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HIV medical providers' perceptions of the use of antiretroviral therapy as non-occupational post- exposure prophylaxis (nPEP) in two major metropolitan areas

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Abstract

Intro—In 2005, the Centers for Disease Control and Prevention expanded its recommendation of post exposure prophylaxis (PEP) use in the workplace to include non-occupational exposures (nPEP). The availability and extensive use of nPEP has not achieved widespread acceptance among health care providers of high-risk populations, and public health and primary care agencies have been sparse in their implementation of nPEP promotion, protocols, and practices.

Methods—We conducted a survey of HIV providers (n=142, response rate = 61%) in Miami-Dade County (Florida) and the District of Columbia (DC) that focused on their knowledge, attitudes, beliefs and practices related to the delivery of nPEP. We then analyzed differences in survey responses by site and by history of prescribing nPEP using bivariate and multivariate logistic regression.

Results—More DC providers (59.7%) reported ever prescribing nPEP than in Miami (39.5%%, $p < 0.048$). The majority of practices in both cities did not have a written nPEP protocol and rarely or never had patients request nPEP. Multivariable analysis for history of prescribing nPEP was dominated by having patients request nPEP (OR = 21.53) and the belief that nPEP would lead to antiretroviral resistance (OR = 0.14), as well as having an nPEP written protocol (OR = 7.49).

Discussion—Our findings are consistent with earlier studies showing the underuse of nPEP as a prevention strategy. The significance of having an nPEP written protocol and of patient requests for nPEP speaks to the importance of using targeted strategies to promote widespread awareness of the use of HIV antiretroviral medications as a prevention intervention.

Keywords

Non-occupational exposure; Antiretroviral prophylaxis; HIV prevention; HIV medical providers

Introduction

The incidence rate of human immunodeficiency virus (HIV) in the United States still persists at approximately 50,000 new HIV infections annually and remains a significant public health burden.[1] Prevention strategies continue to focus on decreasing disease transmission and incidence rates of new infections annually. The use of oral chemoprophylaxis by HIV uninfected persons prior or immediately after exposure to HIV are promising prevention efforts.[2–5] Post-exposure prophylaxis (PEP) has been studied extensively and demonstrated a protective effect through animal transmission models[6–8], perinatal clinical trials[9], and observational[10,11] and case report[12,13] studies of health care workers after occupational exposures. These occupational studies have derived effectiveness data from health care workers that has suggested a 79–81% reduction in HIV infection attributed to the use of antiretroviral medications after a high-risk exposure.[10,11]

In response to this accumulating data on the efficacy of nPEP and the need for more widespread national guidelines on its use in medical facilities[14], the Centers for Disease Control (CDC) expanded its recommendation of post exposure prophylaxis (PEP) use in the workplace in 2005 to include non-occupational exposures (nPEP).[15] The use of nPEP is now recommended for uninfected persons seeking care less than 72 hours following exposure to potentially-infected blood, genital secretions, or other bodily fluid in the setting of significant sexual or injection-drug encounters with an individual of known positive serostatus.[15] These revised guidelines also encourage adjunct behavior modification and risk

reduction counseling to address behavioral and social cofactors that predispose nPEP users to high risk engagement. When the HIV status of the source is unknown, the CDC states that "no recommendations are made either for or against the use of" nPEP and instead advises clinicians to prescribe nPEP based on a "case by-case" evaluation, depending on what is known about the source and exposure. This puts considerable responsibility and discretion on the physician, due to the high prevalence of undiagnosed infection in high risk populations and the fact that the vast majority of patients presenting for post-exposure care do not know the HIV status of the exposure source. One 2003 Rhode Island emergency department study reported that less than 2% of post exposure patients knew that their exposure source was HIV-positive.[16] Similarly, a 10-year 2010 retrospective cohort study of nPEP requests in a hospital out-patient clinic found that 77% of exposure sources had unknown serostatuses, leading investigators to endorse the feasibility and efficiency of a prevention approach that involved the tracing and testing of the exposure source.[5]

nPEP has not achieved widespread acceptance among health care providers of high-risk populations.[17] Many concerns have been raised, including patient non-adherence, pharmacological toxicities and adverse effects in otherwise healthy individuals, development of viral resistance and selection for resistant virus, the potentially high cost of therapy for patients without insurance or with inconsistent insurance coverage, and the difficulty in accessing medical care from a physician within the recommended 72 hours, given that persons most likely to benefit from nPEP may be estranged from the health care system.[15,18,19] Controversy also persists over the cost-effectiveness of nPEP in comparison to other HIV prevention methods, such as behavior modification counseling[20,21], or only in very limited circumstances, such as following receptive but not insertive anal intercourse[18,22], and whether continued emphasis on nPEP and HIV prevention may divert resources from HIV-positive patients to HIV-negative patients[23].

Nonetheless, emerging evidence has supported nPEP use as a practical, cost-effective method of HIV prevention and mitigated concerns about nPEP-induced behavioral disinhibition. Feasibility studies have documented seroconversion prevention and yielded high percentage values of nPEP completion rates amongst nPEP users, despite some subjective reports of side effects.[17,24] Cost-effectiveness has been demonstrated through empirically based economic analysis of a large-scale nPEP feasibility program implemented in San Francisco, where nPEP was administered to patients with varying sources and levels of exposure risk.[25] A similar 2004 study conducted empirical, model-based analysis of nPEP cost-effectiveness in 96 metropolitan statistical areas in the United States and derived a cost-effectiveness ratio comparable to that of existing behavioral counseling interventions.[24] Though nPEP was found to be most cost-effective in metropolitan statistical areas (MSAs) with larger populations of men who have sex with men (MSM), especially those with high HIV prevalence, the results suggested that the use of antiretroviral medications following non-occupational exposures to HIV could be a cost-effective adjunct to existing HIV prevention efforts.

