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High levels of concomitant behavioral health disorders among patients presenting for HIV non-occupational post-exposure prophylaxis at a Boston community health center between 1997 and 2013

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Abstract

A paucity of information regarding mental health exists for patients presenting for HIV non occupational post-exposure prophylaxis (nPEP). We reviewed electronic medical records of 894 adult nPEP patients seen at a large Boston community health center between 1997 and 2013. Of 821 patients with consensual sexual exposures, 88.3% were men who have sex with men, and 40.0% had a mental health diagnosis. Diagnoses included: depression (24.4%), anxiety (21.9%), attention deficit disorder (7.8%), post-traumatic stress disorder (3.3%), and psychotic disorders (3.3%). Of 129 patients with substance use disorders, alcohol dependence (65.9%) and crystal methamphetamine (43.4%) predominated. Unprotected receptive anal intercourse was associated with psychotic disorders (aOR=4.86;95% CI:1.76–13.5) and substance use disorders (aOR=1.89;95% CI:1.28–2.80). Substance use at the time of exposure was associated with: depression (aOR=1.95;95% CI:1.36–2.80), anxiety (aOR=2.22;95% CI:1.51–3.25), attention deficit disorder (aOR=1.96;95% CI:1.18–3.27), and substance use disorder (aOR=4.78;95% CI:3.30–6.93). Mental illness should be screened for and addressed at nPEP visits to optimize HIV risk-reduction.

Keywords

HIV; PEP; nPEP; syndemic; mental illness

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All study procedures were approved by the Fenway Health Institutional Review Board.

INTRODUCTION

Approximately 50,000 people become HIV-infected in the United States each year (1), reflecting an urgent need to expand HIV prevention efforts. Mental illness has been shown to be associated with behaviors that increase HIV transmission risk in multiple studies since the early years of the epidemic. Such behaviors include having multiple sex partners, unprotected anal sex, inconsistent condom use, trading sex for money, drugs, or a place to stay, casual sexual encounters, sexual activity after use of drugs, drug dependence in general, and decreased sexual self-efficacy (2–7). Studies have additionally demonstrated that HIV is more prevalent among patients with severe mental illness in various settings (8–10). People who become HIV-infected in the United States are more likely to report having multiple sex partners, exchanging sex for drugs or money or housing, stimulant or alcohol use during sexual activity, inconsistent condom use, and casual sexual encounters than those who are not infected (2,3,11,12). While nonoccupational post-exposure prophylaxis (nPEP) has long been recommended for biomedical HIV prevention after high-risk exposures (13), nPEP is underutilized (14–17). In addition, nPEP completion rates are poor in some settings (18–26), and few studies have explored underlying psychosocial factors that may impede nPEP adherence or have demonstrated the benefit of additional behavioral counseling for select high-risk patients (27,28).

Psychosocial and mental health problems have been shown to frequently be interrelated among men who have sex with men (MSM). The frequent co-occurrence and interaction of these conditions meet the definition of *syndemics*, (i.e. synergistic epidemics). Among MSM, studies have demonstrated how multiple co-occurring mental health or psychosocial conditions combine and interact to augment HIV transmission, for example, via an increase in unprotected anal sex (4,29,30). Although this relationship has been well described among MSM in terms of both HIV risk and HIV prevalence in the United States, to date no studies have considered the role of syndemics in the context of nPEP, and few have assessed the role of syndemics in event-level HIV risk behavior.

Since the publication of the latest CDC guidelines in 2005 (13), comorbid mental illness among nPEP users has not received significant attention. A better understanding of behavioral health issues in nPEP users is relevant for HIV prevention efforts, particularly in light of studies demonstrating the efficacy of pre-exposure prophylaxis (31–33). In this study, we report the prevalence of mental health disorders among patients presenting for nPEP at the largest center providing this service in New England from 1997 to 2013, and assess the relationship between individual mental health conditions, as well as syndemic mental health conditions, and event-level substance use and unprotected receptive anal intercourse (URAI).

