## **ORIGINAL ARTICLE**

# Characteristics of human immunodeficiency virus exposure and predictors of time until access to postexposure prophylaxis: a prospective observational study

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**Background and objective.** The efficacy of postexposure prophylaxis (PEP) after human immunodeficiency virus (HIV) contact relies on administering the treatment within 4 hours of contact with the virus. This study aimed to evaluate predictors of the time that elapses between HIV exposure and emergency department arrival.

**Methods.** Prospective observational study carried out at Hôpital Bichat, a university teaching hospital in Paris, France. All emergency visits for occupational or nonoccupational exposure to HIV in 2016 and 2017 were included.

**Results**. A total of 1475 cases were studied; 598 patients responded to the follow-up survey. A delay of 4 hours or more between HIV exposure and the emergency department visit was associated with type of contact: health care occupational exposure, other occupational exposure, or sexual intercourse (P < .001). We found significant differences between individuals exposed during sexual contact versus occupational exposure with respect to knowledge of the PEP program pathway (65.2% vs 46.9%, respectively), previous use of PEP (23.9% vs 13.1%), alcohol intake (36.2% vs 18.5%), drug use (34.6% vs 8.6%), and chemsex (sexualized drug use) (26.1% vs 0%) (P < .001, all comparisons). Predictors of time until start of PEP among individuals exposed during sexual intercourse were knowledge and prior use of the PEP pathway (P < .001), drug use (P = .03), and chemsex (P < .001). Predictors among occupationally exposed individuals were prior knowledge of the PEP pathway and drug use (P < .001).

**Conclusions.** Delay in seeking PEP after HIV exposure is greater among individuals exposed during sexual intercourse. Knowledge of the PEP program and prior use of it are associated with less delay. Exposure during sexual intercourse, alcohol and drug use, and chemsex are associated with longer delays, especially in men who have sex with men.

Keywords: Postexposure prophylaxis. Human immunodeficiency virus (HIV) exposure. Quality indicators. Time intervals. Emergency department. Awareness.

### Características de la exposición al VIH y factores predictores del tiempo de acceso a la profilaxis posexposición: estudio observacional prospectivo

**Objetivos.** La eficacia de la profilaxis posexposición al virus de la inmunodeficiencia humana (VIH) depende de un tiempo inferior a 4 horas entre la exposición y la administración del tratamiento. Este estudio evalúa los factores predictores del tiempo entre la exposición al VIH y la llegada a urgencias.

Métodos. Estudio observacional, prospectivo, realizado en el Hospital Universitario de Bichat (París, Francia). Se incluyeron todas las consultas en urgencias en 2016 y 2017 por exposición al VIH –ocupacional y no ocupacional–.

**Resultados.** Se incluyeron 1.475 pacientes, de los que 598 completaron una encuesta de seguimiento. El retraso ( $\geq 4$  horas) entre la exposición al VIH y la consulta en urgencias se asoció con el tipo de exposición al VIH: trabajadores sanitarios, otras exposiciones y sexuales (p < 0,001). Se encontraron diferencias entre la exposición sexual y otras: conocimiento del circuito de PEP: 65,2% y 46,9% (p < 0,001), uso previo de PEP: 23,9% y 13,1% (p = 0,001), uso de alcohol: 36,2% y 18,5% (p < 0,001), uso de drogas: 34,6% y 8,6% (p < 0,001), y *chemsex:* 26,1% y 0% (p < 0,001). En la exposición sexual, los siguientes factores predicen el retraso: conocimiento y uso previo del circuito de PEP (p < 0,001) disminuyen el riesgo de retraso > 4 horas, y uso de drogas (p = 0,03) y *chemsex* (p < 0,001) lo aumentan; en la exposición ocupacional, el conocimiento del programa PEP lo disminuye y el uso de drogas lo aumenta (p < 0,001).

**Conclusión.** El retraso en la consulta posexposición al VIH es mayor en la exposición sexual. El conocimiento del programa de PEP y su uso previo determinaban un retraso menor. En la exposición sexual, el consumo de alcohol, drogas y *chemsex*, implican un retraso mayor, en especial en hombres que tienen relaciones sexuales con hombres.

Palabras clave: Profilaxis posexposición. Exposición al VIH. Indicadores de calidad. Intervalo de tiempo. Servicio de urgencias. Concienciación.