Attracting much attention is the concept that nPEP availability will lead to "treatment optimism" and attenuated risk perception, leading to continued or heightened engagement in high risk behavior, commonly referred to as "behavioral disinhibition."[18,19] It has even been speculated that nPEP could cause net harm, protecting only a few nPEP users at the expense of widespread increased risk behavior and, consequently, increased disease transmission.[19] Concerns about nPEP-induced behavioral disinhibition and promotion of risky behavior have been disproven through various studies, with some even demonstrating that, instead, the distribution of nPEP may have a beneficial effect on behavior by acting as an ''educable moment."[26] The 1999–2003 randomized HIV prevention trial EXPLORE studied approximately 4,300 MSM men in six national cities and showed that, although nPEP users

remained a high risk group, nPEP use did not appear to lead to increased sexual risk.[27] Similarly, a 2009 cohort study of Australian MSM concluded that the use of nPEP was not associated with changes in HIV risk behavior.[28] In a 2004 Brazilian cohort study of MSM, the use of nPEP also did not appear to be associated with increases in reported high-risk behavior; on the contrary, there was a slight decline in reported risk-behavior in the cohort overall, and frequent use of nPEP was not noted despite its ease of access made available by the study team.[29] Furthermore, instances of repeat nPEP use by a single individual has not been attributed to behavioral disinhibition and increased risk behavior, but instead to maintenance of the individual's baseline risk-taking behavior prior to nPEP use.[25]

Despite the evidence that nPEP is a safe and feasible method of HIV prevention, awareness of nPEP amongst the high-risk populations that would most benefit from its use, including MSM, remains low. Reported rates of nPEP awareness have been at its highest in California (47%),[30] but a multicity study of minority, homosexual men attending gay pride parades found that only 21.4% of MSM were aware of the use of antiretroviral medication for HIV prevention.[31] Factors strongly associated with nPEP knowledge in these studies included high numbers of reported sexual partners, HIV-positive serostatus, older age, and higher affluence. Most recently, a 2011 survey of MSM who engage in high risk behavior at New York City bathhouses revealed that only 36% of respondents were aware of the use of antiretroviral medication to prevent disease transmission.[32] Furthermore, knowledge was positively associated with respondents' disclosure of their MSM behaviors to their primary care physicians. Less than half of respondents overall (46.5%) had disclosed their high-risk behavior patterns to a healthcare provider, despite high rates of primary care utilization (98.3%). These results underscore the importance of taking a sexual history as part of the medical history and clinical examination and the significant role that primary care providers can potentially play in expanding nPEP awareness and education amongst high-risk MSM by having a better understanding of patients' sexual practices.

Despite the CDC recommendations, few public health and primary care agencies have implemented nPEP promotion and practices. For example, a 2008 survey of New York state emergency room directors inquired about their knowledge of nPEP practices and protocols at their specific sites.[33] Protocols had been developed for consensual sexual exposures at 59% of facilities, far less than for sexual assault exposures (95%). In regards to practice, patients presenting to the emergency room following a consensual exposure were significantly less likely to be given an nPEP prescription compared to victims of sexual assault. Since prior studies had shown that New York physicians offered nPEP after exposures of unknown risk more often than those from other states, this study likely overestimated nPEP practices, inferring that nPEP is even more underutilized nationwide.[34] A 2011 cross-sectional survey of point-of-care health care sites in Los Angeles County inquired about nPEP availability and found that just 14.5% of venues offered nPEP services, while only 8.5% offered services to uninsured and/or Medicaid patients.[35] Of all venue types - including primary care clinics, HIV/infectious disease subspecialty care clinics, and community-based organizations offering HIV prevention services - hospital emergency departments were more than five times more likely to provide nPEP services.

To better inform ways in which the CDC and other governmental agencies can work with health departments to reduce new HIV infection, link individuals to HIV-related care and treatment, and facilitate a more collaborative national response to this epidemic, the CDC's Division of HIV/AIDS Prevention (DHAP) funded the three year demonstration project titled "The Enhanced Comprehensive HIV Prevention Planning (ECHPP) Project."[36] The major aim of this project is to develop a plan in alignment with the National HIV/AIDS Strategy that maximizes the impact of HIV prevention strategies on reducing HIV incidence in twelve participating MSAs most affected by HIV/AIDS, including Miami and

Washington D.C. All of these municipalities were chosen for having the highest prevalence of individuals living with HIV/AIDS and collectively represent 44% of the estimated AIDS cases nationwide. These goals include assessing the optimal combinations and impact of local prevention, care and treatment approaches and the evaluation of current ECHPP implementation and utilization activities within these select jurisdictions to better inform the development of an optimal combination of behavioral, biomedical, and structural intervention activities to drive decision making and maximize impact on HIV prevention. Within this context, the University of Miami Miller School of Medicine and George Washington University ECHPP teams, along with the Miami-Dade County and District of Columbia health departments, developed a survey of HIV healthcare providers as one of many steps taken to address the implementation of HIV prevention planning strategies in these two MSAs and address the CDC's ECHPP evaluation goals. Questionnaire items were developed to support each of the ECHPP study aims, including the aim to "investigate the availability, accessibility, and acceptability of prescribing and obtaining Post-Exposure Prophylaxis (PEP) by both HIV primary care providers and persons at high risk for HIV" in both Miami-Dade County and the District of Columbia. Additionally, the D.C. ECHPP team, in collaboration with both the Miami and DC Developmental Centers for AIDS Research (D-CFAR) and the DC and Miami Department of Health HIV/AIDS, Hepatitis, STD and TB Administration (HAHSTA), sought to conduct preliminary analysis and review of existing nPEP policies and protocols, as well as their applicability to the District of Columbia and Miami-Dade county, as part of an ECHPP demonstration project specific to nPEP feasibility, cost-effectiveness, and provision to populations at highest risk (ECHPP Strategy #4).

