

MESTRADO
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Knowledge and uptake of Post-Exposure Prophylaxis (PEP) among users of the Community Screening Network in Portugal

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M

2020

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SEDE ADMINISTRATIVA

FACULDADE DE **MEDICINA**

INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR

Acknowledgements

First of all, I would like to thank my supervisor Professor Dr. Henrique Barros for his guidance, advise and collaboration throughout my master's research thesis.

To my co-supervisor Paula Meireles, from the bottom of my heart I truly appreciate your effort in making this study a success, without your help it would not have been possible to finish. You are an inspiration for me, I am so grateful for your understanding, dedication, collaboration and assistance during this time.

To my parents, to whom I owe my entire life I dedicate this title to both of you. You are my rock, my loyal fans. Thank you so much for your unconditional support both morally and financially, may God bless you always.

To my friends from the master's program, I am beyond blessed to have met wonderful people from all around the world. Especially Walaa Kinaan and Leopoldo Lucio Da Mata who more than friends they became family. Thank you for cheering me up everyday and supporting me through tough times - you both are my angels.

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List of Abbreviations

AIDS – Acquired Immunodeficiency Syndrome
aMase – Advancing migrant access to health services in Europe
ART- Antiretroviral Treatment
CDC –Center for Disease Control
CI – Confidence intervals
EU - Europe
FTM - Female to Male
FSW – Female sex workers
HIV – Human Immunodeficiency Virus
IDU – Injected drug users
MTF- Male to Female
MSM- Men who have Sex with Men
MSW – Male sex workers
NPEP – Non-occupational Post-Exposure Prophylaxis
NYC – New York City
PEP- Post-Exposure Prophylaxis
PrEP- Pre-Exposure Prophylaxis
PLWHA – People living with HIV/AIDS
PWID – People who injected drugs
PEPSE – Post exposure prophylaxis for sexual exposure
PR – Puerto Rico
SW- Sex Workers
SPSS—Statistical Package of Social Sciences
STI – Sexually Transmitted Infection
STD – Sexually transmitted disease
SAP – Stops Aids Program
SWOP – Sex worker outreach program
TasP – Treatment as prevention
TW – Transgender women
UNAIDS – Joint United Nations Programme on HIV and AIDS
US – United States
WHO- World Health Organization

WOC – Cis-gender women of color

YMSMOW – Young men who have sex with men of color

RESUMO:

Introdução: Os medicamentos antirretrovirais (ARVs) para a prevenção do HIV, como a profilaxia pós-exposição (PEP), têm sido usados para reduzir o risco de infecção pelo HIV. O início da medicação deve ser imediatamente ou até 72 horas após a exposição e por um período de 28 dias para uma eficácia adequada. O conhecimento e a da PEP ainda são escassos entre os grupos populacionais-chave, como homens que fazem sexo com homens (HSH), profissionais do sexo (SW) ou migrantes devido à informação limitada sobre a PEP.

Objetivos: Os objetivos deste estudo foram: (1) Avaliar o conhecimento da profilaxia pós-exposição entre indivíduos, principalmente considerados como grupos populacionais-chave, como homens que fazem sexo com homens, profissionais do sexo ou migrantes que frequentam uma das comunidades- estruturas baseadas no teste de HIV da Rede de Rastreo em Portugal (2) para avaliar a utilização da PEP entre os grupos mencionados acima.

Métodos: A Rede de Rastreo é um estudo prospectivo em curso realizado em 25 centros de rastreo de 16 organizações em Portugal. O CheckpointLX foi o primeiro centro de testagem comunitário a ser lançado em abril de 2011. Conforme mencionado, o CheckpointLX e entre outras organizações fizeram parcerias com esta rede. Todos os maiores de 18 anos que fizeram o teste em um desses centros de janeiro de 2016 a dezembro de 2018 foram convidados a participar. Usamos informações básicas. Calculamos a proporção de conhecimento e utilização de PEP ao longo da vida dos participantes com relação as características sociodemográficas e a combinação das três populações-chave - HSH, migrantes e profissionais do sexo. Também calculamos as razões de prevalência e IC 95% usando a regressão log-binomial.

