Published in final edited form as:

AIDS Behav. 2020 November ; 24(11): 3124–3131. doi:10.1007/s10461-020-02866-6.

HIV post-exposure prophylaxis (PEP) awareness and non-occupational PEP (nPEP) prescribing history among U.S. healthcare providers

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Abstract

Non-occupational post-exposure prophylaxis (nPEP) has been clinically recommended since 2005. HIV providers and non-HIV providers ($n = 480$) practicing within above-average HIV prevalence ZIP codes of the 10 U.S. cities with greatest overall HIV prevalence participated in a cross-sectional survey between July 2014 and May 2015. Providers were asked about their awareness of post-exposure prophylaxis (PEP) and nPEP prescribing experience for patients with potential sexual exposures to HIV, which we coded into a PEP prescribing cascade with three categories: 1) PEP unaware, 2) PEP aware, no nPEP prescribing experience, and 3) nPEP prescribing experience. Overall, 12.5% were unaware of PEP, 43.5% were aware but hadn't prescribed nPEP, and 44.0% had prescribed nPEP for potential sexual exposures to HIV. Fewer providers practicing in the U.S. South had ever prescribed nPEP compared to providers in other regions ($\chi^2=39.91$, $p<0.001$). HIV providers, compared to non-HIV providers, were more likely to be classified in the nPEP prescription group compared to the PEP aware without nPEP prescription group ($RRR=2.96$, $p<0.001$). PrEP prescribers, compared to those PrEP unaware, were more likely to be classified in the nPEP prescription group compared to PEP aware without nPEP prescription group ($RRR=12.49$, $p<0.001$).

Keywords

HIV; post-exposure prophylaxis; pre-exposure prophylaxis; providers; prescription

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Conflict of Interest: AEP receives research funding from Gilead Sciences, Inc. All other authors declare that they have no conflict of interest.

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

INTRODUCTION

The HIV epidemic continues in the United States (US), with nearly 40,000 new infections diagnosed each year (1). On February 5th, 2019, the US announced a plan to *End the HIV Epidemic* (2), which called for a greater focus on expanding the availability of biomedical interventions. These include treatment as prevention (TasP), pre-exposure prophylaxis (PrEP), and post-exposure prophylaxis (PEP). PrEP reduces the risk of HIV acquisition when taken before and after potential exposure through once-daily and on-demand (e.g., “2-1-1”) dosing schedules (3–11), whereas TasP is a strategy of linking individuals living with HIV to treatment and reducing their viral load to undetectable levels, which eliminates the risk of sexual HIV transmission (12–15). Although more recent attention has been placed on TasP and PrEP (3–8, 12–15), non-occupational post-exposure prophylaxis (nPEP) is a highly effective method of secondary HIV prevention (16–22), has been clinically recommend by the Centers for Disease Control and Prevention (CDC) since 2005 (23), and is endorsed by the World Health Organization to help curb the HIV epidemic worldwide (24). nPEP involves taking a 28-day course of a three- or four-drug regimen of HIV antiretrovirals as soon as possible—and within 72 hours—after an exposure or potential exposure to HIV (25, 26).

Promoting PrEP for HIV prevention is an ideal primary prevention approach, but exposure to HIV or engagement in condomless sexual behavior with HIV-positive or unknown status partners is not always anticipated. Engagement in condomless sexual behavior may be infrequent or sporadic—a known barrier to PrEP uptake and persistence (27–29)—and even individuals prescribed PrEP can have lapses in adherence that result in a recommended course of nPEP antiretrovirals prior to reinitiating PrEP (25). Thus, there is need to make all of the currently known biomedical HIV prevention approaches—including PrEP and nPEP, as well as TasP for those diagnosed with HIV—widely available to end the HIV epidemic in the US.