Methods

All study activities were approved by the Institutional Review Boards at George Washington University, District of Columbia Department of Health, University of Miami and Columbia University.

Participants

Between March 2012 and March, 2013, a survey was conducted of HIV providers in Miami-Dade County (Florida) and the District of Columbia (DC) that focused on their knowledge, attitudes, beliefs and practices related to the delivery of nPEP, pre-exposure prophylaxis (PrEP), and prevention and care issues with people living with HIV/AIDS (PLWHA).

Our target sample population consisted of infectious disease and HIV providers who had treated at least one HIV-positive patient in the year preceding the administration of the survey. We selected these providers as the target sample for this survey with the understanding that our findings would best represent providers who are at the forefront of HIV treatment and prevention strategies and should have highest provision of nPEP as a method to prevent new infections. The majority of HIV providers in Miami and DC provide care to non-HIV infected subjects as Infectious Disease specialists, STD clinic providers and/or primary care providers. In addition, due to the nature of their clinical practice, HIV providers tend to be more informed and up-to-date about current HIV guidelines, the use of antiretroviral medications, including dosing and side effects, and the required initial and follow- up medical work-up of a person exposed to HIV. These characteristics explain why patients either self-refer themselves or are referred by their primary doctors or partners to an HIV provider in the event of a non-occupational HIV exposure. Although any primary care physician can prescribe antiretroviral medication, Infectious Diseases Specialists or Emergency Physicians in most centers are responsible for nPEP,[5] and government-sponsored websites such as AIDS.gov recommend seeking nPEP at a private doctor's office, emergency room, urgent care clinics or a local HIV clinic.[37]

A variety of sources were used in compiling the clinician lists for each city, including the American Academy of HIV Medicine, AIDS Education and Training Center (AETC), state Infectious Disease Society, Ryan White Part A and B programs, local Medicaid office, health departments, and other local medical societies. This list represented more than 230 providers serving patients with HIV in community-based outpatient clinics/offices and outpatient clinics associated with large hospitals/medical centers.

The initial contact, which was done by mail in Miami and e-mail in DC, included a cover letter explaining the purpose of the study, information on how to complete the questionnaire, and the offer of a $20 incentive for completing the questionnaire. Names were not included with the questionnaire and participants were informed that their responses would be confidential. Using a modified version of Dillman's total design method[38] for mail and telephone surveys, we continued to follow-up with responders for three months using a variety of methods including phone-calls, emails, postcards, questionnaire re-mailings and in-person visits (Miami only).

Survey Administration

Providers were given the opportunity to complete the survey electronically, using the web-based program Survey Monkey[1] for Miami-Dade respondents or the program Research Electronic Data Capture (REDCap)[2] for the DC respondents, or on paper. Each survey took 15–20 minutes to complete. Questionnaire items were developed to support each of the ECHPP study aims, including the aim to "investigate the availability, accessibility, and acceptability of prescribing and obtaining Post-Exposure Prophylaxis (PEP) by both HIV primary care providers and persons at high risk for HIV" in both Miami-Dade County and DC.[14,33,39,40]

Merged Data Set, Sample Size and Response Rate—Once recruitment activities concluded at both sites, the data sets from both cities were shared over a secure network and then aggregated. Analysis of the combined data sets was based on responses from 142 providers out of 231 identified practitioners practicing in these two major metropolitan areas, for a final response rate of 61%. The DC site had a sample size of 124 providers and received responses from 63 providers (response rate of 50.8%). The Miami site received responses from 79 out of a total of 107 identified providers, for a response rate of 73.8%.

Statistical Analysis—We examined differences in survey responses by site and by history of prescribing nPEP using chi-square analysis. We examined any significant differences by history of prescribing nPEP for potential interaction or confounding by site using logistic regression analysis. Finally we created a multivariable model of factors related to history of prescribing nPEP by including all simple relationships with history of prescribing nPEP with a p-value under .10 and using backward elimination. Due to different patterns for missing data across survey questions we used multiple imputation.[41] Because the independent variables were all categorical we used a fully conditional specification for the imputation step.[42,43] We utilized 20 imputed datasets to maximize statistical power.[44]

[1]Survey Monkey is a software program with guided tools for creating, administering and analyzing web-based surveys through a secure, encrypted Internet connection. Location: Palo Alto, California, USA. Main website: www.surveymonkey.com.

[2]Study data were collected and managed using REDCap electronic data capture tools hosted at George Washington University. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Results

Demographics

Most medical providers in the survey were over 40 years old and had more than 10 years of practice with the modal category for both sites being more than 20 years of practice (Table 1). There was a difference across sites in the racial/ethnic distribution with Miami having more Hispanic and fewer White providers. Miami (65.4%) also had more male providers than did DC (50.8%) though this was not statistically significant. The modal category of number of patients seen per month was more than 200 for both Miami (55.8%) and DC (45.2%), with most providers reporting more than 20 HIV positive patients seen in the last 3 months at both sites.

nPEP Experience and Knowledge

More providers in DC (59.7%) reported ever prescribing nPEP than providers in Miami (39.5%, $\chi^2(1) = 6.09$, $p < 0.048$). The majority of practices in both cities did not have a written nPEP protocol and rarely or never had patients ask for nPEP. About a third of practices in the entire sample felt there were barriers to prescribing nPEP at their site. About 82% of providers at each site knew that CDC has formal guidelines for the use of nPEP and most (Miami-67.7%, DC-78.3%) knew that unprotected anal exposure is a higher risk factor for HIV than percutaneous occupational exposure. Substantially fewer providers knew (Miami-41.3%, DC-41.7%) that percutaneous occupational exposure is a higher risk than vaginal exposure.