Resultados: Até o final de dezembro de 2018, encontramos uma proporção de 20% de conhecimento sobre PEP e 10,1% de uso de PEP em grupos-chave que participaram da Rede de Rastreo. O conhecimento foi maior entre os homens (25,3%) que residem em Portugal (20,8%) e tinham entre 25 a 34 anos (27,2%), tinham até ao ensino secundário (22,7%) e se autoidentificaram como gays (49,7%). Assim, os participantes que reportaram ser HSH apenas tinham (n = 1137) (47,3%) de conhecimentos seguidos dos Migrantes - HSH (n = 552) (49,2%). Os participantes que tinham conhecimento adequado são os mesmos participantes que usaram PEP com frequência na vida; homens (11,3%) que residiam em Portugal (6,8%) e tinham entre 25 a 34 anos (11,8%), tinham até ao ensino secundário (12,2%) e se autoidentificaram como gays (12,8%); A utilização de PEP foi considerada mais em Migrantes - HSH (n = 103) (19,7%) seguido por HSH apenas (n = 88) (8,2%).

Conclusão: O conhecimento sobre o PEP na primeira visita a um centro de testes baseado na comunidade foi pobre, portanto, a aceitação do PEP foi pequena. É urgente intensificar os programas educativos e as campanhas publicitárias de forma a aumentar a sensibilização

sobre o PEP, fornecer informações detalhadas sobre o que é o PEP e envolver não só a população em geral, mas também grupos populacionais-chave para a utilização adequada deste método de prevenção. A maioria dos participantes possuem conhecimento inadequado sobre PEP, apenas os usuários de 25 a 34 anos apresentaram maior percentual sobre o conhecimento sobre PEP e responderam que teriam feito uso de PEP durante a vida. HSH prova ter melhor compreensão sobre PEP e, portanto, buscou PEP após se envolver em comportamentos de alto risco. Esses resultados exigem modificações urgentes sobre como a conscientização está sendo disseminada. O aprimoramento das estratégias aumentará o conhecimento sobre PEP, principalmente nas populações de maior risco.

ABSTRACT

Introduction: Antiretroviral medications (ARVs) for HIV prevention such as post-exposure prophylaxis (PEP) have been used to reduce the risk of obtaining HIV infection. Initiation of medication should be immediately or up to 72 hours after being exposed and for a length of 28 day course for proper effectiveness. Knowledge and uptake of PEP is still scarce within key population groups such as men who have sex with men (MSM), Sex Workers (SW) or Migrants due to limited information about PEP.

Objectives: The aims of this study were: (1) To evaluate the knowledge of Post-exposure prophylaxis among individuals, mainly considered as key population groups such as men who have sex with men, sex workers or migrants who attended one of the community-based structures for HIV testing from the Community Screening Network in Portugal (2) to assess uptake of PEP among groups mentioned above.

Methods: The Community Screening Network is an ongoing prospective study conducted at 25 screening centers from 16 organizations from all around Portugal. CheckpointLX was the first community-based testing center to be launched in April 2011. As mentioned, CheckpointLX among other organizations has partnered up with this network. All those over 18 years old who were tested at one of these centers from January 2016 to December 2018 were invited to participate. We used baseline information. We computed the proportion of knowledge and lifetime uptake of PEP according to sociodemographic characteristics and the combination of the three key populations – MSM, migrants and sex workers. We also computed the prevalence ratios and 95% CI using the log-binomial regression.

Results: Until the end of December 2018, we found a proportion of 20% of knowledge about PEP and 10.1% of lifetime use of PEP within key groups who attended the Community Screening. Knowledge was higher among males (25.3%) who reside in Portugal (20.8%) and were between 25 to 34 years of age (27.2%) who had up to secondary level of education (22.7%) and self-identified themselves as gay (49.7%); thus, those participants who selected being MSM only had (n=1137) (47.3%) of knowledge followed by those who were Migrants – MSM (n=552) (49.2%). Those respondents who had adequate knowledge are the same participants who have used PEP frequently in their lifetime; males (11.3%) who reside in Portugal (6.8%) and were between 25 to 34 years of age (11.8%) who had up to secondary educational level of (12.2%) and had self-identified themselves as gay (12.8%); Uptake of PEP was considered more in Migrants – MSM (n=103) (19.7%) followed by MSM only (n=88) (8.2%).

Conclusion: Knowledge about PEP at the first visit to a community-based testing center was poor therefore the uptake of PEP was slight. There is urgent need to intensify educational programs and publicity campaigns in order to increase awareness on PEP, providing detailed

information about what PEP is and to engaged not only the general population but as well key groups for proper usage of this prevention method. Majority of participants had inadequate knowledge of PEP, only those users from 25 to 34 years of age had higher percentage about knowledge of PEP and had answered to have use PEP in their lifetime. MSM proves to have better understanding about PEP and therefore have seek for PEP after engaging in high risk behaviors. These results call for urgent modifications on how awareness is being disseminated; improvement on strategies will increase the knowledge of PEP mainly in populations who are most at risk.