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#### Introduction

An estimated 1.8 million people still contract HIV each year worldwide, including more than 70,000 people in Western and Central Europe and North America<sup>1</sup>. It has been currently accepted that 44% of new cases occur in members of vulnerable populations and their partners, regardless of epidemic type or local context, and that a sexual transmission mode is the most common<sup>2,3</sup>. In addition, more than 35 million healthcare workers (HCWs) are exposed to HIV each year around the world<sup>4</sup>; however, other professionals may be exposed outside the healthcare setting<sup>5</sup>. Postexposure prophylaxis (PEP) is an effective and inexpensive tool for preventing HIV transmission after a potential HIV exposure<sup>6,7</sup>. Once HIV crosses a mucosal or cutaneous barrier, it can be detected 48-72 hr later in lymph nodes and up to five days in blood. Animal and perinatal transmission models, as well as observational studies, indicate that the highest efficacy is reached when the post-exposure treatment is administered as soon as possible and that its effectiveness decreases after 24 to 36 hr after exposure<sup>6,7</sup>. All the recommendations and guidelines emphasize that the effectiveness of PEP is linked to its guickest administration<sup>8-13</sup>. In France, a delay of less than 4 hr is considered optimal<sup>14</sup>.

Furthermore, in France, access to PEP programs relies on a healthcare program including specialized consultations in hospitals and sexual health clinics during daytime and weekdays, and emergency departments (EDs) ensure permanent patient reception<sup>15</sup>. It is widely accepted that most PEPs are initiated in the ED and that the role of the ED is central to the program<sup>16</sup>. The delay between HIV exposure and arrival at the ED for HIV transmission risk assessment and PEP administration is critical in a strategy to optimize the effectiveness of PEP. It has been proposed that some HIV exposure variables could be associated with the delay between HIV exposure and PEP scheme usage. Among them, awareness of the care scheme among the general population and in increased risk populations has been previously studied. In France, awareness of the PEP plan is estimated to be around 22% for the general population and 69% for men having sex with men (MSMs)<sup>17</sup>. Recently, it has also been reported than 74.2% of MSMs seeking PEP for sexual exposure had at least one syndemic clinical condition, including depression or alcohol and drug consumption, and that it was associated with increased risk of HIV exposure<sup>18</sup>. To our knowledge, no study has described the delay between HIV exposure and PEP access, nor the associated factors. The objective of this work therefore, is to describe the delay between HIV exposure and arrival at the ED as well as the variables weighing on the delays between HIV exposure and PEP program usage. These variables include patients; exposure characteristics; and syndemic health conditions such as alcohol, drugs, and chemsex consumption.

#### **Methods**

This was a prospective observational study conducted as part of a continuous quality improvement program for dealing with HIV exposures treated at the BCB Hospital, which is an academic, 1,000-bed hospital located in the metropolitan area of Paris. Its ED receives 85,000 visits each year.

All adults treated at the BCB Emergency Department from January 1st, 2016 to December 31st, 2017, after potential HIV exposure, were included. For each patient who met the inclusion criteria, a standard electronic case report form was completed by the emergency physician. This tool is currently used to optimize the quality of PEP prescription.

HIV exposures were classified as follows: 1) the BCB's HCWs (doctors, nurses, cleaning staff, or hospital security) potentially exposed during accidental contact with blood or other body fluids in the exercise of their duties; 2) other occupational or non-occupational exposures (occupational exposure outside the hospital, including firemen, policemen, residential health staff, housekeeping staff, and maintenance staff); and 3) sexual exposures: they were categorized as heterosexual and MSM. Furthermore, time categories were defined as < 4 hr and  $\geq$  4 hr between potential HIV exposure and arrival at ED. According to the French current recommendations for optimal access time to PEP, 4 hr was defined as the breakpoint<sup>14</sup>. During the ED consultation, patients were routinely referred to follow-up and post-emergency consultations at the HIV Clinic of the BCB Hospital within 48 to 72 hr for the reassessment of the PEP indication, for sexual counseling, and for evaluation of pre-exposure prophylaxis. During this consultation, the following were assessed: patients' knowledge of access to the PEP program; their previous HIV exposure; their prior access to the PEP program; and their alcohol, drug, and chemsex use within 24 hr of the last potential exposure to HIV.

