

# Coronavirus disease 2019 attack rate in HIV-infected patients and in preexposure prophylaxis users

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**Objective:** A new coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) emerged in China during late 2019 and resulted in the coronavirus disease 2019 (COVID-19) pandemic which peaked in France in March–April 2020. Immunodeficiency, precariousness and promiscuity could increase the risk of COVID-19 in HIV-infected patients and in preexposure prophylaxis (PrEP) users. No epidemiological data are available in these two populations. We report COVID-19 attack rate in HIV-infected patients and in PrEP users in the Rhône department, France, and compared it with the general population.

**Design:** Retrospective analysis of a laboratory database.

**Methods:** COVID-19 testing strategy in France was centered on symptomatic infections, hospitalized patients and symptomatic healthcare workers while most asymptomatic cases were not confirmed. SARS-CoV-2 positivity rate on PCR assays and COVID-19 attack rate were determined in HIV-infected patients and in PrEP users. COVID-19 attack rate in the general population was estimated from health authorities' database and demographic data. A corrected attack rate taking into account the laboratory representativeness was calculated.

**Results:** From March to April 2020, 24 860 samples from 19 113 patients (HIV-infected 77, PrEP users 27, others 19 009) were assessed for SARS-CoV-2 PCR assay. The positivity rate appeared similar in HIV-infected patients (15.6%), in PrEP users (14.8%) and in other patients (19.1%). The crude/corrected COVID-19 attack rate appeared similar in HIV-infected patients (0.31/0.38%) and in PrEP users (0.38/0.42%), and of the same order as the estimated attack rate in the general population (0.24%).

**Conclusion:** The risk of symptomatic COVID-19 in France appeared similar in HIV-infected patients and in PrEP users compared with the general population.

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## Introduction

A novel human betacoronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged from Wuhan, China, in December 2019, resulting in the coronavirus disease 2019 (COVID-19) pandemic [1]. This virus infects the respiratory tract leading to various clinical presentations, from asymptomatic forms to severe pneumonia. An older age and comorbidities are associated with more severe infection and worse prognosis [2]. Immunodeficiency and chronic inflammation, as observed in HIV-infected patients, might increase the susceptibility and the severity of COVID-19 as for many infectious diseases. Moreover, immune alterations may impact the cytokine storm observed in most severe cases [3]. In addition, precariousness and promiscuity could also increase the risk of transmission in HIV-infected patients, as well as in preexposure prophylaxis (PrEP) users. However, no excess in morbidity and mortality in HIV-infected patients was found in several recent case series [4–7], while HIV-infected patients were not over-represented in patients hospitalized for severe COVID in several studies [8–10]. There are so far no epidemiological data in these populations.

## Objective

The objective of this study was to report the COVID-19 attack rate in HIV-infected patients and in PrEP users in the Rhône department, France, and to compare it with the attack rate observed in the general population in the same area.

## Design

The current study is a retrospective analysis of a laboratory database using cross-referencing with a near-exhaustive clinical database.

## Methods

### Diagnostic strategy in France

In France, national guidance for COVID-19 testing was centered on symptomatic infections, hospitalized patients and symptomatic healthcare workers [11]. As a result, most asymptomatic cases were not diagnosed using PCR assays.

### Analysis and case definition

All patients with at least one COVID-19 PCR assay performed in the Hospices Civils de Lyon Virology Laboratory in March–April 2020 were included. Tested

samples included nasopharyngeal swabs and endotracheal aspirates. Two methods were implemented, one based on a two RNA dependent RNA polymerase target reverse transcription-PCR designed at the Institut Pasteur, Paris, France [12] and the other based on a fully automated sample-to-result two-target test Cobas 6800 SARS-CoV-2 targeting ORF1, a nonstructural region that is unique to SARS-CoV-2 and a conserved region in the structural protein envelope E gene for pan-Sarbecovirus detection (Roche Molecular Systems, Branchburg, New Jersey, USA) [13]. Patients with at least one positive result were considered infected. For patients with negative and positive samples and for patients with multiple samples, only the first positive one was retained. Patients with only negative samples were considered uninfected at the time of the first sample. Thus, each patient accounted only once in the study.