Barriers and Facilitators to Prescribing nPEP

A large majority of providers felt that they were more likely to prescribe nPEP if a patient had an HIV+ partner (80.7%) or had been a victim of a sexual assault (79.0%). A much smaller proportion felt they were more likely to prescribe nPEP if a patient had a partner of unknown HIV status (26.5%) or if the patient had a history of no condom use (27.1%). There were significant differences in impact of history of STIs and being a person who injected drugs (PWID) on likelihood of prescribing nPEP. Providers in Miami reported they were less likely to prescribe to a patient with a history of STIs than in DC (Miami-29.3% more likely, DC-45.9% more likely, $\chi^2(4) = 15.04$, $p < 0.0039$, see Table 1 for all categories of response). Similarly, providers in Miami were less likely to prescribe nPEP to a PWID than were providers in DC (Miami-29.3% more likely, DC-54.1% more likely, $\chi^2(4) = 16.93$, $p < 0.0020$, see Table 1 for all categories of response). Very few providers felt they would be likely to prescribe nPEP to patients with a history of irregular clinic visits (13.6%) or a history of non-adherence to medication (11.0%).

Attitudes toward nPEP

Most providers agreed (80.3%) that it was possible to prescribe nPEP at their clinic; however fewer providers in Miami, compared to DC, felt there was adequate time to prescribe nPEP ($\chi^2(2) = 9.03$, $p < 0.0109$). About a third of providers at each site (Miami-37.3%, DC-31.2%) also felt there were barriers to prescribing nPEP at their facilities. Significantly more providers in Miami (40.5%) felt that nPEP will promote HIV resistance than did providers in DC (12.7%; $\chi^2(2) = 15.38$, $p < 0.0005$). Similarly significantly more providers in Miami (48.1%) than in DC (14.3%) felt that nPEP would promote risky behavior ($\chi^2(2) = 18.13$, $p < 0.0001$).

Bivariate Relationships with History of Prescribing nPEP

Medical providers who had prescribed nPEP were more likely to be associated with larger practices ($\chi^2(4) = 9.96$, $p < 0.0411$, Table 2). Those in practices that care for more than 200

patients in a month were more likely to have prescribed nPEP than those in practices with under 50 patients (OR=5.16, 95% CI[1.51,17.67]). Providers in practices where more than 20 HIV positive patients were seen in the prior 3 months were more likely than those in practices with 20 or fewer HIV positive patients seen to have prescribed nPEP (OR = 3.77, 95% CI[1.38, 10.32]). Similarly, providers who themselves had seen more than 20 HIV positive patients in the prior 3 months were more likely to have prescribed nPEP (OR=2.50, 95% CI[1.12, 5.61]). Those practices with providers who had prescribed nPEP were also more likely to have a written nPEP protocol ($\chi^2(2) = 6.17$, $p < 0.0456$, Table 2). Whereas, providers who did not know if their site had a written nPEP policy were less likely to have prescribed nPEP than those that did know that their site had a written nPEP policy (OR = 0.26, 95% CI[0.72, 0.97]). Providers who had patients that requested nPEP were more likely to have prescribed nPEP than providers who did not have patients that requested nPEP (OR = 34.16, 95% CI[11.68, 102.58]). Providers who had prescribed nPEP were more likely than those who had not prescribed nPEP to know that the CDC has formal guidelines for the use of nPEP ($\chi^2(2) = 6.21$, $p < 0.0448$), however this was no longer significant after controlling for site. Providers who believed nPEP provision was feasible in their practice were more likely than those who felt nPEP provision was not feasible to have prescribed nPEP ($\chi^2(4) = 11.20$, $p < 0.0037$). Providers who had prescribed nPEP endorsed that they were more likely than those who had not prescribed nPEP to prescribe to patients who had a partner of unknown HIV status ($\chi^2(4) = 10.32$, $p < 0.0353$). Additionally, providers who had prescribed nPEP were less likely than those who had not prescribed nPEP to believe that nPEP will promote antiretroviral resistance ($\chi^2(2) = 31.01$, $p < 0.0001$). Those who believed nPEP would not create resistance were more likely to have prescribed nPEP than those who were neutral (OR = 3.17 95% CI[1.33, 7.57]) or those who felt nPEP would create antiretroviral resistance (OR=13.66, 95% CI[4.49, 41.58]. Finally those providers who felt nPEP would not increase risk behavior were significantly more likely to have prescribed nPEP than those who felt that nPEP would increase risk behavior (OR = 6.49, 95% CI [2.50, 16.81].

Multivariate Model for History of Prescribing nPEP

Table 3 shows the initial multivariable model for history of prescribing nPEP, which was dominated by having patients that request nPEP (aOR = 21.53 95% CI[6.50, 71.34]) and provider belief that nPEP would lead to antiretroviral resistance (aOR = 0.14, 95% CI[0.04, 0.55]). We re-estimated the multivariate model excluding “having patients that request nPEP” as a predictor to examine other multivariable predictors related to practice and provider attitudes. In this model, belonging to a practice which saw more than 20 HIV positive patients (aOR = 6.33, 95%CI [1.94, 20.67]) and having a written protocol for nPEP (aOR = 7.49, [1.47, 38.27]) were both associated with higher odds of having prescribed nPEP. Reporting barriers in a practice to prescribing nPEP was associated with lower odds of having prescribed nPEP (aOR = 0.33 95% CI[0.13, 0.83]). Agreeing that nPEP may cause antiretroviral resistance was associated with much lower odds of having prescribed nPEP (aOR = 0.05, 95% CI[0.02, 0.19]) and feeling neutral about the possibility of increased antiretroviral resistance was associated with lower odds of having prescribed nPEP (aOR = 0.22, 95% CI[0.08, 0.61]), both relative to those who disagreed that nPEP would increase antiretroviral resistance.