1. Introduction

1.1 HIV/AIDS Background

HIV/AIDS was first discovered around the 1980s where the first cases were describe in gay men in the United States.¹ As seen, HIV/AIDS continues to have devastating outcomes globally with more than 36 millions people living with this chronic disease.^{2,3} Although, a set of prevention methods are available, in 2018 1.7 million people became newly infected with HIV.^{3,4}

UNAIDS has aspire to reach the 90-90-90 goals by 2020 - 90% of people living with HIV diagnosed, 90% of those living with HIV on antiretroviral treatments (ART) and 90% of people receiving ART having undetectable viral load^{5,6} and the 95-95-95 by 2030. Globally estimates shows that 62% of people living with HIV were seeking treatment from those, an 53% of people have undetectable levels of viral load.⁷ Implementation strategies are needed to increase awareness about HIV, its prevention, early diagnosis and treatment.

It has been found that in low and middle income countries mainly in Sub-Sahara Africa there is a (97%) of HIV existing cases. However, there has been a decrease in HIV burden in this region due to the improvement in treatment coverage and availability of prevention methods. On the other hand, an incrementation of HIV cases has been observed in Eastern Europe, Central Asia and Russia, most likely due to limited access of Antiretroviral treatment (ART), stigmatization and the exchange of syringe in high-risk groups.^{3,8,9}

1.2 HIV in Portugal

By the 1980s and early 1990s, Portugal was on the top list of European countries with a significantly high number of HIV infected people. Injected drug users were the core of a brutal outbreak in Portugal.⁵ However, over the years risk behaviors and therapeutics have given optimistic outcomes to control the epidemic presented in Portugal.¹⁰ The introduction of new prevention treatments has decrease the HIV transmission and yet increased the life expectancy of HIV patients.¹¹ In Portugal, the first HIV/AIDS case was diagnosed in 1983. From 1983 until 2017, there were 57.574^{12,13} diagnosed cases of HIV, constituting an alarming public health issue over the past decades. Portugal is one of the countries with highest prevalence of HIV in Western Europe. HIV epidemic is more pronounce in larger cities namely Lisbon and Porto metropolitan areas.¹⁴

In Portugal, heterosexual transmission has been the main transmission mode representing 42% of new HIV cases in 2018.¹⁵ A considerable proportion one-third (40%) of cases of heterosexual transmission are migrants who come from countries with a high generalized HIV epidemics.⁸ Transmission related to sex between men accounted for (48%) in 2018. However this proportion, is higher when looking to specific cities such as Lisbon (65%) and Porto (55.3%).¹⁴ HIV cases due to unsafe infection practices presented a decrease in recent year, representing in 2018 (5.8%) out of the 29,704 new cases reported.⁸

1.3 Key population groups

Key population groups are considered those that are at higher risk of HIV acquisition. UNAIDS has identified these groups as men who have sex with men (MSM), female sex workers (FSW), people who inject drugs (PWID) and migrants; they are mainly considered high risk groups because they come from countries with global epidemics. In most countries, key population groups still face inadequate coverage and limited access to information, prevention, treatment and care; among stigmatization and discrimination these groups should be provided accessibility to equitable services.¹⁶

1.3.1 MSM

In 2011, the HIV prevalence among MSM was 13 times higher than the general population.¹⁷ This epidemic has always affected the MSM community by the number of new HIV infections. Therefore, the high incidence cases are shown to be emerging in countries from Middle East, North Africa, and Sub-Saharan Africa.¹⁸

MSM are at higher risk of HIV due to social and behavioral factors, condom-less sex, multiple sex partners, stigmatization and depression from society can lead to the uptake of substance use and might increase the chances of acquiring HIV transmission.^{17,19} Anal sex constitutes as a higher transmission of HIV when compared to vaginal sex¹⁹, with differences whether it is receptive or insertive anal sex accounting for one of the main reasons HIV is still persistent among this group.¹⁷

1.3.2 Sex workers

Sex workers are a vulnerable group at high risk of HIV infection. In 2016, Eastern Europe and Central Asia reported 103,438 new HIV diagnosed cases among SW.²⁰ Globally, there is a 12% of prevalence rate among sex workers with a large variation in regions in Europe. An

estimation of (30.7%) of sex workers were HIV positive in 26 countries accounting for (12%) of the general population.^{21,22}

Different factors such as financial issues, sociocultural context, and work environment are some of the reasons SW tends to engage which causes unsafe behavioral actions.²³ SW are susceptible and undergo in physical and sexual assault leading to an increase of contracting HIV infection. Stigmatization, discrimination and legal issues are barriers faced by this group which increases the access for services for HIV care.^{24,25}