Expanding the availability of biomedical HIV prevention interventions will require healthcare providers to participate in the initiative by prescribing PrEP and nPEP. Prior evidence has found many healthcare providers are unaware of interventions such as PrEP and lack the knowledge and skills required to prescribe it (30–42), but knowledge of PrEP has increased slowly after continued clinical trial data and publication of the CDC guidelines (43, 44). In contrast, nPEP has been recommended since 2005, and little is known about healthcare providers’ nPEP prescribing history nearly a decade after these guidelines were published. Given the utility of the previously developed PrEP prescribing cascade (41), we aimed to develop a PEP prescribing cascade for nPEP prescription after patients’ potential sexual exposures to HIV to advance a portfolio of biomedical HIV prevention strategies as the US aims to end the HIV epidemic. A PEP prescribing cascade could be particularly useful in intervention planning given suboptimal rates of nPEP knowledge and prescription reported in previous studies with samples of providers practicing in the US South (45, 46). In this study, we sought to determine PEP awareness and nPEP prescribing history among HIV providers and non-HIV providers practicing in all four major regions of the US.

METHODS

As described previously (41, 42), an online survey of HIV providers and non-HIV providers was conducted between July 2014 and May 2015. We recruited providers practicing in the 10 US cities with greatest HIV prevalence—further restricted to ZIP codes within these cities where HIV prevalence was at least 0.5% (1)—through national databases from professional organizations. To be eligible, providers had to: (1) be working at least 4 hours per week in an outpatient setting; (2) have patients ages 13–64 years in their practice; and (3) describe their practice specialty as Family Medicine, Internal Medicine (IM), IM/Pediatrics, Obstetrics/Gynecology, Infectious Diseases, or HIV Medicine. Of the estimated 2,088 providers invited to participate in the study, 525 enrolled and 480 provided full data used for analysis. Participation was incentivized with a \$100 honorarium. All study procedures were approved by the Institutional Review Board of the Medical College of Wisconsin.

Measures

Demographics and professional characteristics.—We asked respondents to report their age, gender, and race/ethnicity. Providers were also asked to report their location of practice by postal ZIP code, professional position (physician, nurse practitioner, or physician's assistant), and practice type (private hospital or clinic or public/other settings). Individuals were coded as an HIV provider if they provided HIV-related care to patients living with HIV, regardless of professional or specialty training, with the remaining providers considered non-HIV providers.

PrEP awareness and prescribing experience.—Providers were asked about their PrEP awareness and prescribing history, which we coded into a 3-category PrEP awareness and prescribing experience variable: 1) PrEP unaware, 2) PrEP aware, no prescribing experience, and 3) PrEP prescribing experience. Specifically, we determined PrEP awareness by asking: “Are you aware of the concept of HIV PrEP (pre-exposure prophylaxis), which is prescribing regularly-scheduled HIV medications to HIV-uninfected individuals to help prevent them from getting HIV?” with yes/no response categories. PrEP prescribing experience was determined by asking the following: “Have you ever prescribed PrEP?” with yes/no response categories.

PEP awareness and nPEP prescribing experience.—Providers were asked about their PEP awareness and nPEP prescribing experience for patients with potential sex-related HIV exposures, which we coded into the PEP prescribing cascade with three categories: 1) PEP unaware, 2) PEP aware, no nPEP prescribing experience, and 3) nPEP prescribing experience. Specifically, providers were given the following description of PEP: “The following questions are about HIV post-exposure prophylaxis, or PEP. PEP is the practice of giving an individual antiretroviral medications immediately after that individual has had a potential exposure to HIV, for a period of 28 days. This is commonly done in healthcare settings following a needlestick injury to a healthcare worker. However, PEP can also be prescribed to individuals who have had potential sexual exposures or injection-related exposures to HIV.” Providers were then asked about PEP awareness: “Were you previously

aware of the practice of HIV PEP (before reading the definition above)?" with yes/no response categories. nPEP prescribing experience for sex-related HIV exposures was ascertained with the following question: "Have you ever prescribed PEP to a patient following a (potential) sexual exposure to HIV?" with yes/no response categories.

Data Analysis

Descriptive data were assessed using frequency measures. Bivariate analyses were conducted using χ^2 comparisons and analysis of variance (ANOVA) for categorical and continuous independent variables, respectively. We examined associations between providers' demographics, US region of practice, provider type, professional position, clinic/hospital type, and PrEP awareness and prescribing experience and their location on the PEP prescribing cascade using fully-adjusted multinomial logistic regression.