Discussion

This study of HIV providers’ knowledge, attitudes, beliefs, and practices towards the use of nPEP was carried out in two U.S. cities that have been disproportionately impacted by the HIV/AIDS epidemic.[45–47] Both are southern cities that have the highest rates of HIV/AIDS in the U.S. across populations of men who have sex with men, persons at risk for HIV

through heterosexual transmission, and substance use.[46–52] Both Miami and DC were included in the CDC-funded ECHPP project so that their local health departments, in collaboration with community leaders and key stakeholders, could develop a plan and enhance prevention strategies to reduce HIV incidence, increase access to HIV care for persons living with HIV, and decrease the HIV-related health disparities outlined in the National HIV/AIDS Strategy. Expanding use of nPEP was one of the suggested ECHPP HIV prevention strategies.

Study findings document low provision of nPEP by HIV providers participating in our survey. Less than half of HIV providers in Miami and a little more than half of HIV providers in DC have ever prescribed nPEP. Of unexpected note to the study team was the statistically significant difference in nPEP provision between the two major cities, as well as the significant differences in attitudes related to nPEP. Given that both DC and Miami are two cities with high HIV prevalence selected for inclusion within ECHPP, we would expect to see similar nPEP provision and attitudes regarding nPEP between the two cities. Further exploration is warranted to assess city-specific differences in HIV prevention education, awareness and policy to determine why nPEP practices and attitudes are not comparable between two heavily HIV-prevalent MSAs. Still, it is important to note that in both cities, there are few providers that promote the availability of nPEP services at their clinic. For example, throughout the city of DC, there is only one program funded by the DC Department of Health to provide nPEP to sexual assault victims.

Furthermore, since the providers sampled in our survey were the medical providers most expected to receive frequent referrals and requests for nPEP due to their expertise in HIV medicine, provision among non-HIV providers in these communities is most likely even lower. With respect to knowledge, approximately 20% of survey respondents were not aware of the CDC guidelines and less than half of respondents were aware that percutaneous exposure carried greater risk than unprotected vaginal exposure. These findings were unanticipated given that, of all medical specialists, HIV providers should be well-informed of relevant HIV guidelines, current prevention strategies and transmission risks. Lastly, with regard to practitioners' greatest concerns regarding nPEP, two of the top responses were behavioral disinhibition and cost, despite the body of evidence[25–29] noted earlier that disproves these concerns. These findings also point out that, for the group of individuals responsible for the patients' health, the providers, there is a significant opportunity for education. In this regard, web-based resources, as well as collaboration with AIDS Education and Training Centers, can be brought to bear on this education to assist in providing accurate information regarding in whom nPEP use should be considered, the risks of using it, and resources to assist providers in how to deliver nPEP. Awareness of the opportunities and the potential barriers should be addressed at all layers of care including prevention efforts in Department of Health facilities and education campaigns as well as urgent care centers, emergency rooms, and physician practices. With the ongoing changes in health care reform, it is clear that those providing care to individuals at risk for infection, be it an HIV specialist or primary care provider, must have the opportunities, knowledge, and tools to assist in making well-informed clinical decisions pertaining to HIV prevention.

While the majority of HIV providers surveyed in this study indicated being aware of CDC guidelines regarding the use of nPEP, the majority of providers indicated that there were no written nPEP protocols in their clinics and that they had never received requests from patients to prescribe nPEP. Notably, having a written protocol and being asked by a patient to provide nPEP were among the factors that were most strongly related to nPEP provider prescribing behaviors. This finding speaks to the importance of subjective norms and how HIV providers' prevention practices are influenced both by demand from their patients and encouragement from their clinic administrators. The development and implementation of

written protocols in clinics and hospitals nationwide will likely require collaboration at both the clinician level and the institutional administrative level to identify and address institutional barriers to nPEP provision.

Interventions which encourage patients to ask for prevention strategies that might work best for them should be developed and implemented. Recent efforts to enhance health literacy and to get patients to advocate for themselves have increasingly been recognized as an important prevention strategy. nPEP is not something that is currently offered to patients when appropriate. It follows that efforts to educate persons at risk for HIV about this underused prevention strategy and encourage them to initiate a dialogue with their provider about opportunities for potential interventions could improve clinical outcomes. For example, in DC, social marketing campaigns for routine HIV testing emphasized provider-initiated testing, but advertisements were also geared toward patients and empowering them to ask for the test. Also, Fenway Health has recently launched a TalkPEP.org campaign where they are seeking to raise awareness of PEP and encourage people to “talk PEP” with their social networks, partners, and providers.[53] Further targeted education strategies need to be developed and implemented to raise generalized awareness and knowledge about the use of nPEP that will ideally help foster an ongoing dialogue within the patient-doctor relationship about HIV prevention.

Physician and patient awareness of the effectiveness of PrEP for MSM and women who are adherent to their medication regimens may also have a positive impact on the use of nPEP. Many of the previous concerns raised among clinicians regarding the use of nPEP, including patient non-adherence, pharmacological toxicities, high costs, and concerns about how use of nPEP could result in “behavioral disinhibition,” are also being raised about PrEP.[15,18,19] There are several operational research studies underway to address many of these concerns related to PrEP, as well as the impact of provider attitudes about nPEP on the acceptability and provision of PrEP, and vice versa.[54,55] As findings emerge, it is possible that clinicians will re-evaluate concerns related to nPEP and PrEP and use the emergence of PrEP as an intervention approach to educate patients about nPEP as an important and underused biomedical HIV prevention strategy.[54] Additionally, further research comparing provider attitudes and practices with respect to nPEP versus PrEP would be beneficial. Specifically, identifying how providers choose between the use of nPEP and PrEP in specified situations can play a pivotal role in prevention policy and protocols; for example, nPEP may be a more appropriate strategy in the case of sexual assault, but not for a patient involved in an ongoing serodiscordant partnership. While both nPEP and PrEP were queried in this survey, the focus of this paper was specific only to provider attitudes and practices related to nPEP.