1.3.3 Migrants

It is estimated that there are around 244 million of migrants worldwide.²⁶ Factors such as lower knowledge on how HIV is transmitted, poor economical status, limited access to the health care services, lower education, language barriers, stigmatization and discrimination may put them at higher risk of HIV.^{27,28,29} The migration process may increase the fear to fight for their rights. The legal status is a potential detonating reason to lead them to interact in high-risk sexual behaviors and it promotes higher levels of social and behavioral challenges.^{30,31,32,33}

1.3.4 Barriers faced by key population groups in response to HIV

Key population groups tend to face difficult situations when it comes to limited access to the health care system. In particular, stigmatization, inequity, criminalization are the hardest barriers to overcome.³⁴ For this, prevention methods should be established for the sake of their integrity. Countries differ from one another by their policies and regulations, some countries still follow strict regimens including the death penalty if laws are not being followed. There are more than 100 countries that do not permit any work related with sex, 76 countries still do not agree with relationships between people of the same sex^{35,36} and IDU still face discrimination.

For example, sex workers are constantly being forced to interact in unprotected sex, this group tend to have high exposure to HIV and sexually transmitted diseases (STD) and might not be entitled to negotiate the use of condoms.^{22,23} Promoting educational programs for key population groups with accurate information about HIV will help nourish their knowledge and promote the uptake of pharmacological preventive treatments^{37,38} for those users who receive misinformation about their rights.^{39,40} It is essential to provide accessible friendly services to endorse anti-stigma and anti-discrimination practices for key population groups.⁴¹

1.4 Overview of Post-Exposure Prophylaxis

1.4.1 History of PEP and How PEP works

WHO Guidelines had implemented new strategies for occupational and non-occupational PEP exposures in 2005, becoming available in 2006⁴² addressing standards needed for the health care and non-health sector. PEP is the treatment of antiretroviral drugs taken to prevent HIV acquisition after being potentially exposed to the virus through unprotected sexual activities, the sharing of needles or body fluids.⁴³ PEP is recommended to be taken within a window frame of 72 hours of exposure; if taken sooner treatment becomes more effective after being exposed.⁴⁴

HIV screening test must be performed before initiating treatment and followed by a 4-week (28-day) pill intake.⁴³ PEP should be only given to patients who are HIV-negative or are unaware of their status from the last time of engaging in any sexual activities. PEP should only be given in emergency situations.⁴⁵ Therefore, if for any reason the screening results are HIV-positive for the patient, then PEP should be discontinued.

PEP has been proven to be effective when used for occupational exposures but not yet been proven to be effective in non-occupational exposure.⁴⁶ Studies from several countries have shown that non-occupational PEP (nPEP) followed by sexual exposure as well as sexual assault has not had enough attention within the medical care system and yet has been underutilized.^{47,48} nPEP is generally prone to be used when unprotected sex has been practiced, drug use or any other mucosal or wound exposure.⁴⁴ However, PEP has not reached its full successful potential when it comes to preventing transmission because of the lack of use, late initiation of prophylaxis, knowledge about treatment and the side effects.^{49,33}

Risks and benefits of the intake of PEP need to be considered when an individual suspect they have been exposed to HIV, which is mainly by blood and body fluids or sexual exposure with high risk act performed.⁵⁰ Unfortunately, observations from occupational and non-occupational use of PEP show that it is not 100% effective. There are some factors that may affect the efficacy of PEP such as the time when individuals begin using PEP, not willing to complete the full 4 weeks of treatments, the exchange of intravenous syringe drug use and the number of sexual encounters.⁴⁶

1.4.2 Knowledge of PEP

Individuals who are HIV-positive tend to be more aware of the use of PEP as a prevention method. However, not in all situation PEP awareness align with the consistency of knowledge about it. For example, in a study conducted on the awareness of PEP after being sexually exposed in HIV positive women, it shows that 80% of those women had not heard of PEP following sexual exposure (PEPSE), less than 10% had any idea on the effectiveness of duration⁵¹ only 19% among gay and bisexual men were aware of PEP⁵² and only 28% of awareness was found in a Boston study survey⁵³ in comparison with having knowledge about PEP it was found that only 20% of women from a London study had heard of PEP.⁵¹