## Geographical context

The Rhône department is one of the 95 territorial divisions of metropolitan France, centered on the second largest French city, Lyon. As a reference Laboratory for respiratory viruses, our laboratory performed most COVID-19 PCR tests in the Auvergne-Rhône-Alpes administrative region and all tests in the Rhône department during the first weeks of the epidemic, then became less exhaustive when external laboratories opened. A representativeness ratio was determined weekly, based on the number of COVID-19 diagnosed in our laboratory, divided by the total number of diagnoses registered by Health authorities during the same period in the department.

## Representativeness

In France, HIV-infected patients and PrEP users are mostly followed at hospital, since antiretroviral treatment including PrEP is mandatorily initiated at hospital and requires a hospital prescription at least every 12 months. In the Rhône administrative department, the clinical and biological data are registered in a database covering every public hospital in the Rhône and the surrounding departments. Based on compulsory HIV diagnosis declarations and antiretrovirals reimbursement, this database covers more than 95% of HIV-infected patients and PrEP users living in the Rhône department. Each HIV-infected adult patient and PrEP user attending at least one visit between January 2019 and April 2020 was enrolled. The number of at-risk patients in each subgroup was based on the total number of patients in this group minus the number of patients deceased before March 2020. The HIV-infected group and the PrEP group were mutually exclusive. Patients not belonging to either group were considered as ‘other patients’.

**Statistics**

SARS-Cov-2 positivity rate on biological samples was calculated in the overall population. Attack rate analysis was restricted to patients domiciled in the Rhône department. A crude attack rate was first determined by dividing the number of cases in each subgroup by the number of patients in this group. A corrected attack rate was then determined by applying the weekly representativeness ratio to the weekly number of diagnosis, thus giving a corrected number of cases, which was divided by the total number of patients. This corrected rate was based on the assumption that the positivity rate was the same in external laboratories as in our laboratory. Since the most severe COVID-19 cases were highly concentrated in Lyon’ University Hospital where our Laboratory is located, this assumption probably overestimates the positivity rate in external laboratories, thus providing the worst hypothesis scenario.

The attack rate in the general population was estimated by dividing the total number of diagnoses registered by Health

authorities in the Rhône department by the estimated adult population living in the department in January 2020 [14] (<https://www.insee.fr/fr/statistiques/fichier/1893198/estim-pop-dep-sexe-gca-1975-2020.xls>).

Factors potentially associated with COVID-19 such as age, sex, HIV positivity and PrEP use, were studied using a univariable and multivariable logistic regression model. Analyses were performed using R (R Foundation for Statistical Computing, Vienna, Austria). Confidence intervals (CIs) were calculated using Poisson distribution.

**Ethics**

All patients gave consent to the use of their clinical and biological data in the study. The study was approved by the Hospices Civils de Lyon ethics committee (no. 19–51) and is registered on the ClinicalTrials.gov website (NCT04379245).

