

# Adherence and Characteristics of HIV Post-Exposure Prophylaxis for a Population in Tel Aviv of Men Who Have Sex with Men

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**ABSTRACT:** **Background:** Pre-exposure prophylaxis (PrEP) for populations at high risk for human immunodeficiency virus (HIV) is still not available in Israel.

**Objectives:** To analyze post-exposure prophylaxis (PEP) treatment adherence rates among adult men in Tel Aviv, Israel, who have sex with men (MSM), and to obtain data on the demographics of PEP users, exposure types, timeline of exposure and PEP administration, incidence of side effects, number of treatments per individual, and satisfaction with selected elements of treatment provision.

**Methods:** The authors conducted an observational cohort study of adult MSM who requested PEP treatment in the Tel Aviv Sourasky Medical Center. Information from patients receiving treatment between January 2013 and June 2014 was obtained through telephone interviews by means of a 30-item questionnaire.

**Results:** Of 336 individuals requesting PEP treatment, 255 (75.9%) were adult MSM, and 100 (39.2%) satisfactorily completed the interview. The average age of the study cohort was 32.4 years (standard deviation of 7.5). Ninety-one (91%) reported completing a full 28-day course of treatment, 84% reported side effects, and 20% underwent multiple courses. Satisfaction was high for interactions with the HIV specialists. Patient experience with PEP treatment in the emergency room setting, and follow-up were inadequate and deficient.

**Conclusions:** PEP adherence rates in Tel Aviv were significantly higher than previously reported. PEP should be administered in designated community settings. PrEP as a general treatment policy might suit the MSM population in Tel Aviv.

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**KEY WORDS:** human immunodeficiency virus (HIV), post-exposure prophylaxis (PEP), pre-exposure prophylaxis (PrEP), men who have sex with men (MSM)

of homosexual men in California and New York over 30 years ago [1]. By the end of 2014, the World Health Organization estimated that 36.9 million people were living with HIV globally, and that two million had been newly infected that year [2]. There are several populations at high risk of infection, including intravenous (IV) drug users and people who engage in unprotected sexual intercourse. In the United States, although men who have sex with men (MSM) are estimated to represent only 4% of men [3], they accounted for 63% of new HIV infections in 2010, representing a 12% rise compared to the 2008 figures [4]. The two main groups of individuals who request post-exposure prophylaxis (PEP) are health care personnel and the general public. The former group is infected in a medical setting and usually receives professional and prompt medical care. The non-health care population is separated into subgroups based on lifestyle, exposure type, infection route and their relative infection rates. Of all the routes of infection, the most prevalent is unprotected sexual contact, closely followed by the use of contaminated syringes among IV drug users [5]. A single unprotected exposure to a known HIV-positive source through anal receptive sexual contact leads to an estimated 138 infections per 10,000 incidents, while unprotected anal insertive sexual contact poses a much lower risk, estimated to be 11 infections per 10,000 incidents [6].

As a rule, the higher the viral load of the source, the higher the rate of infection. Chronically untreated or acutely infected patients pose a higher risk of infection compared to individuals on an effective anti-retroviral treatment regimen, whose risk of infection is practically nil [7,8]. When first exposed, and for a short 72 hour window of time, PEP consisting of a combination of three medications over the course of 28 days may reduce the rate of infection by up to 81% [9-11]. U.S. and European guidelines allow physicians in those countries to also prescribe pre-exposure prophylaxis (PrEP), which has been gaining recognition as the recommended treatment for high-risk populations, such as MSM. Unfortunately, those guidelines have yet to be approved for use in many countries, including Israel.

In Israel 8449 new cases of HIV/AIDS were registered between 1981 and 2014. In 2014, 468 new cases were reported,

**A**cquired immune deficiency syndrome (AIDS) is a severe viral syndrome caused by human immunodeficiency virus (HIV) infection, which was first reported in a small number

with an incidence of 56.4 new cases per million population [12]. In search of ways to improve treatment efficacy, we looked at the characteristics of this heterogeneous population, the routes of infection, and the rates of adherence. We also sought to expose the weaknesses of Israel's health care system in managing exposure cases and in communicating preventive measures to specific high-risk populations. A previous study in Israel on PEP requests and administration was generalized to various types of HIV exposure, including health care personnel and the general public, and did not address treatment adherence rates. In addition, there was no focus on MSM as a group, which constitutes the largest population applying for PEP in Tel Aviv [13].