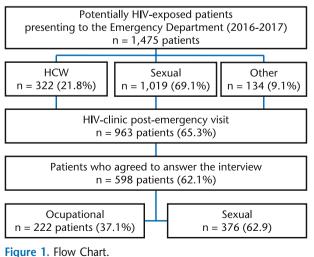
Data collection and storage by the Urqual<sup>®</sup> EDspecific electronic medical record was approved by the French National Commission for Data Protection and Liberties. Data was extracted from the hospital database and then anonymized. The Emergency Ethics Committee for Biomedical Research of the Assistance Publique-Hôpitaux of Paris approved this study.

To describe the study population, continuous variables were expressed as a mean and a standard deviation, and categorical variables as numbers of patients and percentages. A Chi-2 or Fisher's test and a Student's t-test or Kruskal-Wallis test were used to compare categorical and continuous variables, respectively, between the studied groups. Moreover, to assess the association between time categories, type of HIV exposure, and the studied variables, we used multiple logistic regressions. Variables that demonstrated near statistical significance (p < 0.2) were included in a multivariate stepwise multiple logistic regression model. The significance threshold was set at p < 0.05, and statistical analyses were performed using Statistica® software (Stat Soft).

#### Results

During the 2-year study period, 1,475 patients were registered after potential HIV exposure (2016: 658 (44.6%) and 2017: 817 (55.4%)). The study flowchart is shown in Figure 1, and patients' characteristics are shown in Table 1. The time delay (hours) between HIV exposure and ED arrival was significantly different between the study groups – HCWs:  $4.2 \pm 9.6$ , other:  $8.4 \pm 10.5$ , and sexual:  $25.6 \pm 41.6$  (p < 0.001). We also found significant differences between groups in terms of gender distribution, arrival times, HIV source, and PEP prescription. The dispersion of delay between HIV exposure to ED arrival time as a function of the groups is presented in Figure 2. We found that 555 of the 1,475 patients (37.6%) arrived at the ED in less than 4 hr, whereas this percentage was 77.9% for HCWs, 46.3% for other, and 21.1% for sexual (p < 0.001). In addition, we discovered that 52 out of 1,475 patients (3.5%) arrived after 48 hr, mainly for sexual exposures (44/52 (84.6%)). In the logistic regression analysis, a delay  $\geq$  4 hr was associated with the type of HIV exposure: HCWs Odd Ratio (OR) 1, other OR 3.99 [CI 95% 2.88-4.82], and sexual OR 15.97 [CI 95% 8.32-23.2]. Table 2 lists the predictors of  $\geq$  4 hr delays from HIV exposure to ED arrival depending on the types of HIV exposure.

Of the 1,475 HIV potential exposures treated in the ED, 963 patients (65.3%) consulted the HIV clinic within 72 hr after accessing the ED. Among them, 598 patients (62.1%) completed the survey. Some differences were found between those who were sexually exposed (SE) and those who were occupationally exposed (OE). For instance, 245/376 SEs (65.2%) knew about the PEP program versus only 104/222 OEs (46.9%) (p = 0.001). The previous PEP program was used by 90/376 SEs (23.9%) and 29/222 OEs (13.1%) (p = 0.001). We also noticed alcohol use in 136/375 SEs (36.2%) vs. 41/222 OEs (18.5%) (p < 0.001); drug use in 130/376 SEs (34.6%) vs. 19/222 OEs (8.6%) (p < 0.001); and chem-



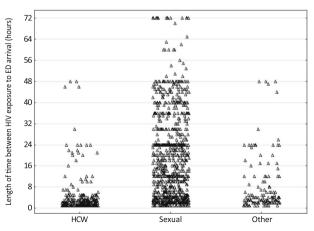
HCW: healthcare workers.

| Table 1. Main characteristics of the study population |  |
|---|--|
| (1,475 patients)                                      |  |

