. Henry, B. Pilmis, C. Rouzaud, M. Morgand, F. Touam, C. Louisin, C. Duvivier, O. Lortholary, R. Guery, F. Danion, J. Lourenco, P. Parize, N. Etienne, M. Launay, C. Rouzioux, V. Avettand Fenoel; Paris (La Pitié): M.A. Valantin, F. Caby, R. Tubiana, R. Agher, S. Seang, L. Schneider, R. PaLich, C. Blanc, C. Katlama; Reims: J.L. Berger, Y. N'Guyen, D. Lambert, D. Lebrun, I. Kmiec, M. Hentzien, V. Brodard, F. Bani-Sadr; Saint-Etienne: E. Botelho-Nevers, A. Gagneux-Brunon, A. Frésard, F. Lucht; Strasbourg: P. Fischer, M. Partisani, C. Cheneau, M. Priester, ML. Batard, C. Bernard-Henry, E. de Mautort, D. Rey; Toulouse: M. Alvarez, N. Biezunski, A. Debarb, C. Delpierre, P. Lansalot, L. Lelièvre, G. Martin-Blondel, M. Piffaut, L. Porte, K. Saune, P. Delobel; Tourcoing: F. Ajana, I. Alcaraz, V. Baclet, A. Boucher, P. Choisy, T. Huleux, B. Lafon-Desmurs, H. Melliez, A. Meybeck, A. Pasquet, M. Pradier, O. Robineau, N. Viget, M. Valette. All members of DAT/AIDS group gave their consent to be listed.

Funding

No funding was obtained for this study.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

CL analyzed, interpreted the data and contributed to the drafting of the manuscript. VOB coordinated the retrieval of questionnaires from the centers and participated to the analysis and interpretation of data. IPM: made the conception and design of the study and contributed to the drafting of the manuscript. OC, LC, TH, AGB, AM, AC, BB, LH, EC, AC, LHM, VOB, CJ, CD: contributed to the acquisition of data and revisited the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Data are extracted from electronic medical record: NADIS® who has been approved by the French National Commission on Informatics and Liberty (CNIL 2001/762876; MR 003: 2044467 v.0), and all patients signed an informed consent before being included in this database.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details

¹APHM Hôpital Sainte-Marguerite, Service d'Immuno-hématologie clinique, Aix-Marseille University, Marseille, France. ²Service des maladies infectieuses et tropicales, CHU Bichat, Paris, France. ³Service des maladies infectieuses et tropicales, Hospices Civils de Lyon, Lyon, France. ⁴Service Universitaire des maladies infectieuses et du voyageur, CH Tourcoing, Tourcoing, France. ⁵Service d'Infectiologie, CHU Sainte-Etienne, Groupe Immunité des Muqueuses et Agents Pathogènes, Institut Presage, Université de Lyon, Lyon, France. ⁶Infectious and Tropical Diseases Department, University Hospital Montpellier, Montpellier, France. ⁷UMI 233/INSERMU1175, IRD, University Montpellier, Montpellier, France. ⁸Service des maladies infectieuses et tropicales, CHU de Martinique, INSERM CIC 1425 and Université des Antilles EA 4537, La Martinique, France. ⁹Maladies Infectieuses et tropicales, CHU HOTEL DIEU, Nantes, France. ¹⁰APHP-Hôpital Necker-Enfants Malades, Service de Maladies Infectieuses et Tropicales, Centre d'infectiologie Necker-Pasteur, F-75015 Paris, France. ¹¹Institut Pasteur, Centre Médical de l'Institut Pasteur, Centre d'infectiologie Necker-Pasteur, F-75015 Paris, France. ¹²Université Paris Descartes, Sorbonne Paris Cité, Equipe d'Accueil EA 7327, F-75015 Paris, France. ¹³IHU Imagine, F-75015 Paris, France. ¹⁴Service des maladies infectieuses et tropicales, CHR d'Orléans –La Source, Orléans, France. ¹⁵Service des maladies infectieuses et tropicales, CHU de Nice, Nice, France. ¹⁶Service de Médecine Interne, CHU Kremlin Bicêtre, AP-HP, Kremlin Bicêtre, France. ¹⁷Service des maladies infectieuses et tropicales, CHU Besançon, Besançon, France. ¹⁸Service des maladies infectieuses et tropicales, CHU Clermont Ferrand, Clermont Ferrand, France. ¹⁹Aix-Marseille Univ, INSERM, IRD, SESSTIM, APHM Sainte-Marguerite, Clinical Immuno-Hematological Unit Marseille, Aix Marseille Univ, Marseille, France. ²⁰Immuno hematological Unit service d'Immuno- hématologie Clinique, Centre d'Informations et de Soins de l'Immunodéficience Humaine et des Hépatites virales, 270 boulevard de Sainte Marguerite, 13009 Marseille, France.