RESULTS

A total of 480 providers completed the survey and were included in this analysis (see Table 1). Roughly half (52.7%) of participants were cisgender men and 54.6% were White. Mean age of the sample was 50 years old. Geographical representation was diverse, with greater than 35 respondents practicing in each of the 10 US cities with greatest HIV prevalence: Atlanta, Chicago, Dallas, Houston, Los Angeles, New York City, Miami, Philadelphia, San Francisco, and Washington DC; 41.7% of providers practiced in the South. About half (53.1%) were considered non-HIV providers, with the remaining considered HIV providers. Most (85.2%) were physicians, and nearly half (48.8%) practiced within a private hospital or clinic. Among all providers, 87.5% were aware of PEP and 44.0% had ever prescribed nPEP for potential sexual exposures to HIV. The PEP prescribing cascade is illustrated in Figure 1, stratified by provider type.

Providers were classified into three groups for analysis; 12.5% ($n = 60$) were unaware of PEP, 43.5% ($n = 209$) were aware of PEP but hadn't prescribed nPEP for potential sexual exposures to HIV, and 44.0% ($n = 211$) had prescribed nPEP for potential sexual exposures to HIV. In bivariate analyses (see Table 1), differences in location on the PEP prescribing cascade were found by providers' race/ethnicity and practice type, with a greater percentage of White and Black providers classified in the nPEP-experienced group, as well as a greater percentage of providers working within public hospitals, clinics, AIDS service and other organizations in the nPEP-experienced group. nPEP prescribing experience differed by US region; 34% of providers practicing in the South were classified in the nPEP-experienced group. In contrast, 40.0% of providers in the Midwest, 48.6% in the Northeast, and 58.6% in the West were classified in the nPEP-experienced group. Lastly, providers who had prescribed PrEP were more likely to be in the nPEP-experienced group—77.4% of providers who had prescribed PrEP had also prescribed nPEP for potential sexual exposures to HIV.

We present findings of our fully-adjusted multinomial regression (see Table 2) in stepwise progression through the PEP cascade. Compared to those classified in the PEP-aware with no nPEP prescribing experience group, providers classified in the PEP-unaware group were more likely to be Asian (as compared to White; relative risk ratio [RRR] = 4.19, $p < 0.01$) and nurse practitioners (as compared to physicians; $RRR = 4.68$, $p < 0.05$). Compared to

providers practicing in the South, those practicing in the Northeast, Midwest, and West were less likely to be in the PEP-unaware group compared to PEP-aware without nPEP prescribing experience ($RRRs = 0.13\text{--}0.31$, $p\text{-values} < 0.05$).

Among providers aware of PEP, HIV providers (compared to non-HIV providers) were more likely to be classified in the nPEP-experienced group ($RRR = 2.96$, $p < 0.001$). PrEP prescribers (compared to those PrEP unaware) were also more likely to be classified in the nPEP-experienced group compared to PEP-aware without nPEP prescription group ($RRR = 12.49$, $p < 0.001$).

DISCUSSION

The primary aims of this study were to determine PEP awareness and nPEP prescribing history for potential sexual exposures to HIV among HIV providers and non-HIV providers practicing within above-average HIV prevalence ZIP codes of the 10 U.S. cities with greatest overall HIV prevalence to identify potential areas for intervention as the US aims to expand nPEP and other biomedical HIV prevention interventions. In our sample, PEP awareness was high overall, but a large drop-off was evident between PEP awareness and nPEP prescription for potential sexual exposures to HIV, suggesting the need for greater training to help providers implement biomedical HIV prevention into their care delivery. The drop-off between PEP awareness and prescription of nPEP was more severe among non-HIV providers compared to HIV providers, which may indicate the need for greater training and resources for this group of providers, especially given that general providers are much greater in number in the US than HIV specialists (approximately 288,000 vs. 5,000), and therefore more accessible to patients who need such HIV prevention services (47, 48).