|   | HCW<br>N = 322<br>n (%) | Other<br>occupa-<br>tional<br>N = 134<br>n (%) | Sexual<br>N = 1,019<br>n (%) | р       |
|---|-------------------------|--|------------------------------|---------|
| Sex   |                         |  |                              | < 0.001 |
| Female  | 72 (22.4)               | 87 (64.9)                                      | 827 (81.2)                   |         |
| Male  | 250 (77.6)              | 47 (35.1)                                      | 191 (18.8)                   |         |
| Type of day   |                         |  |                              | < 0.001 |
| Weekdays  | 253 (78.6)              | 91 (67.9)                                      | 653 (64.1)                   |         |
| Weekend days  | 69 (21.4)               | 43 (32.1)                                      | 366 (35.9)                   |         |
| Arrival time to ED  |                         |  |                              | 0.003   |
| 8 am to 7 pm  | 210 (65.2)              | 84 (62.7)                                      | 547 (53.7)                   |         |
| 8 pm to midnight  | 74 (23)                 | 30 (22.4)                                      | 285 (28)                     |         |
| Midnight to 7 am  | 38 (11.8)               | 20 (14.9)                                      | 187 (18.4)                   |         |
| HIV status of the contact person                            |                         |  |                              | < 0.001 |
| Negative  | 191 (59.3)              | 109 (81.3)                                     | 547 (80.1)                   |         |
| Unknown   | 86 (26.7)               | 6 (4.5)  | 104 (10.2)                   |         |
| Positive  | 45 (14)                 | 19 (11.2)                                      | 99 (9.7)                     |         |
| PEP first dose in the ED                                    |                         |  |                              | < 0.001 |
| No  | 263 (81.7)              | 113 (84.3)                                     | 282 (27.7)                   |         |
| Yes   |                         |  | 737 (72.3)                   |         |
| Time interval from HIV<br>exposure to ED arrival<br>(hours) |                         |  |                              | < 0.001 |
| < 4 hours   | 267 (82.9)              | 81 (60.4)                                      | 257 (25.2)                   | < 0.001 |
| $\geq$ 48 hours   | 2 (0.6)                 | 6 (2.2)  | 44 (4.6)                     | < 0.001 |
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ED: emergency department; HCW: healthcare workers PEP: post-exposure prophylaxis.

sex use in 98/376 SEs (26.1%) vs. 0/222 OEs (0%) (p < 0.001). In some cases, drugs were cannabis, benzodiazepines, and cocaine. Among the SEs, in heterosexuals and MSMs respectively, we found the following: knowledge of the PEP program in 41/136 (30.2%) vs. 204/240 (85%) (p < 0.001), previous PEP program use by 13/136 (9.7%) vs. 77/240 (32.1%) (p < 0.001), alcohol use by 38/136 (27.9%) vs. 98/142 (40.8%) (p = 0.01), drug use by 47/136 (34.6%) vs. 83/240 (34.6%) (p = 1), and chemsex use by 6/136 (4.4%) vs. 92/240 (38.3%) (p < 0.001).



**Figure 2.** Delay between HIV exposure and arrival at the emergency department.

ED: emergency department; HCW: healthcare workers.