Received: 10 October 2018 Accepted: 18 March 2019

Published online: 25 March 2019

References

1. Lot F, Bourdillon F. Découvertes de séropositivité VIH et de sida en 2015. *Inst Veille Sanit* 2017.
2. Éditorial DF. Contrôler durablement l'épidémie VIH en France. *Bull Épidémiol Hebd*. 2017;18:346–7.

3. Gourlay AJ, Pharris AM, Noori T, Supervie V, Rosinska M, van Sighem A, et al. Towards standardized definitions for monitoring the continuum of HIV care in Europe. *AIDS Lond Engl*. 2017;31:2053–8.
4. LeVasseur MT, Goldstein ND, Tabb LP, Olivieri-Mui BL, Welles SL. The Effect of PrEP on HIV Incidence Among Men Who Have Sex With Men in the Context of Condom Use, Treatment as Prevention, and Seroadaptive Practices. *J Acquir Immune Defic Syndr* 1999 2018;77:31–40.
5. ANSM. L'ANSM établit la RTU de Truvada dans la prophylaxie pré-exposition au VIH - Point d'information. 2015. <http://ansm.sante.fr/S-informer/Points-d-information-Points-d-information/L-ANSM-etablit-la-RTU-de-Truvada-dans-la-prophylaxie-pre-exposition-au-VIH-Point-d-information>. Accessed 7 Mar 2018.
6. HAS. La prophylaxie pré-exposition (PrEP) au VIH par TRUVADA. 2017. https://www.has-sante.fr/portail/upload/docs/application/pdf/2017-03/ct_eval_236_bum_truvada_cd_08032017_v4.pdf. Accessed 14 June 2018.
7. Morlat P, Agence nationale de recherches sur le sida (France), France, Conseil national du SIDA, France, Ministère des affaires sociales et de la santé. Prise en charge médicale des personnes vivant avec le VIH: rapport 2013 [pour le] Ministère des affaires sociales et de la santé : recommandations du groupe d'experts. Paris: la Documentation française; 2013.
8. ANSM. Truvada dans la prophylaxie Pré-exposition (PrEP) au VIH : fin de la Recommandation Temporaire d'Utilisation - Informations importantes concernant le bon usage de Truvada® dans l'indication « Prophylaxie pré-exposition (PrEP) » au VIH - Brochure destinée aux prescripteurs. 2017.
9. Lot F, Cazein F, Ndeikoundam N, Pillonel J, Pioche C, Viriot D, et al. Infection par le VIH et IST bactériennes. Point épidémiologique du 26 novembre 2018. *Inst Veille Sanit Santé Publique Fr* 2018.
10. Pugliese P, Cuzin L, Cabié A, Poizot-Martin I, Allavena C, Duvivier C, et al. A large French prospective cohort of HIV-infected patients: the Nadis cohort. *HIV Med*. 2009;10:504–11.
11. Smith DK, Chang M-H, Duffus WA, Okoye S, Weissman S. Missed opportunities to prescribe Preexposure prophylaxis in South Carolina, 2013–2016. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2018.
12. Brown AE, Mohammed H, Ogaz D, Kirwan PD, Yung M, Nash SG, et al. Fall in new HIV diagnoses among men who have sex with men (MSM) at selected London sexual health clinics since early 2015: testing or treatment or pre-exposure prophylaxis (PrEP)? *Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull*. 2017;22.
13. Jia Y, Aliyu MH, Jennifer Huang Z. Dynamics of the HIV epidemic in MSM. *Biomed Res Int*. 2014;2014:497543.
14. Mravčik V, Pitoňák M, Hejzák R, Janíková B, Procházková I. HIV epidemic among men who have sex with men in the Czech Republic, 2016: high time for targeted action. *Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull*. 2017;22.
15. Stahlman S, Lyons C, Sullivan PS, Mayer KH, Hosein S, Beyrer C, et al. HIV incidence among gay men and other men who have sex with men in 2020: where is the epidemic heading? *Sex Health*. 2017;14:5–17.
16. Sewell J, Cambiano V, Miltz A, Speakman A, Lampe FC, Phillips A, et al. Changes in recreational drug use, drug use associated with chemsex, and HIV-related behaviours, among HIV-negative men who have sex with men in London and Brighton, 2013–2016. *Sex Transm Infect*. 2018.
17. Frankis J, Flowers P, McDaid L, Bourne A. Low levels of chemsex among men who have sex with men, but high levels of risk among men who engage in chemsex: analysis of a cross-sectional online survey across four countries. *Sex Health*. 2018;15:144–50.
18. González-Baeza A, Dolengevich-Segal H, Pérez-Valero I, Cabello A, Téllez MJ, Sanz J, et al. Sexualized drug use (Chemsex) is associated with high-risk sexual behaviors and sexually transmitted infections in HIV-positive men who have sex with men: data from the U-SEX GESIDA 9416 study. *AIDS Patient Care STDs*. 2018;32:112–8.