It has been said that having low levels of awareness and knowledge about PEP affects the opportunity to access PEP correctly, which is still a problem that keeps arising across population groups.⁵⁴ For example, in a study conducted in France, there were 2932 participants were 2280 were sexually active; the mean age of participants being aware of PEP was of 41 years who tend to have lower level of education and unemployed.⁵⁵ From those, 30% reported they had never heard of PEP. However the lack of awareness was not properly distributed among participants in this study. Immigrant women and men were less informed about PEP in comparison to homosexual men who were more aware of PEP than male and female IDU and heterosexuals.⁵⁵

In the United Kingdom (UK), a study conducted among nurses showed the increase of percentage on awareness (72%) and knowledge (21%) for the use of PEP out of the 402 sample presented in non-occupational exposure at their clinic.⁵⁶ Factors that might have mitigated the increases on the knowledge and awareness could have been public healthcare access the high risk sexual behavior and the improvement to access PEP.⁵⁶ A survey conducted in San Francisco, California in 2008 showed that 47% of uninfected gay/ bisexual men have heard about PEP. There was a higher increase of awareness in individuals who presented sexually transmitted disease (STD) by 56% in comparison to the Stop Aids Project (SAP) population that showed 41% of awareness. In this study, awareness of PEP was more prominent in the population age of 25 years and older.⁵⁷ Lack of knowledge regarding PEP can negatively influence the timely access to this prevention method and increase the odds of acquiring HIV. Education on how to obtain PEP and its benefits, and increased accessibility are need particularly for those whose status is HIV-negative but has been sexually exposed.

1.4.3 Uptake of PEP

A search on a systematic review and meta-analysis on 56 articles in May 2018, showed an increase on prescription medical records for nPEP among MSM from 57% to 88.1%. 28 studies reported the use of PEP among MSM users of 8.1% (95% CI: 5.6% to 10.5%) being unprotected sex (insertive and anal) the primary reason of use.⁵⁸ Although, PEP has been used among MSM users; the needs of awareness and knowledge are still being underutilized. In another study conducted in Mombasa, Kenya among Female SW and Male SW, only a few participants were aware of PEP; from a total of 44 only 16 (36%) of participants had heard of PEP surpassing MSW more aware of PEP than FSW. Knowledge about PEP does play a significant role for the uptake of PEP. Insufficient PEP promotion leads to insufficient knowledge and to insufficient use of PEP.⁵⁹

Another study conducted in Spain, The Spanish Survey, also explains that the main problem Spain faces when it comes to having low awareness about PEP is due to limited public campaigns. Only people who attend facility centers obtained information about PEP. The Spanish study consisted of 2545 people who were tested for HIV out of which half have had a previous HIV screening test (42% heterosexual men and 36% women and 22% of gay men); from those with a previous study 22% have heard of PEP (34% gay men and 16.5% heterosexual men or women) only 48 (2%) of individuals have ever taken PEP accounting for (23 gay men and 12 heterosexual men and 13 women). The study shows how gay men were no more likely to have used PEP than heterosexuals.⁶⁰

Factors presented can be the lack of knowledge, cost and implications on when PEP should be administered. Proper training of personnel as well, is found to be an obstacle for an effective implementation strategy for patients seeking for PEP from health care professionals.⁶¹

1.5 Studies

The following table show the studies which have assessed knowledge about PEP and uptake of PEP among key populations in different countries.

Table 1 – Summary of characteristics of studies about their knowledge and uptake of PEP in key population groups from other countries					
Cohort Name, Country	Number of participants, year, follow-up, cohort groups	Aim	Recruitment	Knowledge and use of PEP (%)	Factors associated with lack of knowledge and use
North America					
Survey of PEP knowledge, Access and use among at-risk Populations in NYC: (United States) ⁶²	- 540 participants - **179-YMSMOW, 183-TW, - 178-WOC - June 2016 –February 2017	1. To understand how to increase the uptake of PEP within key populations 2. To assess PEP knowledge, access and usage among YMSMOC, TW and WOC	- In person - Online recruitment - Partnering with organizations and Venus that serve key populations	59.2% were aware of PEP 86.2% among YMSMOC 62.6% among TW 33.5% among WC - Low level: who tried to get PEP but could not get it: 14.9% of YMSMOC 9.7% of TW 8.8% of WC	- Expand education and outreach - Low awareness of PEP is determined by the stereotype belief about PEP
Multi-stage design to study rectal microbicide safety and acceptability in young MSM (AUTHORS) in Boston, Pittsburg and San Juan Puerto Rico (United States) ⁶³	- 228 participants - MSM - December 2010 – June 2012	1. Awareness of and experiences with PEP and PrEP in a sample of MSM.	- Newspapers - Craigslist - Social media - Posting in MSM - websites - Face to face interviews in clinics - Bars, clubs and social events	41% had heard of PEP; 16% from San Juan; 64% from Boston; 47% from Pittsburg; (10 point-scale): 9.1 participants are especially likely to use PEP; - Compare to PR, Pittsburg were 5.7 times more likely to have heard of PEP (CI: 2.1-15.5; p= 0.001) and those from Boston 10.1 times more likely (CI: 3.7-27.5; p,0.001).	- Education is needed to raise awareness, primary barrier