|  |              | Logistic regr  | ession           |         | Multivariate logistic regression |         |  |
|--|--------------|----------------|------------------|---------|----------------------------------|---------|--|
|  | < 4 hours    | $\geq$ 4 hours | OR (95% CI)      | р       | OR (95% CI)                      | р       |  |
| ealth care workers                     |              |                |                  |         |                                  |         |  |
| Gender (Male)                          | 69 (35.6)    | 3 (64.4)       | 0.17 (0.05-0.55) | < 0.001 |                                  |         |  |
| Type of day (Weekend-day)              | 60 (87)      | 9 (13)         | 0.70 (0.31-1.46) | 0.3     |                                  |         |  |
| Time of ED arrival                     |              |                |                  | 0.08    |                                  |         |  |
| 8 am to 7 pm                           | 167 (79.5)   | 43 (20.5)      | 1 (ref.)         |         |                                  |         |  |
| 8 pm to midnight                       | 64 (86.5)    | 10 (13.5)      | 0.52 (0.31-0.89) |         |                                  |         |  |
| Midnight to 7 am                       | 36 (94.7)    | 2 (5.3)        | 0.27 (0.1-0.81)  |         |                                  |         |  |
| Risk of HIV transmission               |              |                | ,                | 0.05    |                                  |         |  |
| Low                                    | 64 (81)      | 15 (19)        | 1 (ref.)         |         |                                  |         |  |
| Intermediate                           | 150 (82.9)   | 31 (17.1)      | 0.7 (0.49-1)     |         |                                  |         |  |
| High                                   | 53 (85.5)    | 9 (14.5)       | 0.35 (0.22-0.42) |         |                                  |         |  |
| HCW category                           | ()           | . ()           |                  | 0.09    |                                  |         |  |
| Students                               | 66 (86.8)    | 10 (13.2)      | 1 (ref.)         | 0.07    |                                  |         |  |
| Nurses                                 | 123 (82.6)   | 26 (17.4)      | 1.11 (0.82-1.21) |         |                                  |         |  |
| Physician-surgeon                      | 15 (68.2)    | 7 (31.8)       | 1.31 (1.12-1.58) |         |                                  |         |  |
| HCW workplace                          | 15 (00.2)    | 7 (51.0)       | 1.51 (1.12-1.50) | < 0.001 |                                  | < 0.001 |  |
| HCW from Bichat hospital               | 209 (87.8)   | 29 (12.2)      | 1 (ref.)         | < 0.001 | 1 (ref.)                         | < 0.001 |  |
| •                                      |              |                |                  |         | · · ·                            |         |  |
| HCW from other hospital or care center | 58 (69)      | 26 (31)        | 3.16 (2.88-6.1)  | 0.07    | 2.89 (1.64-5.1)                  |         |  |
| Contact HIV status                     | 1 ( 2 (05 2) | 20(147)        | 1 ( ()           | 0.07    |                                  |         |  |
| Negative                               | 163 (85.3)   | 28 (14.7)      | 1 (ref.)         |         |                                  |         |  |
| Unknown                                | 71 (82.6)    | 15 (17.4)      | 1.42 (1.15-1.68) |         |                                  |         |  |
| Positive                               | 33 (73.3)    | 12 (27.7)      | 2 (1.32-2.63)    |         |                                  |         |  |
| PEP prescription                       | 41 (69.5)    | 18 (30.5)      | 2.23 (1.79-2.76) | < 0.001 | 1.96 (1.57-2.44)                 | < 0.001 |  |
| Other occupational                     |              |                |                  |         |                                  |         |  |
| Gender (Male)                          | 57 (65.5)    | 30 (34.5)      | 0.54 (0.4-0.8)   | 0.1     |                                  |         |  |
| Type of day (Weekend-day)              | 31 (72.1)    | 12 (27.9)      | 0.47 (0.21-1.4)  | 0.05    |                                  |         |  |
| Time of ED arrival                     |              |                |                  | 0.02    |                                  |         |  |
| 8 am to 7 pm                           | 43 (51.2)    | 39 (48.8)      | 1 (ref.)         |         |                                  |         |  |
| 8 pm to midnight                       | 20 (66.7)    | 9 (33.3)       | 0.4 (0.32-0.56)  |         |                                  |         |  |
| Midnight to 7 am                       | 18 (90)      | 5 (10)         | 0.16 (0.1-0.31)  |         |                                  |         |  |
| Risk of HIV transmission               |              |                |                  | 0.01    |                                  |         |  |
| Low                                    | 29 (58)      | 21 (42)        | 1 (ref.)         |         |                                  |         |  |
| Intermediate                           | 3 (60)       | 2 (40)         | 0.49 (0.38-0.68) |         |                                  |         |  |
| High                                   | 31 (77.5)    | 9 (22.5)       | 0.24 (0.14-0.47) |         |                                  |         |  |
| Professional category                  |              |                |                  | 0.6     |                                  |         |  |
| Policeman-Fireman                      | 27 (52.9)    | 24 (47.1)      | 1 (ref.)         |         |                                  |         |  |
| Other                                  | 18 (47.4)    | 20 (52.6)      | 1.09 (0.99-1.19) |         |                                  |         |  |
| Contact HIV status                     |              | ( )            | · · · · ·        | 0.6     |                                  |         |  |
| Negative                               | 13 (57.6)    | 3 (42.4)       | 1 (ref.)         |         |                                  |         |  |
| Unknown                                | 11 (57.9)    | 8 (42.1)       | 1.09 (0.98-1.2)  |         |                                  |         |  |
| Positive                               | 57 (57.6)    | 42 (42.4)      | 1.16 (1.1-1.26)  |         |                                  |         |  |
| PEP prescription                       | 16 (76.2)    | 5 (23.8)       | 0.42 (0.14-1.24) | 0.1     |                                  |         |  |
| exual                                  | 10 (70.2)    | 5 (25.0)       | 0.42 (0.14-1.24) | 0.1     |                                  |         |  |
| Gender (Male)                          | 225 (27.2)   | 602 (72.8)     | 0.54 (0.36-0.81) | 0.003   |                                  |         |  |
| Type of day (weekend-day)              | 92 (25.1)    |                | · · ·            | 0.005   |                                  |         |  |
|  | 92 (23.1)    | 274 (74.9)     | 1.00 (0.77-1.32) |         |                                  | < 0.001 |  |
| Time of ED arrival                     | 65 (11 0)    | 100 /00 1)     | 1 (rof)          | < 0.001 | 1 (rof)                          | < 0.001 |  |
| 8 am to 7 pm                           | 65 (11.9)    | 482 (88.1)     | 1 (ref.)         |         | 1 (ref.)                         |         |  |
| 8 pm to midnight                       | 88 (30.9)    | 197 (69.1)     | 0.33 (0.28-0.38) |         | 0.32 (0.31-0.38)                 |         |  |
| Midnight to 7 am                       | 104 (55.6)   | 83 (44.4)      | 0.11 (0.09-0.14) | 0.00    | 0.1 (0.09-0.14)                  |         |  |
| Risk of HIV transmission               |              |                |                  | 0.02    |                                  |         |  |
| Intermediate                           | 181 (23.6)   | 586 (76.4)     | 1 (ref.)         |         |                                  |         |  |
| High                                   | 76 (31.2)    | 168 (68.8)     | 0.68 (0.5-0.94)  |         |                                  |         |  |
| MSM                                    |              |                |                  | < 0.001 |                                  | < 0.001 |  |
| No                                     | 106 (41.4)   | 150 (58.6)     | 1 (ref.)         |         | 1 (ref.)                         |         |  |
| Yes                                    | 438 (57.7)   | 321 (42.3)     | 0.52 (0.39-0.69) |         | 0.48 (0.36-0.66)                 |         |  |
| Contact HIV status                     |              |                |                  | 0.4     |                                  |         |  |
| Negative                               | 201 (24.6)   | 615 (75.4)     | 1 (ref.)         |         |                                  |         |  |
| Unknown                                | 27 (27.3)    | 72 (72.7)      | 0.92 (0.83-1.02) |         |                                  |         |  |
| Positive                               | 29 (27.9)    | 75 (72.1)      | 0.84 (0.69-1.05) |         |                                  |         |  |
| PEP prescription (yes)                 | 203 (27.5)   | 534 (72.5)     | 0.62 (0.44-0.87) | 0.005   |                                  |         |  |