## PATIENTS AND METHODS

The study population includes MSM older than 18 years of age who were treated with PEP in the Tel Aviv Sourasky Medical Center between January 2013 and June 2014. The primary objective of this observational cohort study was to analyze PEP treatment adherence. The secondary objective was to obtain data on the demographics of PEP users, exposure types, timeline of exposure and PEP administration, incidence of side effects, number of PEP treatments per individual, type of follow-up, and satisfaction with selected elements of treatment provision.

Telephone interviews were conducted by a single physician (N.O.) during the 3 month period July to October 2014. During that time five attempts were made to contact each of the 255 patients.

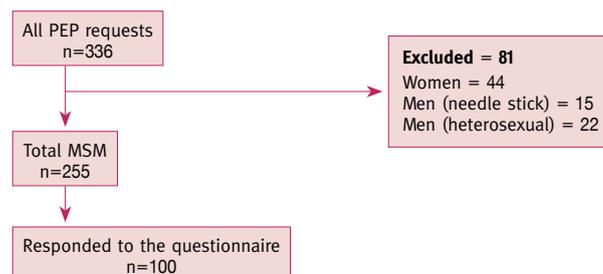
The questionnaire was approved by Sourasky's ethics committee, and each participant verbally approved participation in the study. The structured questionnaire designed for the current investigation consisted of 30 items and the respondents were asked to score each one from 1 to 5 (1 = do not agree at all, 5 = agree entirely). At the end of each interview the participants were asked to evaluate, in their own words, their level of satisfaction with the whole process of administering the PEP treatment. All PEP regimens were protease inhibitor-based.

## RESULTS

A total of 336 patients visited the hospital's emergency room (ER) for the purpose of obtaining PEP after having been exposed to a suspected HIV source during the study period; 255 (75.9%) of them involved adult MSM [Figure 1]. A full telephone interview was completed by 100 men (39.2%), who comprised the study group and their data were analyzed. Non-respondents could not be reached by phone, or heard the introduction and chose not to participate in the study.

The average age of those PEP recipients who responded to the interview was 32.4 years [standard deviation (SD)  $\pm$  7.5] at

**Figure 1.** Population that requested PEP treatment



**Table 1.** Treatment characteristics of respondents

	Full 28 day course (n=91)	Partial course (n=9)	Total population (n=100)
Age, years Average (SD)	32.63 ( $\pm$ 7.58)	30.89 ( $\pm$ 7.36)	32.47 ( $\pm$ 7.57)
<b>Hours since exposure</b>			
≤ 24	68	7	75
≤ 48	18	2	20
≤ 72	5	0	5
> 72	0	0	0
<b>Side effects</b>			
Mild to moderate	56	4	60
Severe	35	5	40
<b>No. of PEP courses</b>			
One	66	6	72
Two	14	2	16
> two	4	0	4
No answer	7	1	8
<b>Regular (twice yearly) HIV testing</b>			
No	28	1	29
Yes	63	8	71
<b>Type of sexual contact</b>			
Penetrative	34	3	37
Receptive	23	4	27
Both	27	2	29
Other	7	0	7

SD = standard deviation

the time of treatment administration [Table 1]. Ninety-one of the respondents (91%) reported having completed a full 28 day course of treatment.

The respondents waited an average of 20.4 hours (SD  $\pm$  19.0) from the time of exposure until arrival at the ER. Side effects, which were rated according to the extent to which they interfered with daily activities, were reported by 84 participants (84%), and 40% of the total population reported them as being severe.

