

Efficiency and relevance of post-exposure prophylaxis prescription by emergency physicians: a monocentric retrospective study

Xavier Eyer MD, MSc^{1,2}, Youri Yordanoff MD, PhD^{3,4}, Dominique Pateron MD, PhD^{3,4}, Patrick Plaisance MD, PhD^{1,2}, Anthony Chauvin, MD, PhD^{1,2}

1 Emergency Department, Lariboisière Hospital, Assistance des Hôpitaux de Paris – Nord, Paris Cité University, Paris, France

2 Paris Cité University, Paris, France

3 Emergency Department, Saint-Antoine Hospital, Assistance Publique-Hôpitaux de Paris, Sorbonne University, Paris, France

4 Sorbonne Université, Paris, France

Corresponding Author:

Xavier Eyer MD, MSc

Emergency Department, Lariboisière Hospital, Assistance des Hôpitaux de Paris – Nord, Paris Cité University, Paris, France

Telephone: 0033 (0)149956169 - Email: xavier.eyer@aphp.fr

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ABSTRACT

Background:

Preventing infection with HIV remains a major public health challenge. Exposed persons are offered support and quick access to the post-exposure prophylaxis (PEP) by hospital emergency services. This study aimed to investigate the accuracy of the prescription of emergency PEP for patients with sexual fluid exposure in a French emergency department (ED) by comparing data in medical files and actual prescriptions.

Methods:

We retrospectively collected data for patients consulting for sexual exposure in a single Parisian ED from 2015 to 2016. For each patient, researchers independently checked whether the emergency physician prescribed PEP according to French guidelines. Our primary outcome was the appropriateness of the emergency PEP prescription after sexual fluid exposure. We calculated the Cohen weighted kappa coefficient with its 95% confidence interval (CI) for determining the agreement in indication for PEP.

Results:

We included 346 patients in the analysis. Half of the patients were men who had sex with men (n=178). The most frequent sexual exposure was anal insertive or receptive (n=177; 51%). PEP was prescribed in 94% of cases (n=328). In 33 cases (10%) the indication for PEP was not clear, but PEP was prescribed in 17 cases (52%). The Kappa value for determining the indication for PEP was 0.55 (95% confidence interval 0.36-0.74), indicating poor agreement for prescription. The agreement was lowest for men who had sex with men: 0.29 (0.05-0.53).

Conclusion:

Strategies are needed to improve the relevance of the prescription of PEP in French EDs to avoid the excess secondary effects and cost.

Keywords: Sexual exposure; emergency medicine; post exposure prophylaxis

Introduction

Preventing infection with HIV type 1 (HIV-1) and 2 (HIV-2) remains a major public health challenge. [1] Emergency post-exposure prophylaxis (PEP) is an antiretroviral therapy for people exposed to risk of HIV transmission. PEP should be taken as soon as possible and at the latest, within 48 hrs of exposure. [2] Exposed persons are offered support and quick access to the PEP by hospital emergency services as exposure to HIV (occupational and non-occupational), is frequently managed in hospital emergency departments (EDs). [3,4] Guidelines for initiating PEP in EDs are regularly updated. [5] The recommendations in France do not differ from those for US, United Kingdom or Italy in terms of risk stratification, the PEP indication primarily is relying on the description of the source partner. [6-8]

Since 2011, the number of new cases of HIV diagnosed in France has been stable, about 6.000 per year. [9] Although PEP has real clinical impact, its use has some secondary effects (i.e., liver toxicity, hypersensitivity reactions). [10,11] As well, in France, the cost of one PEP kit is 800 to 1,000 Euros and completely financed by public funds. Despite the important role of EDs in quelling the HIV epidemic, studies of emergency-physician prescribing practices is limited. [12,13]

To our knowledge no study has investigated emergency-physician practices in prescribing PEP in France. We hypothesized that emergency physicians over-evaluate the risk of transmission of HIV after non-occupational body fluid exposure and therefore over-prescribe emergency PEP. Our aim was to describe emergency PEP prescription after body fluid exposure (mainly sexual) in a single emergency department.

METHODS

Study design and setting

We performed a retrospective study, from January 1, 2015 to December 31, 2016 in a single ED in Paris, France. The ED where the study was led is part of a teaching hospital and receives 90,000 yearly visits. In 2011, the incidence of HIV in Paris and its suburbs was 39/100.000, higher than that in France. [14] In France, patients who consult in an ED for non-occupational body fluid exposure are assessed by emergency physicians and are prescribed PEP according to the French guidelines. [15] When indicated, the emergency physician prescribes emergency PEP for 5 days, blood

tests during the consultation are not recommended. Each patient will then be referred for specific infectious diseases consultation (Centre Diagnostic Anonyme et Gratuit) at the end of the 5-day course. There, an infectious-disease specialist evaluates the need to continue the treatment for 28 days and performs blood tests, including HIV-1 and -2, hepatitis B and C virus and syphilis.