ED: emergency department; HCW: healthcare workers; MSM: men having sex with men; PEP: post-exposure prophylaxis.

|                                 | Logistic regression       |                           |                  |         |  |  |  |
|---------------------------------|---------------------------|---------------------------|------------------|---------|--|--|--|
|                                 | < <b>4 hours</b><br>n (%) | ≥ <b>4 hours</b><br>n (%) | OR (IC 95%)      | Р       |  |  |  |
| Ocupational exposures (n = 222) |                           |                           |                  |         |  |  |  |
| Knowledge of the PEP plan (yes) | 93 (89.4)                 | 11 (10.6)                 | 0.06 (0.03-0.13) | < 0.001 |  |  |  |
| Previous use PEP (yes)          | 19 (65.5)                 | 10 (34.5)                 | 0.76 (0.33-1.73) | 0.5     |  |  |  |
| Alcohol (yes)                   | 24 (58.5)                 | 17 (41.5)                 | 1.07 (0.54-2.14) | 0.8     |  |  |  |
| Drugs (yes)                     | 2 (10.5)                  | 17 (89.5)                 | 2.69 (1.79-4.03) | < 0.001 |  |  |  |
| Chemsex (yes)                   | 0                         | 0                         | ND               | ND      |  |  |  |
| Sexual exposure (n = 376)       |                           |                           |                  |         |  |  |  |
| Total                           |                           |                           |                  |         |  |  |  |
| Knowledge of the PEP plan (yes) | 100 (40.8)                | 145 (59.2)                | 0.53 (0.33-0.82) | < 0.001 |  |  |  |
| Uso previo de PEP (yes)         | 53 (58.9)                 | 37 (41.1)                 | 0.28 (0.17-0.46) | < 0.001 |  |  |  |
| Alcohol (yes)                   | 43 (31.6)                 | 93 (68.4)                 | 1.34 (0.82-2.1)  | 0.2     |  |  |  |
| Drugs (yes)                     | 39 (30.0)                 | 91 (70.0)                 | 1.66 (1.05-2.61) | 0.03    |  |  |  |
| Chemsex (yes)                   | 21 (21.4)                 | 77 (78.6)                 | 2.55 (1.48-4.37) | < 0.001 |  |  |  |
| Heterosexual                    |                           |                           |                  |         |  |  |  |
| Knowledge of the PEP plan (yes) | 22 (53.7)                 | 19 (46.3)                 | 0.31 (0.14-0.67) | 0.003   |  |  |  |
| Previous use PEP (yes)          | 9 (69.2)                  | 4 (30.8)                  | 0.2 (0.06-0.69)  | 0.01    |  |  |  |
| Alcohol (yes)                   | 7 (18.4)                  | 31 (81.6)                 | 3.1 (1.22-7.68)  | 0.02    |  |  |  |
| Drugs (yes)                     | 9 (19.1)                  | 38 (80.9)                 | 3.15 (1.35-7.34) | 0.007   |  |  |  |
| Chemsex (yes)                   | 0 (0)                     | 6 (100)                   | NA               |         |  |  |  |
| HSH                             |                           |                           |                  |         |  |  |  |
| Knowledge of the PEP plan (yes) | 78 (38.2)                 | 126 (61.8)                | 0.62 (0.28-1.36) | 0.23    |  |  |  |
| Previous use PEP (yes)          | 44 (57.1)                 | 33 (42.9)                 | 0.27 (0.16-0.49) | < 0.001 |  |  |  |
| Alcohol (yes)                   | 36 (36.7)                 | 62 (63.3)                 | 0.99 (0.55-1.76) | 0.9     |  |  |  |
| Drugs (yes)                     | 30 (36.1)                 | 53 (63.9)                 | 1.03 (0.59-1.8)  | 0.9     |  |  |  |
| Chemsex (yes)                   | 21 (22.8)                 | 71 (77.2)                 | 2.8 (1.55-5)     | < 0.001 |  |  |  |