Several limitations of our data should be noted. First, non-responders may have differed from respondents in terms of their reporting of prescribing practices. The small number of non-responders with available data limits the conclusions that can be made regarding nonresponse bias. Second, the data obtained were self-reported and not confirmed through patient interviews or clinical records. Third, there are small differences in the methods used between each city, such as the form of the initial contact and Miami’s use of the Dillman’s total design method for follow-up communications, which may account for differences in study findings. Finally, our survey sampled HIV care providers with high volumes of HIV-positive patients practicing in Miami and Washington, D.C.; therefore, our findings may be of limited generalizability outside of these two cities or other ECHPP EMAs with high HIV prevalence, among non HIV providers, or among those with smaller patient volumes. Future studies assessing nPEP practices and attitudes may consider surveying other populations of medical providers, such as primary care physicians, who may not receive as many patient requests/referrals for nPEP or be as aware of current nPEP recommendations and/or advances in HIV medicine. This could help determine the population(s) of providers with

the potential to make the most use of nPEP, and to further target nPEP education and HIV prevention strategies accordingly.

Despite these limitations, our findings are consistent with previous studies that have shown the underuse of nPEP as a prevention strategy. HIV prevention researchers worldwide are recognizing the need for a combination HIV prevention approach that takes advantage of multiple HIV prevention strategies, and nPEP is a strategy that has been shown to be both effective and cost-effective.[10,11,24,25] Given the recent publication of trials showing the efficacy of PrEP, it may be the right time to renew efforts to increase use of nPEP and to develop strategies to support its successful implementation.

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Table 1

Descriptive Characteristics of Respondents, by Site

Characteristics of Respondents		Miami	Washington DC	Total	Chi square p-value
		N (%)	N (%)		
Years Practicing					
	Less than 5	3 (4.0)	6 (9.5)	9.0(6.5)	0.1291
	5–9	7 (9.3)	11 (17.5)	18(13.0)	
	10–14	12 (16.0)	14 (22.2)	26(18.8)	
	15–19	13 (17.3)	5 (7.9)	18(13.0)	
	20 or more	40 (53.3)	27 (42.9)	67(48.6)	
Age					
	Under 39	9 (12.3)	17 (27.0)	26(19.1)	0.1158
	40–49	27 (37.0)	15 (23.8)	42(30.9)	
	50–59	19 (26.0)	20 (31.8)	39(28.7)	
	60 or older	18 (24.7)	11 (17.4)	29(21.3)	
Race/Ethnicity					
	White	28 (35.9)	42 (68.9)	70(50.4)	**<.0001**
	Black	9 (11.5)	9 (14.8)	18(12.9)	
	Hispanic	31 (39.7)	2 (3.3)	33(23.7)	
	Other race	10 (12.8)	8 (13.1)	18(12.9)	
Gender					
	Male	51 (65.4)	32 (50.8)	83(58.9)	0.0800
	Female	27 (34.6)	31 (49.2)	58(41.1)	
Field of Practice					
	Infectious Disease	42 (53.2)	29 (46.0)	71(50.0)	
	Non-Infectious Disease	37 (46.8)	34 (54.0)	71(50.0)	0.40
Patients seen in one month					
	0–50	11 (14.3)	8 (12.9)	19(13.7)	0.6008
	51–100	11 (14.3)	11 (17.7)	22(15.8)	
	101–150	5 (6.5)	8 (12.9)	13(9.4)	

Characteristics of Respondents		Miami	Washington DC	Total	Chi square p-value
		N (%)	N (%)		
	151–200	7 (9.1)	7 (11.3)	14(10.1)	
	200+	43 (55.8)	28 (45.2)	71(51.1)	
More than 20 HIV positive patients in practice in last 3 months					
	Yes	63 (79.8)	53 (84.1)	116(81.7)	0.5025
	No	16 (20.3)	10 (15.9)	26(18.3)	
More than 20 HIV positive patients under own care in last 3 months					
	Yes	56 (70.9)	48 (76.2)	104(73.2)	0.4781
	No	23 (29.1)	15 (23.8)	38(26.8)	
Ever Prescribed nPEP to a patient					
	Yes	30 (39.5)	37 (59.7)	67(48.6)	**0.0476**
	No	45 (59.2)	25 (40.3)	70(50.7)	
	Unsure	1 (1.3)	0 (0)	1(0.7)	
Practice has written nPEP protocols in place?					
	Yes	16 (21.1)	19 (31.2)	35(25.5)	0.3628
	No	52 (68.4)	35 (57.4)	87(63.5)	
	Unsure	8 (10.5)	7 (11.5)	15(10.9)	
In past 6 months, how many times have you encountered patients who requested nPEP?					
	Often (>once/week)	1 (1.33)	4 (6.5)	5(3.6)	0.1573
	Occasionally (few × a month)	10 (13.3)	14 (22.6)	24(17.5)	
	Rarely (<once/month)	29 (38.7)	22 (35.5)	51(37.2)	
	Never	35 (46.7)	22 (35.5)	57(41.6)	
Are there barriers to prescribing nPEP in your facility?					
	No	47 (62.7)	42 (68.9)	89(65.4)	0.4506
	Yes	28 (37.3)	19 (31.2)	47(34.6)	
CDC has formal guidelines regarding the use of nPEP (Answer: True)					
	True	52 (82.5)	51 (82.3)	103(82.4)	0.9991
	False	1 (1.6)	1 (1.6)	2(1.6)	
	Don't know	10 (15.9)	10 (16.1)	20(16.0)	