Of the 100 respondents, 20 (20%) reported having undergone more than one course of PEP, with an average of 2.3 courses per individual. Seventy-one respondents claimed that they underwent regular HIV tests, while 24 (24%) reported having undergone only one post-exposure blood test. Ninety-seven respondents (97%) had requested treatment after possible expo-

sure through unprotected sexual contact, of whom 38% reported penetrative sexual contact, 28% reported receptive contact, and 30% reported a combination of the two.

Both the ER visit and the treatment procedures were perceived as stressful events, while approval ratings for the HIV medical clinic were high [Table 2]. The media were the main source of information on the availability of PEP treatment [Table 2].

## DISCUSSION

Tel Aviv is home to Israel's largest LGBTQ community (lesbian, gay, bisexual, transgender and queer), including a substantial MSM population. Tel Aviv Sourasky Medical Center is a tertiary center serving multiple populations at high risk of HIV infection, including MSM and other high-risk populations, such as African immigrants and IV drug users. The adherence of such high risk individuals to PEP as a preventive strategy has never been investigated in Israel.

The PEP administration process is complex and based on the specific characteristics of the exposed person and the circumstances of the exposure [14]. Other than side effects, erroneously delivered PEP treatment is costly and may have serious economic implications. The recommended treatment policy is to administer PEP when the exposure was via a high risk route from an HIV-positive source or from a source at high risk for an HIV infection, and to do so within 72 hours [15]. A threshold of 0.1% infection risk is generally used when deciding to prescribe PEP [16].

Full adherence to treatment in this study was 91%, which is higher than reported in the literature among comparable populations. The latter values varied between 24% and 78%, and they were especially low among sexual assault victims compared to the known high-risk groups [17]. The overall treatment adherence rate was determined in a meta-analysis by Ford and colleagues [18] who reviewed 97 publications with 21,462 initiations of PEP treatment. The average rate of full adherence to the 28 day regimen was 56.6%. MSM had the highest rate of any subgroup, with an adherence of 67.2%. The major reasons for early treatment withdrawal were side effects, primarily nausea or general fatigue [17]. Factors that contributed to a higher adherence rate were detailed explanations of the importance of adherence, regimens with once-daily treatment or fewer medications, the presence of supporting measures to treat side effects, and professional mental health support [19].

In Israel, PEP treatment is primarily administered after visits to the ER due to a lack of community-based solutions. Visiting the ER to initiate PEP treatment is inherently not ideal. None of the respondents had any medical conditions that required an ER visit or hospital care other than their application for PEP. Visiting a busy ER is usually associated with a lack of discretion and lack of privacy. Presumably, patients might respond

**Table 2.** The questionnaire

<b>General</b>	
Were you apprehensive about undergoing PEP treatment?	2.27*
Did you expect to be criticized by the medical staff?	1.89
Were you nervous about requesting treatment? Score your level of anxiety.	3.41
Were you expecting a long and complex bureaucratic process?	2.38
How complex was the actual process?	2.06
Did you think the details of your exposure would be given to government agencies?	1.85
How much weight did the issue of confidentiality have on your final decision?	1.28
Was the process of purchasing the treatment simple?	3.54
Was being followed on the treatment with your family physician problematic?	2.27
Would you have preferred getting initial treatment in a more discreet setting than the emergency room?	4.14
Would you have preferred the follow-up process to be done in a dedicated clinical setting?	3.98
Would you have preferred to be followed by the same physician who initiated your PEP treatment?	3.44
<b>Satisfaction with the HIV clinic physician</b>	
To what degree was the physician a reassuring factor?	4.57
Was the physician patient?	4.59
Did the physician supply you with sufficient relevant information?	4.46
<b>Source of knowledge on PEP availability†</b>	
Friends	27
Personal knowledge	22
Partner	10
Media	37
Israel AIDS Task Force	3
Family physician	4
No response	14

Respondents were asked to score the item from 1 to 5 according to the level of agreement with each question: 1 = do not agree at all, 5 = agree entirely. They were able to choose more than one answer

\*Averages of all responses

†Number of respondents who chose the response

better to medical guidance in a more discreet setting involving less hurried attention on the part of the physician. In addition, post-exposure seekers visiting the ER to receive PEP within the initial 72 hour timeframe are often subjected to long waiting periods before being seen by a physician. Some patients who visit the ER toward the end of this timeframe may find that the wait obliges them to start the treatment later than recommended.