19. Pakianathan M, Whittaker W, Lee MJ, Avery J, Green S, Nathan B, et al. Chemsex and new HIV diagnosis in gay, bisexual and other men who have sex with men attending sexual health clinics. *HIV Med*. 2018.
20. Bracchi M, Stuart D, Castles R, Khoo S, Back D, Boffito M. Increasing use of "party drugs" in people living with HIV on antiretrovirals: a concern for patient safety. *AIDS Lond Engl*. 2015;29:1585–92.
21. Staltari O, Loporini C, Caroleo B, Russo E, Siniscalchi A, De Sarro G, et al. Drug-drug interactions: antiretroviral drugs and recreational drugs. *Recent Patents CNS Drug Discov*. 2014;9:153–63.
22. Baecke C, Gysens IC, Decoutere L, van der Hilst JCH, Messiaen P. Prevalence of drug-drug interactions in the era of HIV integrase inhibitors: a retrospective clinical study. *Neth J Med*. 2017;75:235–40.
23. Kojima N, Davey DJ, Klausner JD. Pre-exposure prophylaxis for HIV infection and new sexually transmitted infections among men who have sex with men. *AIDS Lond Engl*. 2016;30:2251–2.
24. Liu AY, Cohen SE, Vittinghoff E, Anderson PL, Doblecki-Lewis S, Bacon O, et al. Preexposure prophylaxis for HIV infection integrated with municipal- and community-based sexual health services. *JAMA Intern Med*. 2016;176:75–84.
25. Nguyen V-K, Greenwald ZR, Trotter H, Cadieux M, Goyette A, Beauchemin M, et al. Incidence of sexually transmitted infections before and after preexposure prophylaxis for HIV. *AIDS Lond Engl*. 2018;32:523–30.
26. Scott HM, Klausner JD. Sexually transmitted infections and pre-exposure prophylaxis: challenges and opportunities among men who have sex with men in the US. *AIDS Res Ther*. 2016;13:5.
27. Malahleha M, Ahmed K, Deese J, Nanda K, van Damme L, De Baetselier I, et al. Hepatitis B virus reactivation or reinfection in a FEM-PrEP participant: a case report. *J Med Case Rep*. 2015;9:207.
28. Solomon MM, Schechter M, Liu AY, McMahan VM, Guanira JV, Hance RJ, et al. The Safety of Tenofovir-Emtricitabine for HIV Pre-Exposure Prophylaxis (PrEP) in Individuals With Active Hepatitis B. *J Acquir Immune Defic Syndr* 1999 2016;71:281–286.
29. Wright E, Grulich A, Roy K, Boyd M, Cornelisse V, Russell D, et al. Australasian society for HIV, viral hepatitis and sexual health medicine HIV pre-exposure prophylaxis: clinical guidelines. Update April 2018. *J Virus Erad*. 2018;4:143–59.
30. Ross EL, Cinti SK, Hutton DW. Implementation and Operational Research: A Cost-Effective, Clinically Actionable Strategy for Targeting HIV Preexposure Prophylaxis to High-Risk Men Who Have Sex With Men. *J Acquir Immune Defic Syndr* 1999 2016;72:e61–e67.
31. ANSM. Suivi de l'utilisation de Truvada® ou génériques pour une prophylaxie pré-exposition (PrEP) au VIH à partir du SNIIRAM. 2018. <http://ansm.sante.fr/S-informer/Points-d-information-Points-d-information/Utilisation-de-la-prophylaxie-pre-exposition-PrEP-au-VIH-par-Truvada-ou-generiques-entre-janvier-2016-et-juillet-2017-Point-d-information>. Accessed 29 June 2018.
32. Baral S, Logie CH, Grosso A, Wirtz AL, Beyrer C. Modified social ecological model: a tool to guide the assessment of the risks and risk contexts of HIV epidemics. *BMC Public Health*. 2013;13:482.
33. Champenois K, Cousien A, Cuzin L, Le Vu S, Deuffic-Burban S, Lanoy E, et al. Missed opportunities for HIV testing in newly-HIV-diagnosed patients, a cross sectional study. *BMC Infect Dis*. 2013;13:200.
34. Taborelli M, Virdone S, Camoni L, Regine V, Zucchetto A, Frova L, et al. The persistent problem of late HIV diagnosis in people with AIDS: a population-based study in Italy, 1999–2013. *Public Health*. 2017;142:39–45.
35. Darling KE, Hachfeld A, Cavassini M, Kirk O, Furrer H, Wandeler G. Late presentation to HIV care despite good access to health services: current epidemiological trends and how to do better. *Swiss Med Wkly*. 2016;146:w14348.
36. O'Connell S, Enkelmann J, Sadlier C, Bergin C. Late HIV presentation - missed opportunities and factors associated with a changing pattern over time. *Int J STD AIDS*. 2017;28:814–21.
37. Grant R, Liu A, Hecht J, Buchbinder S, Weber S, Crouch P-C, et al. Scale-up of Preexposure prophylaxis in San Francisco to impact HIV incidence. 2015.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more [biomedcentral.com/submissions](https://www.biomedcentral.com/submissions)