Histories of nPEP and PrEP prescription were similar in our sample. Most providers who prescribed PrEP had also prescribed nPEP, but 19.4% of providers ($n = 93$) had only engaged in prescribing one—not both—of these biomedical HIV prevention interventions. A greater number of providers had prescribed nPEP but not PrEP (12.1%) compared to vice versa (7.3%). These findings identify missed opportunities to implement nPEP and PrEP jointly into clinical practice. Many patients who present for nPEP are good candidates for PrEP and should be screened and followed up with accordingly, particularly because some patients who initiate nPEP become recurrent users of it (49). Moreover, providers should be prepared to recommend a course of nPEP for PrEP patients who experience lapses in adherence around potential HIV exposure events. Interventionists could capitalize on providers' experiences prescribing one of these interventions to support dual implementation, particularly if providers are trained to recommend PrEP to individuals after a course of nPEP antiretrovirals (50), as recommended in the revised CDC nPEP clinical guidelines (25).

Our findings related to nPEP are similar to our initial reports from this study regarding PrEP. We found only 64% of HIV providers and 17% of non-HIV providers had prescribed PrEP, despite high awareness overall (41). Moreover, our prior work focused on constructs of the information-motivation-behavioral skills model (51) found that providers would potentially benefit from greater knowledge of PrEP, increasing positive attitudes about PrEP, and

increasing their confidence or self-efficacy to prescribe PrEP (42). It is plausible that these same theoretical constructs may influence nPEP prescribing, but further research is needed to identify similar and unique barriers to nPEP prescribing, including the potential for a PEP purview paradox analogous to the now diminishing PrEP purview paradox (52, 53). Targeting theoretical constructs to support nPEP prescribing practices could be an opportunity to support nPEP implementation, particularly if interventions aim to jointly increase PrEP and nPEP prescribing practices. Nonetheless, we anticipate providers will have greater control to increase PrEP prescribing practices because many more patients could be prescribed PrEP in general practice compared to nPEP, given the short timeframe from potential HIV exposure required to initiate nPEP (i.e., past 72 hours). However, increasing nPEP availability by advertising nPEP and PrEP jointly with immediate appointment flexibility for patients would be a pertinent approach to making nPEP more accessible to those in need.

More universal training is needed nationwide across professional positions but especially among providers practicing in the US South or within private clinical settings. In particular, we found many more providers classified in the non-nPEP prescription groups who practiced in the South, which aligns with the PrEP-to-need ratio (i.e., the number of PrEP prescriptions per HIV infection reported) findings that identified a greater need for biomedical HIV prevention implementation scale-up in areas of the South because of greater HIV incidence (54). Further outreach and training is also needed across professional positions due to the current shortages and worsening outlook of the number of physicians practicing in primary care (55), but additional research is needed with non-physician providers because of the rather limited number of nurse practitioners and physician assistants included in our study, as well as in the literature more broadly.

Our research extends prior evidence reported from other samples of healthcare providers residing in the Southern US. Most notably, fewer than half of primary care providers practicing in six Southern US cities stated they had a ‘good’ understanding nPEP, and 70% had never prescribed nPEP to a patient (45). Our findings are also similar to another study which found suboptimal nPEP implementation in Washington, DC and Miami. In this study, the largest determinants of nPEP prescription were patients requesting nPEP and whether the clinic had a written protocol to guide nPEP prescription (46). Collectively, this evidence suggests the need for further nPEP implementation scale-up.