Selection of participants

In the evaluated ED, each patient who consults has an electronic medical record. Before discharge, each physician will complete the file and select a discharge diagnosis from a list based on the International Classification of Diseases codes. All pathologies for blood or body fluid exposure are classified under the same code: Z20.9 "subjects exposed to communicable disease without precision". For the study period, we collected data from charts with a discharge diagnosis of blood or body fluid exposure. [16] We included patients ≥ 18 years old, consulting in the ED for non-occupational HIV exposure (sexual exposure). Therefore, the non-inclusion criteria were age < 18 years, patient left without being seen, patient known to have HIV infection, consultation not related to HIV exposure, patient direct discharge to the infectious disease consultation, and occupational exposure.

Outcomes measures

Our primary outcome was the appropriateness of the emergency PEP prescription after sexual fluid exposure. For each patient, we evaluated the appropriateness of the prescription by comparing the emergency physician's decision, or not, to prescribe PEP according to the French PEP national guidelines. When the medical file was incomplete to allow judgment, we decided a priori to consider that PEP was indicated. Secondary outcome was to assess factors associated with non-respect of post-exposure prophylaxis (PEP) recommendations.

Patients and sexual fluid exposure characteristics

Two researchers (XE and AC) independently extracted the following data from the ED electronic medical record using a standardized form: 1) patient demographics data (age and sex); 2) consultation details (day of consultation, period of consultation

[night shift: from 22:00 to 8:00 and day shift from 8:00 to 22:00] and length of stay); 3) details related to the potential HIV exposure; and 4) If PEP was prescribed by the physician. For characterized sexual fluid exposure, researchers collected 1) the sexual practice (heterosexual, men who had sex with men [MSM], multiple partners); 2) risk of hemorrhage (anal, vaginal or buccal); and 3) if known, the HIV status of the patients' partner.

For each included patient, the researchers independently checked whether the emergency physician prescribed PEP according to French guidelines (PEP prescription was recommended, to be considered in view of file data, or not recommended) (Table 1). When assessments differed, the item was discussed until consensus was reached. When needed, a third reviewer assessed the report to achieve consensus.

Table 1: French guidelines for prescription of PEP in emergency Department

	Source person's HIV status			
	Positive	Unknown		
Risk and nature of the exhibition	Detectable viral load	Viral load <50 copies/ml	Group with prevalence high*	Group with prevalence low or unknown
<i>Insertive anal</i>	PEP recommended	PEP not recommended	PEP recommended	PEP not recommended
<i>Receptive anal</i>	PEP recommended	PEP not recommended	PEP recommended	PEP not recommended
<i>Vaginal receptive</i>	PEP recommended	PEP not recommended	PEP recommended	PEP not recommended
Vaginal insertive	PEP recommended	PEP not recommended	PEP recommended	PEP not recommended
<i>Oral receptive with ejaculation</i>	PEP recommended	PEP not recommended	PEP recommended	PEP not recommended
<i>Oral receptive without ejaculation or insertive</i>	PEP not recommended	PEP not recommended	PEP not recommended	PEP not recommended

*High-prevalence group: multi-partner, men who had sex with men (MSM), sex workers, or person from a region with a prevalence of HIV >1% (Africa, Caribbean including French West Indies, South America including French Guiana, Asia), or injecting drug users.

Statistics

Statistical analysis involved use of SAS 9.3 (SAS Inst. Inc., Cary, NC). Data are described with mean (SD) for quantitative variables and number (%) for qualitative variables. We calculated the Cohen weighted kappa coefficient with its 95% confidence interval (CI) for determining the agreement in indication for PEP. A kappa of 1, 0.90–0.99, 0.80–0.89, 0.70–0.79, 0.60–0.69, and <0.60 is considered perfect, excellent, very good, good, moderate, and poor, respectively. [17] Moreover, we performed a multivariate analysis of factors associated with non-respect of PEP recommendations, estimating odds ratios and 95% CIs. The study was developed and results are reported according to the guidelines on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).[18]