**Table 3.** Predictors of  $\geq$  4 hr interval between HIV exposure and ED arrival according to HIV exposure type in type based on the survey conducted at the follow-up visit

PEP: post-exposure prophylaxis.; HSH: men having sex with men; HIV: human immunodeficiency virus.

There was a delay  $\geq$  4 hr in 241/376 SEs (64.1%) and 89/22 OEs (40.1%) (p < 0.001). We also found the following regarding SEs and OEs respectively: 245/376 (65.2%) vs. 104/222 (46.9%) had knowledge of the PEP program (p < 0.001), 90/376 (23.9%) vs. 29/222 (13.1%) had previously used the PEP program (p = 0.001), 136/376 (36.2%) vs. 41/222 (18.5%) had used alcohol (p = 0.001), 136/376 (26.2%) vs. 19/222 (8.6%) had used drugs (p < 0.001), and 98/376 (26.1%) vs. 0/222 (0%) had used chemsex (p < 0.001).

The factors associated with a delay  $\ge 4$  hr among SEs, heterosexuals, MSMs, and occupational groups are presented in Table 3.

#### Discussion

The present study highlights the time delay between HIV exposure and ED arrival which was significantly longer in SEs than in OEs, including HCWs and some other exposed professionals. Similarly, our results indicate that some factors are associated with the delay, including HIV exposure and patient characteristics. Above all, we demonstrated that both knowledge of the PEP access program by those potentially exposed and some syndemic health conditions such as alcohol, drug, and chemsex consumption in the hours before potential HIV exposure are important predictors of the delay between HIV exposure and ED arrival. The delay between HIV exposure and administration of PEP should be as short as possible to guarantee the efficacy of PEP<sup>8-13</sup>. In France, a delay of less than 4 hr between HIV exposure to PEP assessment and administration is recommended<sup>8,14,15</sup>. We assessed the delay between HIV exposure and arrival at the ED to measure the delay in accessing the PEP program, which allows for the assessment of PEP indication and guarantees access to PEP antiretrovirals. Significant differences were found between the study groups in terms of the delays on admission to the ED. More than three quarters of HCWs were consulted within 4 hr; in contrast, this was true only in 46.3% and as low as 21.0% for sexual exposures. On the other hand, our results indicate that a delay exceeding 48hr was significantly more common in the sexual exposure group. In this case they could not benefit from PEP prescription according to French recommendations<sup>8</sup>. Given that the characteristics of HIV exposure were different depending on the exposure type group, and since each one has its own variables, we evaluated the factors associated with a delay  $\geq$  4 hr for each HIV exposure type. We found that among HCWs, some factors are associated with delays  $\geq 4$  hr, including the sex and the workplace of the exposed person. Furthermore, HCWs working within the BCB Hospital had shorter delays than HCWs working in other health facilities. This demonstrates HCWs' capacity to evaluate the risk of HIV transmission and the need to access the PEP program. In multivariate analysis, the workplace of the exposed person and PEP prescription remained significantly associated. Among OEs, and in univariate analysis, we identified that a delay  $\geq 4$  hr was significantly associated with some variables, including time of day, time of ED arrival, and risk of HIV transmission; however, multivariate analysis failed to determine the associated factors with a delay  $\geq 4$  hr. In this group, exposed individuals seem less able to assess the risk associated with their potential exposure to HIV. Our results highlight the need to train and educate these professionals. In the sexual group, some variables were associated with  $a \geq 4$  hr delay: female gender; arrival at ED in the daytime; lower risk exposures, including heterosexual exposures and unknown HIV status of the sexual partner; and PEP prescription. In multivariate analysis, the following predictors remained significant: arrival at ED in the daytime and heterosexual exposure.