Respondents in our survey were like-minded in their preference to be treated outside the ER in a specialized community-based setting for both the initial treatment and the follow-up process [Table 2], although approval ratings for our HIV clinic were high [Table 2]. A discreet community-based specialized clinic operated by staff trained to provide service for sexually transmitted diseases (STDs) would appear to be an appropriate substitute for the ER. A suitable comparable model is Britain's sexual health clinics, which provide specific services including PEP according to the British Association for Sexual Health and HIV guidelines [20]. Establishing this service in Tel Aviv can be beneficial in terms of providing better treatment for STDs and follow-up, PrEP, and psychosocial and educational solutions for patients, while reducing the number of ER visits.

Notwithstanding the higher success rates gained by antiretroviral treatments over time, limiting exposure still remains the best way to avoid infection. Nevertheless, the high infection rates among several populations, including MSM, indicate a high-risk lifestyle, such as having multiple partners and refraining from using condoms. PrEP is a new therapeutic approach that has been approved by the U.S. Food and Drug Administration and the European AIDS Clinical Society. PrEP may be beneficial to high risk populations by lowering the infection rate by up to 92%. It is offered in the United States to high risk populations, among them MSM, who first test negative for HIV, commit to treatment adherence and participate in a regular follow-up schedule [21-23].

Side effects of treatment are a well-known reason for PEP treatment withdrawal. The PEP regimen in Israel is based mainly on protease inhibitor drugs. Given that integrase inhibitors cause fewer side effects [11], it would follow that they should be preferred when choosing a PEP regimen, as recommended in the current U.S. Department of Health and Human Services guidelines and is the norm in Western Europe. This course of action may further increase compliance rates.

Possible explanations for the high compliance rates among our study participants may be a strong determination to avoid the stigma of being HIV-positive, or the high percent of well-educated individuals in the LGBTQ community [24,25].

Only 37% of the respondents heard about PEP through the media; friends were the second most prevalent source [Table 2]. These low rates indicate that government health officials do not utilize all available methods to spread information on the availability of PEP. Targeting popular LGBTQ internet sites and providing smartphone applications may facilitate the dissemination of this essential information directly to the individuals who need it.

One limitation of our study was the lack of information on PEP recipients who did not complete the telephone interview. The only data available on non-respondents, apart from contact information, were age, request date and consensual sexual activity (yes or no). Also known was whether the source was a known HIV-positive individual (yes or no). From this information we could not deduce any differences between the respondent population and the non-respondents. We could not identify a clear reason for the lack of participation, which could be used as a differentiating factor. For those reasons, we did not run comparison analyses on the two populations, but we found no reason to believe these populations differ one from another. Hence, we assume that the analyzed data were representative of the whole study population, although an unforeseen bias should be considered.

We are aware of the possible correlation between participants' willingness to cooperate and those individuals' adherence rates. With this drawback in mind, we still deduce that, in general, the MSM population in Tel Aviv shows a high com-

mitment level to an orderly and strict treatment regimen, as required by patients who are administered PEP.

The relation between PEP and PrEP adherence levels has not been reported previously. Yet, we believe that the high PEP adherence may imply a high PrEP adherence. We believe that PrEP may prove beneficial and should be considered for implementation by the Israeli health officials for high risk MSMs who frequently engage in unprotected sexual contact.

In summary, post-exposure prophylaxis adherence rates in Tel Aviv are significantly higher than comparative rates in other countries. There is not enough credible information published online or throughout the media about PEP. Non-optimal patient experience with PEP treatment in the ER setting suggests that alternative solutions are needed. MSM's commitment to PEP courses, as well as the rate of PEP users who have applied for PEP more than once, suggest that PrEP might be a more suitable approach for HIV prevention in the MSM community in Tel Aviv.

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