**Table 1. Characteristics of the tested population (n = 19 113).**

Characteristic	HIV-infected patients, n = 77		PrEP users, n = 27		Other patients, n = 19 009	
Age (year) median (IQR)	53.0 (41.3–58.6)		33.9 (27.6–40.3)		54.6 (35.6–75.7)	
Age category, n (%)						
<20 years	1 (1.3%)				1009 (5.3%)	
20–40 years	18 (23.4%)		19 (70.4%)		4941 (26.0%)	
40–60 years	40 (51.9%)		8 (29.6%)		4966 (26.1%)	
60–80 years	17 (22.1%)				4227 (22.2%)	
>80 years	1 (1.3%)				3859 (20.3%)	
Unknown					8 (0.04%)	
Male, n (%)	52 (67.5%)		27 (100%)		7696 (40.5%)	
Living in the Rhône department, n (%)	76 (98.7%)		27 (100%)		14 907 (78.4%)	
HIV risk factor, n (%)					NA	
MSM	25 (32.5%)		27 (100%)			
Heterosexual	43 (55.8%)		0			
Other	9 (11.7%)		0			
Born outside Western Europe, n (%)	28 (36.4%)		2 (7.4%)		NA	
CDC stage C	25 (32.5%)		NA		NA	
HIV duration (year) median (IQR)	15.0 (7.0–24.0)		NA		NA	
Antiretroviral duration (year) median (IQR)	12.2 (7.3–23.0)		NA		NA	
PrEP duration (year) median (IQR)	NA		0.9 (0.4–1.6)		NA	
Antiretroviral treatment, n (%)	76 (98.7%)		26 (96.3%)		NA	
Antiretroviral drugs, n (%)					NA	
Boosted PI	9 (11.7%)		NA			
INSTI	48 (62.3%)		NA			
NNRTI	23 (29.9%)		NA			
TDF/TAF	52 (67.5%)		26 (96.3%)			
CD4 <sup>+</sup> cell count/μl, median (IQR)	529 (361–722)		NA		NA	
CD4 <sup>+</sup> cell count >500/μl, n (%)	42 (54.5%)		NA		NA	
HIV viral load <50 copies/ml, n (%)	69 (89.6%)		NA		NA	
COVID-19 positivity rate, n/total (%)	n/Total	%	n/Total	%	n/Total	%
Total	12/77	15.6	4/27	14.8	3632/19 009	19.1
Male	7/52	13.5	4/27	14.8	1503/7696	19.5
Female	5/25	20.0	0/0	NA	2129/11 313	18.8
Crude COVID-19 attack rate in the Rhône	12/3874	0.31 (0.18–0.55)	4/1675	0.24 (0.09–0.64)	NA	
Corrected COVID-19 attack rate in the Rhône (worst case scenario)	14.7/3874	0.38 (0.23–0.64)	7.1/1675	0.42 (0.20–0.88)	NA	

CDC, Centers for Disease control and Prevention; COVID-19, coronavirus infectious disease 2019; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; NA, not applicable; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PrEP, preexposure prophylaxis; TDF, tenofovir disoproxyl; TAF, tenofovir alafenamide.

## Results

### Positivity rate

From 2 February 2020 (week 6) to 26 April 2020 (week 17), 24 860 samples from 19 113 patients (HIV-infected 77, PrEP users 27, others 19 009) were assessed for SARS-Cov-2 PCR assay in our laboratory (Table 1). Overall, 3648 patients were infected (HIV-infected 12; PrEP-users four; others 3632) giving a positivity rate of 19.1% (3648/19 113). This rate increased from 3.2% in patients below 10 years of age to 25.3% in patients over 90 years and was comparable in males (19.5%) and in females (18.8%). The weekly positivity rate increased from 4.3% (week 9), to 32.3% (week 13), and then regularly decreased to 7.0% (week 17). The positivity rate appeared similar in HIV-infected patients [15.6% (12/77)], in PrEP users [14.8% (4/27)] and in other patients [19.1% (3632/19 009)]. Overall, 83% of all COVID-19 diagnoses in the Rhône department in March–April 2020 were performed in our laboratory. The representativeness ratio of the laboratory decreased from 100% during week 10 to 12 to 47% during week 17.

### Attack rate

From January 2019, 4755 HIV-infected patients and 1867 PrEP users were in care in the Rhône department, of

whom 3874 HIV-infected patients and 1675 PrEP users lived in the Rhône department. Twelve HIV-infected patients and four PrEP users were diagnosed with COVID-19, all living in the Rhône department. The crude COVID-19 attack rate in the Rhône department appeared similar in HIV-infected patients [0.31% (95% CI 0.18–0.55%)] and in PrEP users [0.38% (0.23–0.64%)]. The corrected COVID-19 attack rate, taking into account the representativeness of the laboratory (worst case scenario), was 0.38 (0.23–0.64%) for HIV-infected patients and 0.42% (0.20–0.88%) for PrEP users (Table 1).