EXPLORE STUDY (San Francisco, Boston, Seattle, Chicago, NY and Denver) United States ⁶⁴	- 4295 participants MSM - January 1999 – February 2003 - Longitudinal Study	1. Examine knowledge and use of nPEP and its association with HIV risk behaviors	- Advertising - Newspaper - Health care providers	• 315 people reported used nPEP on at least one occasion; • 2037 (47.5%) has heard of nPEP; • Boston and San Francisco had higher levels of nPEP use compared to the other 4 sites, accounting for (3.6% vs. 1.0%) (p<0.001) • 69% of MSM at baseline said they were “very likely” to use PEP after high risk exposure.	- nPEP was not perceived as an alternative for safe sex - Knowledge about nPEP remains low within these
South America					
Biological and Behavioral Surveillance survey (BBSS) – 12 Brazilian cities: São Paulo, Belo Horizonte and Rio de Janeiro – Southeast Region; Curitiba and Porto Alegre – South Region; Brasília and Campo Grande – Central-West Region; Fortaleza, Recife and Salvador – Northeast Region; and, Belem and Manaus – North Region) ⁶⁵	- 4245 participants - (350) FSW from each of the 12 cities - 2016 - Cross-sectional Study	1. To investigate non-disclosure of FSW status to health care providers and its association with access and uptake of preventive health care services	- Respondent-driven sampling (RDS)	• Awareness of PEP was reported by 31% and among FSW who reported engaging in risky behavior per the past. • Six months with PEP indications (49.6%) only (8.3%) used PEP. • 10% of FSW used PEP	- Stigma - Violence - Discrimination - Financial resources from government and donors

Africa					
PrEP and PEP and their experience with HIV/STI healthcare services. Mombasa, Kenya ⁶⁶	- 50 Sex workers (25 FSW, 25 MSW) - December 2014 – May 2015 - Semi-structured qualitative interviews	1. To inform development of a multi-level risk reduction intervention that includes peer-delivered education, distribution of condoms and lubricant	- Bars - Nightclubs	• Only 16 out of 44 SW were aware of PrEP and PEP; • More MSW were aware of PrEP and PEP than FSW (5/23 vs 9/21 and 9/23 vs 7/21 respectively); • Reported use of PEP was also low for both FSW and MSM (3/23 and 4/21); • Only 16% of 44 (36%) had ever heard PEP.	- Knowledge; - Education; - Low Uptake; - Sexual Assault; - Occupational exposure; - Condom malfunction.
(SWOP) The Sex Worker Outreach Program - Nairobi, Kenya ⁶⁷	- 5814 HIV uninfected FSW; - 4-year period (2009-2013); - Cross-sectional analysis.	1. To compare the nature of sex work, risk taking behavior, knowledge of PEP and potential barriers to PEP access and use between repeat PEP and non-repeat PEP	- Hot spot-based mobilization - Snowball	4695 (80.7%) did not request PEP; • 1119 (19.2%) requested PEP; • Out of 1119 PEP users 214 (3.7%) sought PEP more than once; • PEP was accessed by 20% of HIV uninfected FSW	- Fear of stigmatization; - Lack of use: many could be obtained by offering sex without a condom.