Limitations

Our research is not without limitation. First, our sampling strategy only focused in above-average HIV prevalence ZIP codes of the 10 U.S. cities with greatest overall HIV prevalence, potentially limiting generalizability to other urban and rural areas. Additional nationwide research is needed with special attention to other areas most affected by HIV. Second, our response rate was approximately 30%, which could have resulted in selection bias. Based on the study design, it is possible that our results over-report nPEP prescribing experience. Third, our sample primarily comprised of physicians, suggesting the need for additional research with nurse practitioners, physician assistants, and other healthcare professionals (e.g., pharmacists). Fourth, our reported rates of nPEP prescription were

limited to nPEP use with patients who experienced potential sexual exposures to HIV. Future research should assess nPEP prescription practices associated with injection-related exposures and identify any nuances in prescription rates by non-occupational exposure type. Last, our data were collected in 2014–2015, and we have since seen increasing awareness of PrEP (43). Although nPEP had been clinically recommended by the CDC for nearly a decade prior to our survey, it is possible that awareness of nPEP has increased since 2015. Further research is needed to document the longitudinal trends in nPEP awareness and prescription among healthcare providers.

CONCLUSIONS

We found evidence extending prior reports documenting low rates of nPEP prescription by healthcare providers in the US. Although nPEP awareness was high in our sample, interventions are needed to support nPEP prescription practices, optimize clinical protocols for nPEP prescribing, and publicize nPEP availability to their patients, particularly in areas with lower levels of PrEP uptake. Our findings also support the need for further nPEP training among non-HIV providers, who may be more accessible to patients immediately following potential HIV exposure. Last and most importantly, our evidence suggests the need to expand nPEP availability if we are to *End the HIV Epidemic* (2) in the US.

ACKNOWLEDGEMENTS

Funding support was provided by Gilead Sciences, Inc. (IN-US-276-0123, PI: Petroll) and the National Institute of Mental Health (P30-MH052776, PI: Kelly; K01-MH118939, PI: John; K01-MH112412, PI: Quinn). The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

The authors acknowledge the contributions of other members of the study team, especially Drs. Jill Owczarzak, Timothy McAuliffe, Laura Bogart, and Jeffrey Kelly. We also thank our staff at the Center for AIDS Intervention Research and our participants who volunteered their time.

This work was presented in part at the International Association of Providers of AIDS Care (IAPAC) Conference; June 17–19, 2019; Miami, FL.

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Figure 1.

The HIV post-exposure prophylaxis (PEP) prescribing cascade for sexual HIV exposures among HIV providers (n = 225) and non-HIV primary care providers (n = 255) practicing within above-average HIV prevalence ZIP codes of the 10 U.S. cities with greatest overall HIV prevalence.

Table 1

Demographics, provider characteristics, and HIV pre-exposure prophylaxis (PrEP) prescribing practices and their bivariate associations with location on the HIV post-exposure prophylaxis (PEP) prescribing cascade among a U.S. sample of HIV providers and non-HIV primary care providers (n = 480)

Categorical Variables	n	Col. %	PEP Unaware (n = 60)		PEP Aware, No Non-Occupational PEP (nPEP) Prescribing Experience ^L (n = 209)		nPEP Prescribing Experience ^L (n = 211)		χ^2 statistic
			n	Row %	n	Row %	n	Row %	
Gender									
Cisgender female	216	45.0	25	11.6	105	48.6	86	39.8	4.87
Cisgender male	253	52.7	33	13.0	101	39.9	119	47.0	
Transgender or prefer not to answer	11	2.3	2	18.2	3	27.3	6	54.6	
Race/ethnicity									20.84 **
Asian	81	16.9	21	25.9	31	38.3	29	35.8	
Black	53	11.0	4	7.6	24	45.3	25	47.2	
Latinx	39	8.1	4	10.3	22	56.4	13	33.3	
White	262	54.6	24	9.2	113	43.1	125	47.7	
Multi/other or prefer not to answer	45	9.4	7	15.6	19	42.2	19	42.2	
U.S. Region									39.91 ***
Northeast	109	22.7	5	4.6	51	46.8	53	48.6	
Midwest	55	11.5	3	5.5	30	54.6	22	40.0	
South	200	41.7	44	22.0	88	44.0	68	34.0	
West	116	24.2	8	6.9	40	34.5	68	58.6	
Provider type									92.70 ***
HIV provider	225	46.9	14	6.2	60	26.7	151	67.1	
Non-HIV primary care provider	255	53.1	46	18.0	149	58.4	60	23.5	
Professional position									7.34
Physician	409	85.2	51	12.5	187	45.7	171	41.8	
Nurse practitioner	44	9.2	7	15.9	14	31.8	23	52.3	
Physician assistant	27	5.6	2	7.4	8	29.6	17	63.0	
Practice type									13.15 **
Private hospital or clinic	234	48.8	42	18.0	100	42.7	92	39.3	
Public/other settings ²	246	51.3	18	7.3	109	44.3	119	48.4	
PrEP awareness and prescribing experience									181.45 ***
PrEP unaware	68	14.2	27	39.7	35	51.5	6	8.8	
PrEP aware, no prescribing experience	222	46.3	25	11.3	139	62.6	58	26.1	
PrEP prescribing experience	190	39.6	8	4.2	35	18.4	147	77.4	
Continuous Variable	M	SD	M	SD	M	SD	M	SD	ANOVA