METHODS

Participants and Procedures

Data were extracted from electronic medical records for all patients seeking nPEP at a large community health center in Boston, MA from the inception of this center's electronic medical record on July 1, 1997 to August 1, 2013. Medical records were screened for

eligibility for all patients who had a prescription for antiretroviral medication without a diagnosis of HIV. Inclusion criteria included: 1) Age 18 years or older at time of first nPEP course; 2) Documentation of sexual and/or non-occupational intravenous drug needle exposure to HIV as reason for seeking nPEP; and 3) Negative HIV test at time of presentation for each nPEP course. Patients with new HIV infections confirmed within 30 days of nPEP, patients who received a prescription for nPEP but did not follow up in person, patients prescribed PEP for occupational or non-sexual exposure, and patients enrolled in nPEP clinical trials were excluded. Analyses in the present study were restricted to patients who reported consensual sexual exposure. Patients who sought nPEP for sexual assault or needle sharing were excluded. As part of a comprehensive review of the nPEP experience at this Boston community health center, secular trends regarding choice of medication and incident HIV infection after nPEP initiation were analyzed separately (34,35), hence the exclusion of patients that tested positive within 30 days of presentation for nPEP in the current study. While the inclusion of such patients was not thought to influence this particular analysis, those with new diagnoses within 30 days may have had other recent high-risk behaviors preceding that which led to the nPEP presentation. Therefore, it is possible that there is something different about the excluded group compared to those who had a one-time high-risk exposure and presented immediately for care.

Two study investigators performed data abstraction, which consisted of thorough manual review of electronic medical records. De-identified data of those patients who met inclusion criteria were entered into a database that was designed by a group of study team members. Clinical data that did not have a clear coding selection was first discussed by both persons doing data abstraction. Records for which ambiguity remained were referred to the principal investigator, who ultimately advised upon the appropriate coding selection.

Measures

Mental health and syndemic conditions—Data was abstracted from medical records related to depression, anxiety, attention deficit disorder (ADD), substance use disorder, post-traumatic stress disorder (PTSD), bipolar disorder, and/or schizophrenia. Specific substance use disorders included the following: alcohol, crystal methamphetamine, cocaine, MDMA/ecstasy, heroin, other opiates or narcotics, lysergic acid diethylamide (LSD), marijuana, gamma-Hydroxybutyric acid (GHB), ketamine, and benzodiazepines. In order to be coded as having a substance use disorder, patients must have had documentation in their medical record of 1) diagnosis and 2) treatment, or referral for treatment, with psychotherapy and/or pharmacotherapy prior to being started on nPEP based on manual review of the problem list, medication history, and clinic notes in each patient's record. Childhood physical abuse has been associated with high-risk sexual behaviors among MSM and HIV infection (36–39), and PTSD has been reported to be relatively common in young sexual minority men (40), and associated with HIV risk and challenges to engaging in care (41,42), hence the inclusion of PTSD in this study. In order to limit the potential bias of over-diagnosis of mental illnesses, we chose to use include mental health conditions that were treated or referred for treatment rather than rely on medical chart diagnoses or International Classification of Diseases (ICD) codes alone. Due to small numbers, bipolar disorder and schizophrenia were combined and coded as psychotic disorders. A score for the total number of syndemic

mental health conditions was created by summing the number of co-occurring mental health conditions together. The syndemic score ranged from 0 (no co-occurring mental health conditions) to 5 (5 co-occurring mental health conditions).

Event-level sexual risk—Reasons for seeking nPEP (i.e., consensual sexual exposure in which the condom broke or no condom was used, sexual assault, or needle exposure) were extracted from the medical records. For sexual exposures, the type of sexual exposure (oral, anal, or vaginal) and sexual role (insertive and/or receptive) were extracted from medical records. URAI was coded as any anal sexual encounter in which no condom use was attempted in which the patient was the receptive partner. Substance use at the time of exposure was also extracted from medical records and included substances taken immediately prior to or during the sexual encounter per patient report, as documented in the medical record.