Europe

PEP and TasP awareness among Italian MSM, PLWHA and High-risk Heterosexual and Demographic, Behavioral and Social Correlates – Italia ⁶⁸	- 6781 (72.6%) non-HIV positive Heterosexual people - 1874 (20%) non-HIV positive MSM - 694 (7.4%) PLWHA - January–October 2014 - Cross-sectional study	1. To investigate the prevalence of PEP and TasP awareness and their demographic behavioral and social correlates in Italy. 2. Investigates the relations between knowledge about PEP and TasP frequency of unprotected sexual intercourse with casual partners	- Emails - Social network - Web-based communities	• MSM were less knowledgeable about PEP and TasP then were PLWHA. • more knowledge about PEP and TasP were higher in risk heterosexual participants	- stigma - Lack of information about HIV treatments
VESPA study. France ⁵⁵	- 2280 participants; - 26% women; - 41% Homosexual men; - 16% immigrants; - 2003; - Cross-sectional.	1. Evaluate awareness of HIV prophylaxis at national level and to identify factors that may be related to a lack of PEP awareness	- Face-to-face survey	• 30% reported that they had never heard of PEP; • Among men: majority of immigrants' men did not know about PEP; • 1/3 of both IDU and native born heterosexual women did not know about PEP.	- Greater socioeconomic vulnerability - older age - lower levels of education - unemployment
aMase (Advancing Migrant Access to Health Services in Europe) Study- Nine European Countries. Netherlands ⁶⁹	- 417 participants - Migrants, non-migrants and MSM - July 2013 – June 2015 - Cross-sectional	1. The comparison of rich set of data between HIV positive migrants and non-migrants living in the same country	- Questionnaire	• 66% had ever heard of PEP • MSM born in sub-Saharan Africa, Latin America Caribbean and other country in Europe were less likely to have heard of PEP then non-migrant MSM	- Awareness - Accessing health care: migrants have higher possibility than non-migrant MSM; - Language barriers - Knowledge about rights should be improve to access healthcare; - Cultural; - Socioeconomic status; - Poverty; - Discrimination;

2. Aims

In this research study, the primary aim was to describe the knowledge and uptake of post-exposure prophylaxis among key populations for HIV – men who have sex with men, sex workers and migrants users of the community-based screening network centers in Portugal. The specific objectives are:

1. To evaluate the knowledge about post-exposure prophylaxis among people who were tested in one of the community-based centers for HIV, viral hepatitis and syphilis who are part of the Community Screening Network in Portugal in their first visit from 2016 to 2018.
2. To determine the proportion of uptake of post-exposure prophylaxis among the Community Screening Network users in their lifetime measured at their first visit from 2016 to 2018.

Chapter 1.

Knowledge and uptake of Post-Exposure Prophylaxis (PEP) among users of the Community Screening Network in Portugal

Background

The infection caused by the Human Immunodeficiency Virus (HIV) has spread widely throughout the world since the '80s. In Portugal, in 2018 there were estimated 41,000 (95% CI 36,000 – 46,000) people living with HIV of whom 37,000 individuals were receiving antiretroviral therapy.^{1,2} Key populations for HIV such as trans people, men who have sex with men (MSM), sex workers, people who inject drug (PWID), or migrants have a higher risk of acquiring HIV due to factors that influence their social and legal status, stigmatization, discrimination, poverty, and violence.³ In 2019, an estimate of 60% of new HIV cases globally were among key populations, which remains a major concern globally.⁴

In Portugal, heterosexual transmission has been the main transmission mode representing 42% of new HIV cases in 2018.⁵ A considerable proportion one-third (40%) of cases of heterosexual transmission are migrants who come from countries with a high generalized HIV epidemics.⁶ Transmission related to sex between men accounted for (48%) in 2018. However this proportion, is higher when looking to specific cities such as Lisbon (65%) and Porto (55.3%). HIV cases due to unsafe infection practices presented a decrease in recent year, representing in 2018 (5.8%) out of the 29,704 new cases reported.^{5,7}

The introduction of pharmacological prevention tools such as post-exposure prophylaxis (PEP), and more recently pre-exposure prophylaxis (PrEP) constitute important strategies for HIV prevention. Although, guidelines for the use of PEP for non-occupational exposures have been available since 1998 appropriate information about PEP has been limited within potential users and providers.⁸ PEP may be appropriate for individuals who tend to fall in sporadic high risk exposures.⁹ However, there are still major barriers that affect its utilization such as the lack of knowledge about PEP and appropriate information on how soon PEP should be taken, the length of treatment and/or the side effects.¹⁰

In 2017 the European MSM internet survey (EMIS) survey among MSM; (N=113.135) 7% of men who were not diagnosed with HIV and had ever tried to get PEP, (N=113.117) 5% had ever taken PEP and 1.1% have taken the pill more than once. In the same study, MSM were asked “have you heard about PEP?” 61% answered yes, 9% were not sure and 30% have not heard about PEP; this shows that 39% of MSM are still unaware of PEP.¹¹ In the Biological and Behavioral Surveillance Survey (BBSS) conducted in 12 Brazilian cities; 31% of 4245 female sex worker (FSW) participants who had engaged in risky behavioral activities reported to be aware of PEP

and only 10% of FSW have used PEP.¹² In the VESPA study conducted in France; out of 2280 participants (26% women, 41% gay men, 16% immigrants) 30% had never heard of PEP, among men majority of men immigrants did not know about PEP and one-third of both people who injected drugs (PWID) and native born heterosexual women did not know about PEP.¹³ Addition, in the aMase study conducted in 9 European countries on 417 participants (migrants, non-migrants and MSM) 66% had ever heard of PEP, MSM born in Sub-Sahara Africa, Latin America and other Caribbean countries were less likely to have heard of PEP than non-migrants MSM.¹⁴