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Characteristics of Respondents		Miami	Washington DC	Total	Chi square p-value
		N (%)	N (%)		
Unprotected anal > percutaneous occupational exposure risk (Answer: True)					
	True	42 (67.7)	47 (78.3)	89(73.0)	0.3043
	False	15 (24.2)	8 (13.3)	23(18.9)	
	Don't know	5 (8.1)	5 (8.3)	10(8.2)	
Percutaneous occupational > unprotected vaginal exposure risk (Answer: True)					
	True	26 (41.3)	25 (41.7)	51(41.5)	0.9883
	False	28 (44.4)	27 (45)	55(44.7)	
	Don't know	9 (14.3)	8 (13.3)	17(13.8)	
Influence on prescribing nPEP: Patient has a sexual partner who is HIV+					
	Somewhat less likely	1 (1.7)	0 (0)	1(0.8)	0.495
	Neither	1 (1.7)	1 (1.6)	2(1.7)	
	Somewhat more likely	12 (20.7)	8 (13.1)	20(16.8)	
	More likely	44 (75.9)	52 (85.3)	96(80.7)	
Influence on prescribing nPEP: Patient has a partner, unknown HIV status					
	Less likely	6 (10.3)	2 (3.4)	8(6.8)	0.0737
	Somewhat less likely	10 (17.2)	7 (11.9)	17(14.5)	
	Neither	13 (22.4)	17 (28.8)	30(25.6)	
	Somewhat more likely	19 (32.7)	12 (20.3)	31(26.5)	
	More likely	10 (17.2)	21 (35.6)	31(26.5)	
Influence on prescribing nPEP: Patient is a victim of sexual assault					
	Less likely	1 (1.7)	0 (0)	1(0.8)	0.4345
	Somewhat less likely	2 (3.5)	1 (1.6)	3(2.5)	
	Neither	2 (3.5)	2 (3.3)	4(3.4)	
	Somewhat more likely	11 (19.0)	6 (9.8)	17(14.3)	
	More likely	42 (72.4)	52 (85.3)	94(79.0)	
Influence on prescribing nPEP: Patient has history of no condom use					
	Less likely	7 (12.1)	5 (8.3)	12(10.2)	0.9264
	Somewhat less likely	4 (6.9)	6 (10.0)	10(8.5)	

Characteristics of Respondents		Miami	Washington DC	Total	Chi square p-value
		N (%)	N (%)		
	Neither	16 (27.6)	17 (28.3)	33(28.0)	
	Somewhat more likely	16 (27.6)	15 (25.0)	31(26.3)	
	More likely	15 (25.9)	17 (28.3)	32(27.1)	
Influence on prescribing nPEP: Patient has history of STIs					
	Less likely	5 (8.6)	0 (0)	5(4.2)	**0.0039**
	Somewhat less likely	1 (1.7)	6 (9.8)	7(5.9)	
	Neither	8 (13.8)	12 (19.7)	20(16.8)	
	Somewhat more likely	27 (46.6)	15 (24.6)	42(35.3)	
	More likely	17 (29.3)	28 (45.9)	45(37.8)	
Influence on prescribing nPEP: Patient who injects drugs					
	Less likely	10 (17.2)	0 (0)	10(8.4)	**0.002**
	Somewhat less likely	4 (6.9)	1 (1.6)	5(4.2)	
	Neither	12 (20.7)	13 (21.3)	25(21.0)	
	Somewhat more likely	15 (25.9)	14 (23.0)	29(24.4)	
	More likely	17 (29.3)	33 (54.1)	50(42.0)	
Influence on prescribing nPEP: Patient with history of no regular visits					
	Less likely	17 (29.3)	6 (10.0)	23(19.5)	0.0704
	Somewhat less likely	9 (15.5)	14 (23.3)	23(19.5)	
	Neither	19 (32.8)	20 (33.3)	39(33.1)	
	Somewhat more likely	8 (13.8)	9 (15.0)	17(14.4)	
	More likely	5 (8.6)	11 (18.3)	16(13.6)	
Influence on prescribing nPEP: Patient with history of not adhering to medication					
	Less likely	18 (31.0)	11 (18.3)	29(24.6)	0.4178
	Somewhat less likely	14 (24.1)	14 (23.3)	28(23.7)	
	Neither	16 (27.6)	19 (31.7)	35(29.7)	
	Somewhat more likely	6 (10.3)	7 (11.7)	13(11.0)	
	More likely	4 (6.9)	9 (15.0)	13(11.0)	
Patient requests for nPEP in past 6 months					

Characteristics of Respondents		Miami	Washington DC	Total	Chi square p-value
		N (%)	N (%)		
	Often (once/week)	1 (1.3)	4 (6.5)	5(3.6)	0.1573
	Occasionally (few times/month)	10 (13.3)	14 (22.6)	24(17.5)	
	Rarely (less than once/month)	29 (38.7)	22 (35.5)	51(37.2)	
	Never	35 (46.7)	22 (35.5)	57(41.6)	
It is feasible to provide nPEP in my practice					
	Agree	61 (77.2)	53 (84.1)	114(80.3)	0.5893
	Neutral	9 (11.4)	5 (7.9)	14(9.9)	
	Disagree	9 (11.4)	5 (7.9)	14(9.9)	
There is adequate time to prescribe nPEP					
	Agree	50 (63.3)	54 (85.7)	104(73.2)	**0.0109**
	Neutral	18 (22.8)	6 (9.5)	24(16.9)	
	Disagree	11 (13.9)	3 (4.8)	14(9.9)	
nPEP will promote HIV resistance					
	Agree	32 (40.5)	8 (12.7)	40(28.2)	**0.0005**
	Neutral	19 (24.1)	15 (23.8)	34(23.9)	
	Disagree	28 (35.4)	40 (63.5)	68(47.9)	
nPEP will promote risky behavior					
	Agree	38 (48.1)	9 (14.3)	47(33.1)	**0.0001**
	Neutral	16 (20.3)	22 (34.9)	38(26.8)	
	Disagree	25 (31.7)	32 (50.8)	57(40.1)	
Single greatest concern about prescribing nPEP					
	Would lead to increased risk behavior	13 (20.6)	8 (12.9)	21(16.8)	**0.0004**
	Patient noncompliance with therapy	17 (27.0)	7 (11.3)	24(19.2)	
	Develop resistance to anti-retroviral therapy	9 (14.3)	17 (27.4)	26(20.8)	
	Adverse effects of therapy	4 (6.4)	7 (11.3)	11(8.8)	
	Cost of therapy	9 (14.3)	10 (16.1)	19(15.2)	