Demographics—Data including patient's age at the beginning of each nPEP course, self-reported race/ethnicity (coded as white versus all other racial/ethnic identities), insurance status (coded as any insurance or none), whether or not the patient was engaged in primary care at the community health center prior to the nPEP course, self-reported gender identity (male, female, transgender male to female, transgender female to male, or genderqueer), and gender of patient's partners (coded exclusively male partners versus not). Each patient could have had one or multiple nPEP courses over the study period.

Statistical Analysis

Descriptive characteristics for the sample were calculated with medians and interquartile ranges (IQR) for continuous variables and proportions for categorical variables. The prevalence of each mental health condition was calculated for the overall study sample, and by substance use disorder (any or specifically alcohol dependence). Logistic generalized estimating equation (GEE) models were used to assess the relationship between each mental health condition and 1) URAI and 2) substance use in the context of the exposure that led to nPEP intake. A GEE model approach was chosen to account for correlation within subjects induced by the fact that an individual patient could have had used nPEP multiple times. A population averaged GEE model was selected to model average responses in the population, and an exchangeable correlation structure was selected, assuming that observations within a subject were equally correlated. Bivariate logistic GEE models for each mental health condition separately as well as a model for syndemic factors were used to assess the unadjusted relationship, and then separate multivariable models for each mental health condition as well as a model for syndemic factors were built adjusting for variables that were conceptualized to be potential confounding factors or that differed by number of syndemic conditions. Models were adjusted for the following: age, year of nPEP presentation, race/ethnicity (categorized as White, Black, Asian, Latino/a, or other), insurance status (any or none), primary care status (engaged in primary care or not), gender identity (categorized as male, female, or transgender/genderqueer), and if the participant reported an MSM exposure or not. Finally, bivariate and multivariable logistic GEE models were built to assess the association between syndemic mental health conditions (modeled additively) and 1) URAI and 2) substance use at the time of exposure.

RESULTS

Of 894 patients who sought nPEP between 1997 and 2013, 91.8% sought nPEP for reasons other than sexual assault or needle exposure (i.e. condom broke, was removed, or use was not attempted), representing 1,162 unique nPEP courses in 821 patients. Table 1 lists characteristics of the study sample by number of co-occurring mental health conditions. Median age at first nPEP course was 32.5 years (IQR 28.8 to 40.4 years). Most (95.7%) of the sample reported being male, 2.9% were female, 0.5% were transgender males, 0.6% were transgender females, and 0.2% described themselves as genderqueer. Of individuals who self-identified as male, 725 (92.2%) had exclusively male partners and 29 (3.5%) had male and female partners. Thirty-two (3.9%) reported sex with exclusively female partners. Of the 821 patients, 72.9% identified as white, 11.0% as Latino, 6.8% as Black or African American, 5.0% as Asian, and 5.2% as other. More than half of the sample (62.9%) reported receiving their primary care at the community health center.

Table 2 lists the prevalence of underlying mental health conditions in the overall sample and by substance use status (including no substance use disorder, any substance use disorder, and alcohol and crystal methamphetamine use disorders specifically). Of the 821 patients, 60.0% had no documented mental health conditions, 16.7% had 1, 13.3% had 2, 7.4% had 3, 2.4% had 4, and 0.2% had 5 diagnosed mental health conditions, respectively. The prevalence of each mental health condition tended to be higher among individuals with substance use disorders than in the overall study sample.

Table 3 lists the results of separate bivariate and multivariable GEE models assessing the association between each mental health condition and outcomes including 1) URAI and 2) substance use at the time of exposure. In a model adjusted for multiple sociodemographic factors, having a psychotic disorder (aOR 4.86, 95% CI 1.76 to 13.5, $P=0.002$) and substance use disorder (aOR 1.89, 95% CI 1.28 to 2.80, $P=0.001$) were significantly associated with increased odds of engaging in URAI at the time of exposure, compared to all other exposure modalities. In a separate model adjusted for sociodemographic factors, each additional co-occurring mental health condition was associated with a 21% increase in the odds of URAI at the time of exposure (aOR 1.21, 95% CI 1.06 to 1.38, $P=0.005$). Mental health conditions that were associated with increased odds of substance use at the time of exposure included depression (aOR 1.95, 95% CI: 1.36 to 2.80, $P<0.001$), anxiety (aOR 2.22, 95% CI: 1.51 to 3.25, $P<0.001$), attention deficit disorder (aOR 1.96, 95% CI: 1.18 to 3.27, $P=0.01$), and substance use disorder (aOR 4.78, 95% CI: 3.30 to 6.93, $P<0.001$). Each additional co-occurring mental health condition (syndemic) was associated with a 60% increase in odds of substance use at the time of exposure (aOR 1.61, 95% CI 1.40 to 1.85, $P<0.001$).