As of 26 April 2020, 3312 COVID-19 cases were reported by health authorities in the Rhône department, for an estimated population of 1397 909 adults, excluding HIV-infected patients and PrEP users. The COVID-19 attack rate in the general population was thus estimated to 0.24% (0.23–0.24%) in this department (Fig. 1).

The only factor associated with COVID-19 was age, both in univariable [odds ratio (OR) 1.01 per year (1.01–1.01%)] and in multivariable analyses [OR 1.01 per year (1.01–1.01%)], while male gender [OR 0.97 (0.89–1.06)], HIV infection [OR 0.73 (0.44–1.58)] and PrEP use [OR 1.1 (0.38–3.21)] were not.

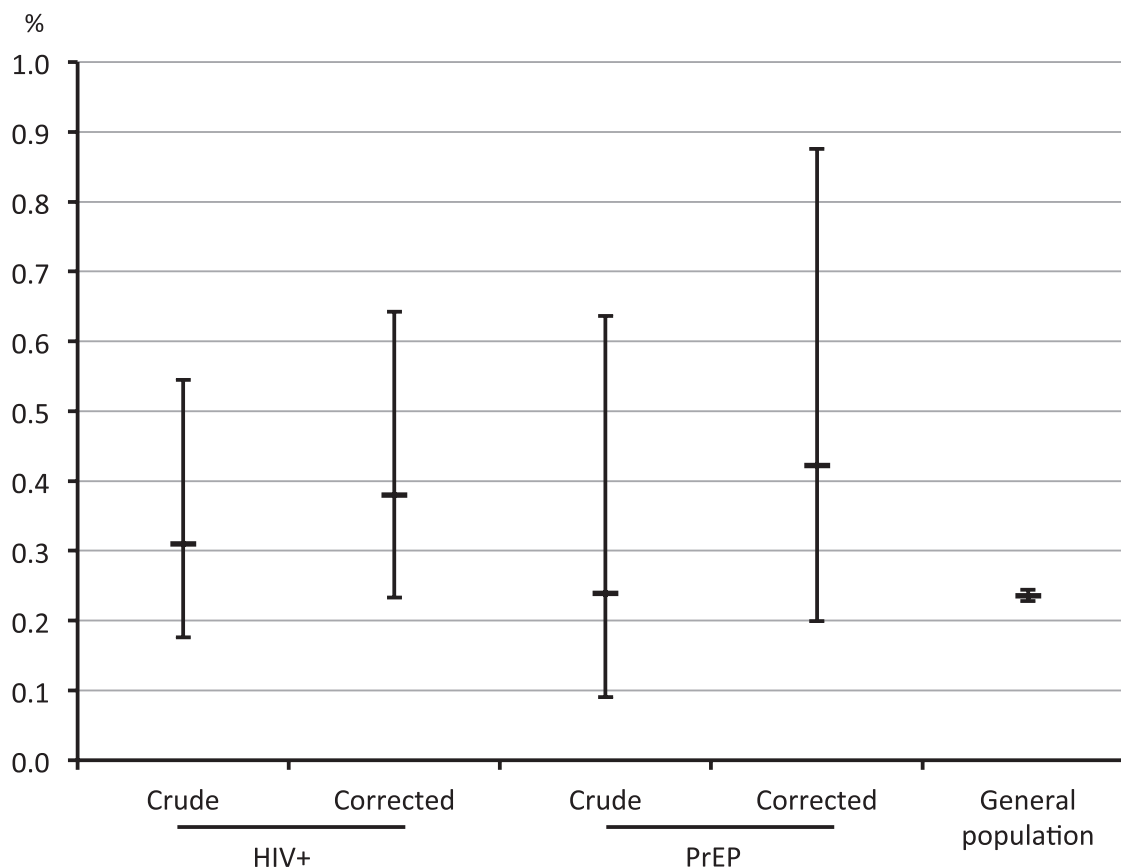


Fig. 1. Crude and corrected coronavirus disease 2019 attack rates in HIV-infected patients ( $n=77$ ) and in preexposure prophylaxis users ( $n=27$ ), and estimated coronavirus disease 2019 attack rate in the general population in the Rhône department, France, March–April 2020. Attack rates are presented together with their 95% confidence intervals (error bars).

## Conclusion

HIV-infected patients and PrEP users had similar SARS-Cov-2 positivity rates and COVID-19 attack rates as the general population during the early 2020 pandemic in the Rhône department, France, and did not appear more susceptible than patients of similar age. Despite the relatively small number of tested patients due to the French diagnostic strategy centered on most severe cases only, these results also suggest that severe cases are not over-represented among HIV-infected patients, as recently reported in several cases series from Europe and the United States [4–7]. In addition, HIV-infected patients accounted for only 0.8–1.4% of patients hospitalized with COVID-19 in three large studies in China [10], the United Kingdom [8] and New York City [9]. While 36.4% of HIV-infected patients in our database were born outside Western Europe, a factor that could contribute to precariousness, and since CD4<sup>+</sup> cell count was below 361/μl in a quarter of our patients, these results are reassuring regarding the epidemiological impact of COVID-19 in this population. However, the limited number of cases precludes conclusions regarding the impact of more severe immunodeficiency on the risk of infection and on the severity of the disease. In addition, SARS-Cov-1 pulmonary infection was attenuated in a complement system knocked out mice model [15], indicating that additional studies are required, by immunodeficiency type.