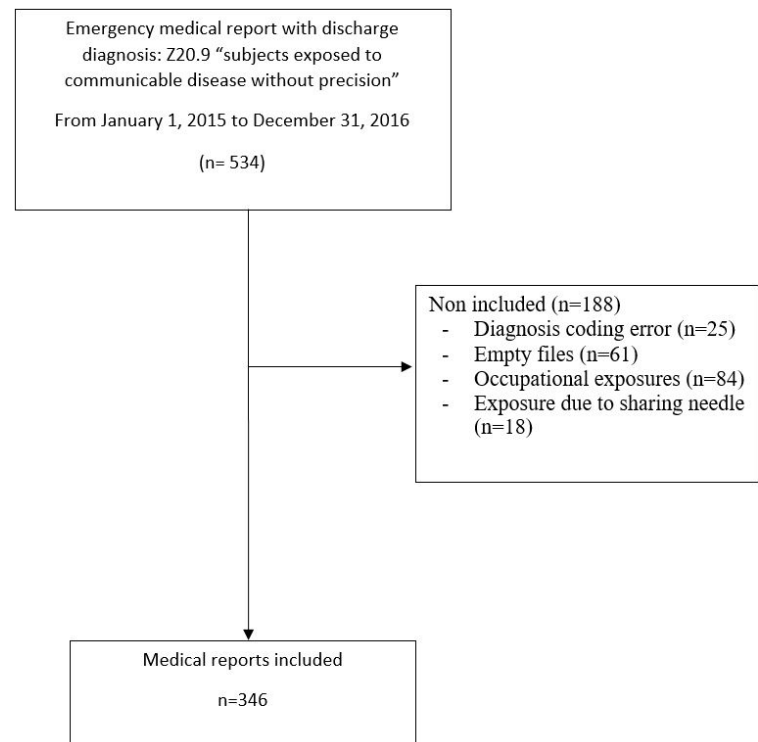
RESULTS

Demographic data

During the study 2-year period, we analyzed 534 consultations for exposure to communicable diseases. Two-thirds of the consultations were for sexual exposure (n=346) (Figure 1).

Most patients were male (n=293; 85%). The mean age was 32 years (SD 10). Sexual orientation for patients did not differ by age (Table 2).

Figure 1: Study flow chart



For 51% (n=178) of cases, the sexual orientation of patients was MSM or bisexual; for 34% (n=117), heterosexual men; and for 15% (n=51), heterosexual women. Most patients consulted during the day rather than during the night shift. Consultations did not differ between the week and weekend. The mean length of ED stay was 126 min (SD 95).

Table 2 : Characteristics of patients consulting hospital emergency departments because of sexual fluid exposure.

	All n(%)	Heterosexual men n(%)	Heterosexual women n(%)	MSM and bisexuals n(%)
Female	53 (15.3)		51 (14.7)	0 (0)
Male	293 (84.7)	117 (33.8)		178 (51.4)
Age (years), mean +/- SD	32.4 +/- 9.3	30.3 +/-9.4	30.4 +/- 8.1	34.1 +/-9.2
Night shift (20:00 to 8:00)	222 (64.2)	62 (17.9)	30 (8.7)	119 (34.4)
Consultation between 8:00 and 20:00	124 (35.8)	45 (13)	21 (6.1)	59 (17.1)
Length of stay (min), mean +/- SD	126 +/-95	124 +/-104	150 +/-106	121 +/-85
Consultation period				
Week	187 (54.1)	59 (14.4)	31 (9)	94 (24)
Weekend	159 (45.9)	58 (14.4)	20 (5.8)	84 (21)

MSM: men who had sex with men

Description of the sexual exposure and source of HIV

Almost all sexual exposures were with a single partner (n=338; 98%). The most frequent sexual exposures were vaginal insertive (n=103; 30%), receptive anal (n=95; 28%) and insertive anal (n=82; 24%) (Table 3). Half of the sexual exposures involved a torn condom (n=174; 50%). Half of the exposures were due to lack of a condom (n=165; 48%): 34 cases for heterosexual

men, 17 for heterosexual women and 67 for MSM or bisexuals. The male condom was the only kind of mechanical protection reported. Seven patients (2%) reported an intact condom and did not have risky sexual exposure. Eight exposures (2%) were in a context of sexual assault.

The positive HIV status was known for 10% (n=34) of source partners: 26 were MSM or bisexual, 5 heterosexual men and 2 heterosexual women. The viral load was reported detectable in 4 cases (12%) and unknown in 30 (88%).

Table 3 : Details of sexual exposure and source partner.