DISCUSSION

In this retrospective study of nPEP use, we observed a high prevalence of mental illness and substance use among primarily MSM presenting for nPEP over a 16-year period. Depression and anxiety were particularly common among individuals presenting for nPEP with any substance use disorder but most notably with alcohol and crystal methamphetamine use

disorders. Several mental health conditions were associated with substance use at the time of exposure and URAI. Similar trends have been previously associated with increased risk of HIV transmission in a large, multi-site cohort of HIV-negative MSM (43) and notably in young MSM aged 16 to 25 (44). Alcohol dependence, in particular, has also been associated with high-risk sex among black MSM in the Boston area, outside of the setting of nPEP (45). While depression and anxiety were associated with URAI, only psychotic disorders and having a substance use disorder were statistically significantly associated with URAI after adjusting for demographic factors. In addition, there was a greater adjusted odds of substance use at the time of exposure among patients with depression, anxiety, and attention-deficit disorder.

A growing literature has described that a combination of psychosocial and behavioral factors may act synergistically, or syndemically, to increase the risk of HIV transmission (4,7,46,47). In this study, we found that the co-occurrence of multiple mental health conditions was associated with increased odds of both event-level substance use and URAI, suggesting a syndemic phenomenon between mental health conditions and event-level HIV risk-taking behavior. To our knowledge, this is the first study to assess the existence of a syndemic among individuals seeking nPEP, as well as a relationship with event-level HIV risk behavior. Comprehensive HIV prevention interventions that address not only sexual risk-taking behavior but mental health conditions may have the greatest potential to mitigate HIV risk among individuals with co-occurring mental health conditions.

While all of the exposures included in the study were high-risk by virtue of the fact that nPEP was prescribed, individuals who reported URAI were most likely to have concomitant mental health and substance use disorders. Given that URAI is associated with more than 10 times the risk of HIV infection than unprotected insertive anal intercourse, vaginal intercourse, or oral intercourse (48), individuals who present for nPEP after engaging in unprotected receptive anal intercourse should also be considered for pre-exposure prophylaxis, particularly if their behavioral patterns suggest recurrent risk, if they remain HIV-uninfected upon completing nPEP. Prior survey data from this setting demonstrated that patients continue to engage in high-risk behavior during nPEP (49), emphasizing the importance of combining behavioral and biomedical approaches to patients presenting for nPEP. Several studies have demonstrated a benefit of offering more intensive behavioral interventions to sexually high-risk patients, including dedicated and more frequent counseling sessions (27,50). Furthermore, behavioral HIV prevention interventions for patients with severe mental illness have been shown to be cost-effective (51,52). Given that this sample of nPEP users shares similar characteristics to high-risk, HIV-uninfected MSM cohorts, it would be logical that nPEP patients that have comorbid mental health diagnoses would be excellent candidates for intensive post-exposure counseling beyond the current standard of care provided to all nPEP patients, although this would need to be corroborated with a randomized study.

Given the high prevalence of mental illness recorded in this study, it is critical that nPEP providers in all settings are trained to screen for mental illness and either begin the indicated treatment while managing nPEP with the client, or make prompt referrals upon diagnosis of a treatable condition. Previous studies have demonstrated that mental illness and alcohol and

intravenous drug use are associated with adverse clinical outcomes and poor antiretroviral medication adherence among HIV-infected individuals (53), which could limit the protective effects of nPEP. If mental illness and substance use are recognized early on, then nPEP may be an opportune moment at which to engage these patients in mental health care and evidence-based behavioral interventions.