Similarly, the risk of COVID-19 did not appear increased in PrEP users, a population with a high degree of social and physical interactions which could potentially increase the risk of transmission. Despite the small number of cases, this result suggests that social distancing was sufficient in this population to maintain transmission at a relatively low level, probably reflecting behavioral changes during the epidemic.

Lopinavir, a protease inhibitor of HIV showed in-vitro efficacy against SARS-Cov-2 but failed to demonstrate clinical efficacy in severe COVID-19 [16]. In addition, the nucleotide analog tenofovir binds to the SARS-COV-2 RNA dependent RNA polymerase and may exert an antiviral action against the virus [17]. Two-thirds of HIV-infected patients and nearly all PrEP-users in our study were currently receiving Tenofovir disoproxil or Tenofovir alafenamide, including 10 of the 12 HIV-infected and the four PrEP users COVID-19 cases. Despite the small numbers, these results do not support a protective role of Tenofovir against COVID-19.

Limitations to this study include the limited number of cases in the two subgroups, the absence of clinical data in the COVID-19 cases and in controls and the fact that mostly symptomatic patients were tested, as recommended in France. Thus, most asymptomatic patients were probably missed, and the attack rates reported in the

study are minimal estimates of infection. However, this study has several strengths, including the accuracy of the subgroup denominators and the high representativeness of our Laboratory in the Rhône department. These results need to be confirmed by other studies in different countries and contexts.

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Authors' contributions: L.C., initiated the study.

All the authors contributed to the design of the study.

C.C., V.I., B.L. and virologists listed in the COVID-HIV-PrEP Study Group, performed the laboratory analyses.

L.C., C.C. and physicians of the COVID-HIV-PrEP Study Group provided clinical care and contributed to the acquisition of clinical data.

C.C. and V.I. drafted the article.

C.B. managed the regulatory process.

L.C. and P.P. analyzed the data.

All authors reviewed the article before submission and gave approval to the final draft.

## Conflicts of interest

There are no conflict of interest.

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