	All (n=346)	Heterosexual men (n=117)	Heterosexual women (n=51)	MSM and bisexual (n=178)
	n (%)	n (%)	n (%)	n (%)
Sexual exposure				
Insertive anal	82 (23.7)	12 (3.5)	0 (0)	70 (20.2)
Receptive anal	95 (27.8)	0 (0)	2 (0.6)	93 (26.9)
Vaginal insertive	103 (29.8)	101 (29.2)	0 (0)	2 (0.6)
Vaginal receptive	46 (13.3)	0 (0)	46 (13.3)	0 (0)
Oral insertive	20 (5.78)	4 (1.2)	3 (0.9)	13 (3.8)
Multiple partners	8 (2.3)	4 (1.2)	0 (0)	4 (1.2)
Mucosal risk factors	8 (2.3)	2 (0.6)	0 (0)	6 (1.7)
Sexual assault	8 (2.3)	1 (0.3)	7 (2.1)	0 (0)
Mechanical protection				
Intact condom	7 (2.1)	2 (0.6)	2 (0.6)	3 (0.9)
Torn condom	174 (50.3)	78 (22.5)	42 (12.1)	72 (2.8)
No condom	165 (47.7)	34 (9.8)	17 (4.9)	67 (19.4)
Source partner characteristics				
HIV status unknown or negative	312 (90.2)	95 (27.5)	49 (14.2)	130 (37.6)
HIV positive	34 (9.8)	5 (1.5)	2 (0.6)	26 (7.5)
Detectable viral load	4 (11.8)	0 (0)	0 (0)	4 (11.8)
High group risk	59 (17.1)	29 (8.4)	13 (3.7)	17 (4.9)
Multiple partners declared by source partner	47 (79.7)	18 (62.1)	11 (84.6)	14 (82.4)
High-prevalence country	6 (10.2)	5 (17.2)	0 (0)	1 (5.9)
Using intravenous drugs	1 (1.7)	0 (0)	0 (0)	1 (5.9)
Undefined risk factor	5 (8.5)	0 (0)	2 (15.4)	2 (11.8)

For 18% of cases (n=59), the source partner was in a high-risk group. The most frequent risk was multiple partners declared by the source partner. Most consulting patients could not say if the source partner had a risk factor (i.e., HIV positive, sharing a syringe, from a country with > 1% prevalence of HIV).

PEP prescription

PEP was prescribed for 328 cases (94%). In 33 cases (10%), the indication for prescription was clearly not recommended, but PEP was prescribed for 17 cases (52%). The only factor associated with the non-adherence to the guidelines was the description of anal sex (insertive or receptive) during the sexual exposure ($p < 0.01$) (Table 4).

For 79 cases (23%), the prescription was clearly recommended, and in all cases emergency physicians followed the recommendations. In 233 cases (67%), emergency physicians prescribed the PEP, but the medical files did not allow for concluding whether PEP was indicated or not. The most frequent missing data were the country origin of the patient, the HIV status and the use of intravenous drugs. Emergency physicians prescribed PEP in almost all of these cases (n=231; 99%).

The Kappa value for interobserver agreement for determining when PEP was indicated was 0.55 (95% CI 0.36-0.74), for poor agreement. The agreement was lowest for MSM patients: 0.29 (0.05-0.53). Table 5 presents the details of agreement.

Table 4: Factors associated with non-respect of post-exposure prophylaxis (PEP) recommendations.

Factors	Odds ratio	P value
MSM	0.32 (0.08;1.34)	NS
Torn condom	1 (0.2;4.38)	NS
Consulting during weekend	1 (0.25;3.93)	NS
Night shift	1.33 (0.33;5.42)	NS
Insertive or receptive anal	16.88 (1.8;158)	<0.01

Table 5: Description of the prescription of PEP and relevance of the prescription

	All (n=346)		Heterosexual men (n=117)		Heterosexual women (n=51)		MSM and bisexual (n=178)	
	Indication for PEP n (%)	Prescription of PEP n (%)	Indication for PEP n (%)	Prescription of PEP n (%)	Indication for PEP n (%)	Prescription of PEP n (%)	Indication for PEP n (%)	Prescription of PEP n (%)
Indication for PEP								
Clearly recommended	80 (23.1)	80 (100)	28 (23.9)	28 (100)	16 (31.4)	16 (100)	37 (20.8)	37 (100)
Questionable indication	233 (67.3)	231 (99)	76 (65)	75 (98.7)	30 (58.8)	29 (96.7)	127 (71.3)	120 (94.5)
Not recommended	33 (9.6)	17 (51.51)	13 (11.1)	6 (46.2)	5 (9.8)	1 (20)	14 (7.9)	9 (64.3)
Kappa (95% CI; p value)	0.55 (0.36-0.74;<0.01)		0.66 (0.41-91;<0.01)		0.73 (0.37-1;1)		0.29 (0.05-0.53;0.006)	