The results of this study must be considered in the context of several limitations. This was a retrospective study that relied on data recorded in electronic medical records. It is possible that there were individuals with undiagnosed or unreported mental health conditions. Some patients either received primary care at another facility or may not have been engaged in primary care at all, so it is unknown whether such participants had mental health conditions diagnosed or followed through with treatment at other health centers. Therefore, the true prevalence of mental illness and substance use may be higher in this sample of MSM who presented for nPEP. Much of the data in this study relied on self-report, including nature of the exposure that led to seeking nPEP (i.e. unprotected anal sex). It is possible that social desirability bias influenced these results, and participants may have reported a broken condom instead of condomless anal sex. Since the chart review was performed manually, human error in either data abstraction, coding, or entering data into the database could have either overestimated or underestimated the prevalence of respective mental health conditions and/or event-level behaviors. We believe this effect was minimal since one of approximately every 20 charts was double checked for precision by at least one of the study investigators during data abstraction and the data entry process. Despite these limitations, our study is the first to consider the role of mental health conditions on HIV risk during exposures that lead to nPEP. These results provide valuable evidence of the role of mental health conditions in HIV risk in this population.

FUTURE DIRECTIONS

Particularly with the increased availability of PrEP, offering a comprehensive nPEP strategy that proactively includes mental health considerations is necessary to ensure a more stable transition to PrEP for patients who engage in recurrent high-risk behavior. Likewise, the expansion of PrEP programs should be an impetus for patient and provider education about nPEP to increase utilization for patients with suboptimal PrEP adherence due to mental illness and substance use, as well as for those not receiving PrEP. Treating mental illness and recreational substance use could also potentially improve nPEP medication completion rates and safer sex, as well as reduce the likelihood of requiring emergent prophylaxis in the future. Chemoprophylaxis alone is unlikely to stem HIV transmission on a global scale without addressing the psychosocial aspects directly and indirectly influencing high-risk behavior. Additional prospective research will be necessary to establish the relationships between mental health, substance use, HIV transmission, and other outcomes among those who utilize nPEP and PrEP.

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Table 1

Demographics of study sample

	Number of Co-Occurring Mental Health Conditions (Syndemic)						Overall (N=821)
	0 (N=493)	1 (N=136)	2 (N=109)	3 (N=61)	4 (N=20)	5 (N=2)	
Age, years (median, IQR)	31.6 (26.3 to 38.6)	35.1 (29.1 to 43.0)	35.0 (28.3 to 41.7)	32.0 (25.9 to 44.0)	36.1 (30.8 to 41.6)	26.7 (22.0 to 31.4)	32.5 (28.8 to 40.4)
<i>Gender identity</i>							
Male	472 (95.7%)	130 (95.6%)	105 (96.3%)	59 (96.7%)	18 (90.0%)	2 (100%)	786 (95.7%)
Female	19 (3.9%)	2 (1.5%)	2 (1.8%)	2 (1.6%)	0	0	24 (2.9%)
Transgender man	1 (0.2%)	2 (1.5%)	1 (0.9%)	0	0	0	4 (0.5%)
Transgender woman	1 (0.2%)	2 (1.5%)	1 (0.9%)	0	1 (5.0%)	0	5 (0.6%)
Genderqueer	0	0	0	1 (1.6%)	1 (5.0%)	0	2 (0.2%)
<i>Race/Ethnicity</i>							
White/Caucasian	309 (60.7%)	116 (85.3%)	90 (82.6%)	57 (93.4%)	17 (85.0%)	2 (100%)	591 (72.0%)
Latino	69 (14.0%)	8 (5.9%)	11 (10.1%)	1 (1.6%)	1 (5.0%)	0	90 (11.0%)
African American	44 (8.9%)	5 (3.7%)	5 (4.6%)	1 (1.6%)	1 (5.0%)	0	56 (6.8%)
Asian	34 (6.9%)	4 (2.9%)	2 (1.8%)	1 (1.6%)	0	0	41 (5.0%)
Other	37 (7.5%)	3 (2.2%)	1 (0.9%)	1 (1.6%)	1 (5.0%)	0	43 (5.2%)
Engaged in primary care at Fenway	240 (48.7%)	98 (72.1%)	97 (89.0%)	59 (96.7%)	20 (100%)	2 (100%)	516 (62.9%)
Any insurance	285 (57.8%)	99 (72.8%)	79 (72.5%)	46 (75.4%)	16 (80.0%)	1 (50.0%)	526 (64.1%)