Age	50.0	8.5	51.2	8.7	50.6	7.8	49.1	9.0	$F(2, 477) = 2.44$
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Note: Percentages may not add up to 100 because of rounding.

*
 $p < 0.05$;

**
 $p < 0.01$;

 $p < 0.001$.

¹ nPEP prescribing experience was limited to potential sexual exposures to HIV and did not include prescription for injection-related exposures.

² Includes public hospitals, clinics, AIDS service organizations, other, and one missing response.

Table 2

Results of the fully-adjusted multinomial regression model predicting location on the HIV post-exposure prophylaxis (PEP) prescribing cascade among a U.S. sample of HIV providers and non-HIV primary care providers (n = 480)

Variables	PEP Unaware		PEP Aware, No Non-Occupational PEP (nPEP) Prescribing Experience ^I		nPEP Prescribing Experience ^I	
	RRR ⁺	95% CI	RRR	95% CI	RRR	95% CI
Age	1.00	0.96–1.04	--	--	0.98	0.95–1.01
Gender (ref: cisgender female)			--	--		
Cisgender male	1.22	0.62–2.40	--	--	1.29	0.77–2.16
Transgender or prefer not to answer	2.80	0.17–47.28	--	--	2.19	0.30–15.86
Race/ethnicity (ref: White)			--	--		
Asian	4.19 ^{**}	1.84–9.50	--	--	1.33	0.65–2.72
Black	0.58	0.16–2.09	--	--	1.35	0.59–3.11
Latinx	0.74	0.23–2.40	--	--	0.76	0.37–1.56
Multi/other or prefer not to answer	1.14	0.31–4.19	--	--	1.30	0.53–3.16
U.S. Region (ref: South)			--	--		
Northeast	0.22 ^{**}	0.08–0.59	--	--	0.85	0.44–1.64
Midwest	0.13 ^{**}	0.04–0.51	--	--	0.76	0.33–1.76
West	0.31 [*]	0.11–0.89	--	--	1.45	0.79–2.68
Provider type (ref: non-HIV primary care provider)			--	--		
HIV provider	1.39	0.56–3.42	--	--	2.96 ^{***}	1.74–5.04
Professional position (ref: physician)			--	--		
Nurse practitioner	4.68 [*]	1.42–15.37	--	--	1.19	0.51–2.79
Physician assistant	1.73	0.26–11.49	--	--	0.58	0.21–1.59
Practice type (ref: public/other settings)			--	--		
Private hospital or clinic	1.97	0.90–4.31	--	--	0.72	0.41–1.28
PrEP awareness and prescribing experience (ref: PrEP unaware)			--	--		
PrEP aware, no prescribing experience	0.26 ^{**}	0.12–0.56	--	--	1.63	0.63–4.22
PrEP prescribing experience	0.27 [*]	0.09–0.84			12.49 ^{***}	4.57–34.10

* $p < 0.05$;

** $p < 0.01$;

*** $p < 0.001$.

⁺RRR = relative risk ratio; this is the multinomial logistic regression coefficient exponentiated (i.e., *eb*).

^InPEP prescribing experience was limited to potential sexual exposures to HIV and did not include prescription for injection-related exposures.