CI, confidence interval

DISCUSSION

Our objective was to investigate the efficiency and relevance of the prescription of emergency PEP with sexual fluid exposure in a French ED. The PEP prescription remains a problem in EDs and in particular when the patient consulting is a MSM or bisexual. In fact, in these cases, in our cohort, the accuracy of the prescription was poor.

Our study is the first to examine PEP prescription for emergency non-occupational blood exposure in France. A recent US study investigated care discrepancies between occupational exposure and non-occupational exposure in EDs.[19] The authors found that, emergency physicians failed to provide PEP in 27.5% of cases of high-risk non-occupational exposure and prescribed PEP correctly in 72.5% of cases (95% CI 66.8-77.5%). In 2008, Merchant et al., reported that PEP prescription after blood or body fluid exposure was low overall and varied by type of exposure.[20] Perhaps lack of knowledge of the indications for PEP by ED clinicians or lack of hospital protocols for PEP might explain the low prescription of PEP, especially after non-occupational exposure.

Our findings are partially in conflict with these studies. In fact, like them, we found that French emergency physicians were not efficient in PEP prescription. However, French emergency physicians seem to over- than under-prescribe PEP. In an emergency situation, with an anxious patient who had a sexual exposure, refusing PEP prescription could be difficult even if the exposure was safe (i.e., vaginal insertive practice without a condom with a source partner with negative rapid-HIV serology findings).

ED accessibility combined with the need to rapidly initiate PEP ensures that the ED is an important resource for patients after a sexual exposure. Information on physician decisions in the care of patients potentially exposed to HIV has been provided by physician surveys.[21] Among emergency physicians who care for patients after non-occupational exposure, only 15% recommended PEP after unsafe sexual practices and injection drug use.

The management of sexual exposure in EDs could be improved in several ways. First, the development of expert consultations could help emergency physicians decide to prescribe or not PEP. Indeed, a free phone consultation with an HIV expert has been developed, the Clinical Consultation Center (CCC).[22] This

service provides clinicians of all experience levels with prompt expert responses to questions about HIV testing and prevention, HIV treatment, HIV–hepatitis co-infection, pre-exposure prophylaxis, perinatal HIV, substance use management, and PEP. If needed, expert consultation is available through the national PEP hotline, at 888-448-4911. Second, as always, the education of emergency physicians needs to be the base. The creation of an emergency specialty in 2017 will be a good opportunity to improve knowledge of the management of fluid exposure.[23] With substantial effort to develop new strategies to prevent HIV infection, emergency physicians must know the molecules, indications and implications. In fact, the prevention strategy could be crucially changed with the development of pre-exposure prophylaxis in high-risk groups.[24] Use of one pill daily can prevent up to 92% of new infections; most recent data show a number needed to treat of 13 to prevent one HIV infection.[25,26] The US Food and Drug Administration has approved the prescription of pre-exposure prophylaxis by EDs. However, this treatment is associated with high rates of gastrointestinal and renal adverse events. So, it cannot be overprescribed by emergency physicians. Also, in contrast to other countries, the adherence and follow-up of patients with PEP in France has never been studied.

LIMITATIONS

There were limitations of this study. First limitation of our study is that it was retrospective. Thus, our results would require a prospective evaluation to confirm the results. Moreover, patient and/or physician interpretations of events leading to potential HIV transmission may be incompletely reported and conversations during consultation may have been inadequately documented. Some medical files did not have sufficient information to judge the appropriateness of care, which may have influenced results. The experience and pressure medical professionals face when patients present to the ED plays an important role in the decision to prescribe or not PEP to such patients. As our study was a monocentric evaluation, these findings may not be generalizable, even in a French setting since the reality in different hospitals is different and the available resources and manpower are different. Finally, a follow up on the outcomes and the results of the patients who received PEP would have been interesting, to see if the Emergency physician made the right judgment call at the time.

CONCLUSIONS

This study showed that emergency physicians in France over-prescribe PEP, which exposes patients to risk of adverse events, and society to economic consequences. EDs must develop new strategies to respect guidelines on its prescription.

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Conflict of interests

The authors declare no conflicts of interest.

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