Prevalence of mental health disorders prior to first NPEP use by any substance use disorder, alcohol use disorder, and crystal methamphetamine use disorder

Table 2

	Among individuals with no substance use disorder (N=692)	Among individuals with any substance use disorder (N=129)	Among individuals with alcohol use disorder (N=85)	Among individuals with crystal meth use disorder (N=56)	Overall (N=821)
Major depressive disorder	129 (18.6%)	71 (55.0%)	52 (61.2%)	28 (50.9%)	200 (24.4%)
Generalized anxiety disorder	114 (16.5%)	66 (51.1%)	49 (57.7%)	23 (41.8%)	180 (21.9%)
Attention deficit disorder	45 (6.5%)	19 (14.7%)	15 (17.7%)	9 (16.4%)	64 (7.8%)
Post-traumatic stress disorder	14 (2.0%)	13 (10.1%)	8 (9.4%)	9 (16.4%)	27 (3.3%)
Bipolar disorder	10 (1.5%)	15 (11.6%)	12 (14.1%)	6 (10.9%)	25 (3.1%)
Schizophrenia	1 (0.1%)	1 (0.8%)	0	0	2 (0.2%)

Table 3

Associations between 1) unprotected anal intercourse and 2) substance use at time of exposure that led to NPEP and preexisting mental health conditions, including a prior diagnosis of depression, anxiety, attention deficit disorder, PTSD, psychotic disorder, substance use disorder, and all mental health conditions summed in an additive fashion (syndemics)

	Unprotected Receptive Anal Intercourse			Any Substance Use at Time of Exposure		
	OR ¹ (95% CI)	P	aOR ² (95% CI)	OR ¹ (95% CI)	P	aOR ² (95% CI)
Depression	1.49 (1.11 to 2.01)	0.008	1.33 (0.96 to 1.84)	1.81 (1.31 to 2.51)	< 0.001	1.95 (1.36 to 2.80)
Anxiety	1.47 (1.07 to 2.01)	0.02	1.23 (0.87 to 1.73)	1.88 (1.34 to 2.64)	< 0.001	2.22 (1.51 to 3.25)
Attention deficit disorder	1.17 (0.73 to 1.87)	0.51	0.92 (0.57 to 1.48)	2.06 (1.27 to 3.34)	0.003	1.96 (1.18 to 3.27)
Post-traumatic stress disorder	1.63 (0.81 to 3.27)	0.17	1.35 (0.66 to 2.76)	1.07 (0.49 to 2.35)	0.87	0.91 (0.40 to 2.09)
Psychotic disorder ³	4.12 (1.65 to 10.3)	0.002	4.86 (1.76 to 13.5)	1.46 (0.70 to 3.03)	0.31	1.55 (0.73 to 3.33)
Substance use disorder	2.17 (1.50 to 3.14)	< 0.001	1.89 (1.28 to 2.80)	4.41 (3.16 to 6.15)	< 0.001	4.78 (3.30 to 6.93)
Syndemic ⁴	1.28 (1.14 to 1.44)	< 0.001	1.21 (1.06 to 1.38)	1.49 (1.33 to 1.67)	< 0.001	1.61 (1.40 to 1.85)

Each line represents a separate model for each mental health condition

¹Logistic generalized estimating equation

²Logistic generalized estimating equation adjusted for age at NPEP visit, race/ethnicity, insurance status (any/none), primary care status, and gender identity

³Includes a diagnosis of bipolar disorder and/or schizophrenia

⁴Models the total number of psychiatric disorders in an additive fashion; bold indicates $P < 0.05$