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Characteristics of Respondents		Miami	Washington DC	Total	Chi square p-value
		N (%)	N (%)		
	Divert resources from treating HIV+	5 (7.9)	0 (0)	5(4.0)	
	Other	6 (9.5)	2 (3.2)	8(6.4)	
	No concerns	0 (0)	11 (17.7)	11(8.8)	

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Table 2

Bivariate relationships of respondent characteristics and having prescribed nPEP in the past

Characteristics of Respondents		Prescribed nPEP[1]	Never Prescribed nPEP[2]	Chi square	p-value[3]
		N (%)	N (%)		
Patients seen in one month					
	0–50	4 (6.0)	15 (22.1)	9.96	**0.0411**
	51–100	12 (17.9)	10 (14.7)		
	101–150	4 (6.0)	8 (11.8)		
	151–200	9 (13.4)	5 (7.4)		
	200+	38 (56.7)	30 (44.1)		
More than 20 Patients with HIV seen in practice in last 3 months					
	Yes	61 (91.0)	51 (72.9)	7.59	**0.0059**
More than 20 Patients with HIV seen by provider in last 3 months					
	Yes	55 (82.1)	45 (64.3)	5.50	**0.0190**
Written nPEP protocols in place					
	Yes	23 (34.9)	12 (17.1)	6.17	**0.0456**
	No	38 (57.6)	48 (68.6)		
	Unsure	5 (7.6)	10 (14.3)		
Patient requests for nPEP in past 6 months[4]					
	Often (>once/week)	5 (7.6)	0 (0.0)	67.28	**<0.0001**
	Occasionally (few × a month)	23 (34.9)	1 (1.4)		
	Rarely (<once/month)	33 (50.0)	18 (25.7)		
	Never	5 (7.6)	51 (72.9)		
There are barriers to prescribing nPEP at my facility					
	Yes	18 (26.9)	29 (42.7)	3.70	0.0543
CDC has formal guidelines regarding the use of nPEP (Answer: True)					
	True	60 (89.6)	42 (73.7)	6.21	**0.0448**
	False	0 (0.0)	2 (3.5)		
	Don't know	7 (10.4)	13 (22.8)		

Characteristics of Respondents		Prescribed nPEP[1]	Never Prescribed nPEP[2]	Chi square	p-value[3]
		N (%)	N (%)		
Influence on prescribing nPEP: Patient has a partner, unknown HIV status					
	Less likely	3 (4.6)	4 (7.8)	10.32	**0.0353**
	Somewhat less likely	5 (7.7)	12 (23.5)		
	Neither more or less likely	15 (23.1)	15 (29.4)		
	Somewhat more likely	23 (35.4)	8 (15.7)		
	More likely	19 (29.2)	12 (23.5)		
Influence on prescribing nPEP: Patient is a victim of sexual assault					
	Less likely	1 (1.5)	0 (0.0)	7.96	0.0932
	Somewhat less likely	0 (0.0)	3 (5.8)		
	Neither more or less likely	1 (1.5)	3 (5.8)		
	Somewhat more likely	7 (10.6)	9 (17.3)		
	More likely	57 (86.4)	37 (71.1)		
It is feasible to provide nPEP in my practice					
	Agree	61 (91.0)	48 (68.6)	11.20	**0.0037**
	Neutral	2 (3.0)	12 (17.1)		
	Disagree	4 (6.0)	10 (14.3)		
nPEP will promote HIV resistance					
	Agree	5 (7.5)	31 (44.3)	31.01	**<.0001**
	Neutral	14 (20.9)	19 (27.1)		
	Disagree	48 (71.6)	20 (28.6)		
nPEP will promote risky behavior					
	Agree	9 (13.4)	33 (47.1)	20.10	**<.0001**
	Neutral	20 (29.9)	18 (25.7)		
	Disagree	38 (56.7)	19 (27.1)		

[1] Denominators are the number that had prescribed nPEP who answered this question. Denominators differ due to missing data

[2] Denominators are the number that had NOT prescribed nPEP who answered this question. Denominators differ due to missing data

[3] Only responses with a p-value smaller than .10 are included in Table 2, all variables in Table 1 were examined

[4]The statistical test collapsed the Often and Occasionally responses due to small cell sizes

Table 3

Multivariable model for having prescribed nPEP in the past

		OR	95% CI
INTIAL MULTIVARIATE MODEL			
Site			
	Miami	0.66	(0.24, 1.82)
	Washington, DC	1.00	
Patient requests for nPEP in past 6 months			
	Have had requests	21.53	(6.50, 71.34)
	Have never had requests	1.00	
nPEP will promote risky behavior			
	Agree	0.14	(0.04, 0.55)
	Neutral	0.40	(0.13. 1.20)
	Disagree	1.00	-
MULTIVARIATE MODEL EXCLUDING PATIENT REQUESTS			
Site			
	Miami	0.84	(0.35, 2.04)
	Washington, DC	1.00	-
More than 20 Patients with HIV seen in practice in last 3 months			
	Yes	6.33	(1.94, 20.67)
	No	1.00	-
Written nPEP protocols in place			
	Yes	7.49	(1.47, 38.27)
	No	2.46	(0.58, 10.43)
	Unsure	1.00	-
Are there barriers to prescribing nPEP at your facility?			
	Yes	0.33	(0.13, 0.83)
	No	1.00	-
nPEP will promote risky behavior			
	Agree	0.05	(0.02, 0.19)
	Neutral	0.22	(0.08, 0.61)
	Disagree	1.00	-