We consider that these elements can reflect the importance of other unassessed factors in this first analysis. We hypothesized that not only knowledge of the PEP program but also some syndemic health conditions are part of those factors. We found that knowledge of the PEP program and its previous use has been more significant in the SE group than in the OE group. Furthermore, PEP program knowledge was found to be between 6% and 85% in HCWs<sup>19-21</sup> and between 22% and 30% in the general population<sup>14</sup>.The PEP program is known by 17% to 88% of people living with HIV and by between 17% and 88% of MSMs<sup>22-29</sup>.

We assessed the association between knowledge of the PEP plan and the optimal delay in access. In both types of exposure - sexual and occupational - knowledge of the PEP program was significantly associated with a shorter delay. Moreover, previous use of the PEP program was significantly associated with this delay only in the SE group. In the heterosexual and MSM subgroups, we found that knowledge of the PEP program was significantly higher in the MSM subgroup, indicating that MSMs have more knowledge of the program and that up to a third of them have already resorted to using it. On the other hand, in the heterosexual subgroup, knowledge of the PEP program and previous PEP program utilization were associated with shorter delays, whereas in MSMs, only previous use of the PEP program has been significantly associated with shorter delays. Our results suggest that knowledge of the program and the ability to plan how to access it are major determinants of rapid program access in all types of HIV exposure.

Furthermore, it has been reported that personal factors such as difficulty or shame in approaching sexuality, constraints in accessing the PEP plan, and even the attitude of caregivers may be limits to the use of the PEP plan<sup>30,31</sup> and that some syndemic health conditions have been associated with increased risk of HIV exposure<sup>18</sup>. In addition, alcohol, drug, and chemsex consumption during the 24 hr before the occurrence of the potentially high HIV exposure was significantly higher in the SE group than in the OE group. Moreover, we found that alcohol consumption and chemsex were higher in MSMs than in heterosexuals<sup>32,33</sup>. which is probably related to a festive use of these drugs<sup>34</sup>. In SEs, drug consumption and chemsex were significantly associated with a delay  $\ge 4$  hr, whereas in OEs, only drug use was associated with a  $\ge 4$  hr delay. Furthermore, in heterosexuals, consumption of alcohol, drugs, and probably also chemsex were associated with longer delays, whereas in MSMs, only chemsex consumption was significantly associated with delays greater than 4 hr. Our results highlight the role of chemsex in MSMs as an explanatory factor for a delay in accessing the PEP program, even though this population has the highest knowledge and prior use of the PEP program, and it is the population with the highest risk of seroconversion to HIV.

The present study has some limitations. First, this is a monocentric study in an academic hospital in the capital. Access to its ED is easy 24 hr a day. This may not be the case in other hospitals where patients have to travel long distances and where transport, especially at night, is less frequent, which could lead them to delay their consultation until the following day. Moreover, patients completed the survey on a voluntary basis in the HIV clinic within 72 hr after accessing the ED. However, 34.7% of patients did not come to the consultation and could not be interviewed, which may represent a bias.

In conclusion, the present study indicates that respect of the ideal consultation time for assessment and access to PEP depends on the level of knowledge and training not only of the persons concerned - both the heterosexual population and MSMs – but also health professionals and other professionals potentially exposed to HIV. This has motivated us to set up and strengthen information campaigns regarding the PEP program for the general population as well as for health professionals and other professionals at risk of HIV exposure. Moreover, our work suggests that other factors must be involved in both the decision and the time of the decision, and the delay between HIV exposure and ED arrival time being longer for sexual than for occupational exposures. Finally, we found that some syndemic clinical conditions such as alcohol, drugs, and chemsex are factors in the delayed decision to opt for PEP, notably chemsex for MSMs.

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