The Community Screening Network is a project launched in 2015 whose purpose was to provide rapid tests for HIV, viral hepatitis, and syphilis at community based settings targeting mainly key populations in Portugal. All 25 participant community-based centers provide free testing as well as counseling, prevention, and support to access diagnosis, treatment, or prophylaxis in the Portuguese National Health Service.¹⁵ The main objectives of this study were to evaluate the knowledge and uptake of PEP among users of the Community Screening Network in Portugal in their first visit from 2016 to 2018.

Methods

The Community Screening Network is an observational study with a longitudinal design that has been established in Portugal since 2015. This project embraces the principles of offering a integrated testing and tailored counseling for its users. For this study, we used cross-sectional data from first visits of eligible individuals from January 2016 until December 2018. A standardized online questionnaire was designed for the data collection. Recruitment of participants were taken from 25 screening organizations who belong to this network. Eligible criteria were being 18 years of age or older, whose HIV testing at enrollment was negative and provided a valid answer (“Yes”, “No”, or “I rather not answer”) to the “Do you know about PEP” and “Have you ever used PEP” questions in the questionnaire at baseline. For this specific study 16,301 individuals met the inclusion criteria. Of those, we excluded from the bivariate analysis 289 participants who answered “I rather not answer”.

Study instrument and variables

The Community Screening Network participant organizations use a harmonized questionnaire available online, with the exception of one of the centers where a cohort of HIV-negative MSM –

The Lisbon cohort of MSM takes place and uses a specific questionnaire. Therefore we have merged the datasets and harmonized the variables needed. The main outcomes of our analysis – knowledge and uptake of PEP questions were collected similarly at both questionnaires and were merged to have them as dependent variables for our study. As independent variables we considered sociodemographic characteristics such as (age, gender, country, education and sexual orientation) and being defined as one of more the key populations – MSM, migrants or sex workers. These have been defined as following: 1. MSM were those who reported to be a cisgender male and reported to have had sex with man over the previous 12 months; 2. migrants were those who have reported to have been born in a country different from Portugal; and 3. SW were those who report to have sex in exchange for drugs or money.¹⁵

Statistical Analysis

Statistical analysis was conducted using IBM SPSS version 24. Knowledge and uptake of PEP were assessed by describing the absolute and relative frequencies. To measure the strength of association between our independent and dependent variables we estimated the prevalence ratio (PR) and the 95% confidence interval using the log-binomial regression in SPSS. Missing values have been excluded from the denominator of proportions for all variables.

Ethical statement

All participants provided verbal informed consent before inclusion. The community screening network study protocol was approved by the ethics committee of Institute of Public Health of the University of Porto (ID CE15045), and the Lisbon Cohort of MSM received from the ethics committee of São João Hospital Center and Medical School, University of Porto, approved the study protocol (ID 104/12).

Results

Table 1. summarizes the sociodemographic characteristics of participants. The most frequent age group 25 and 43 years old (29.1%). The highest proportion of participants from this study were male (58.2%) followed by females (41.2%) and trans people (male to female or female to male) were 0.6% of the study population. Participants were more frequently born in Portugal (60.5%) followed by African countries (17.5%) and Brazil (13.3%). Demographics show an equal distribution of participants across educational levels with basic or less education (38.8%) and

secondary (30.2%) education followed by having a bachelor (17.9%) and those other degrees accounted for (13.0%). Majority (69%) of participants self-identified themselves as heterosexual followed by gay with (20.1%) and last (11.0%) bisexual and/or participants who rather not say or do not use any term for sexual orientation;. Most participants who attend the screening network are migrants (25.3%) followed by MSM (15.9%) and least SW (3.7%); after integrating all three key groups we determine that most were MSM – migrants (7.4%) and migrants – SW (6.3%).

Association between sociodemographic characteristics and the Knowledge of PEP

Three thousand one hundred and ninety-seven of our participants (20.0%) reported to know about PEP. In a bivariate analysis, knowledge of PEP was less frequent among females, participants older than 45 years of age; among those with only the basic education or less and coming from African countries as showed in table 2.

More knowledge was found among transgender participants (55.4%) (PR: 2.19; 95% CI: 1.84-2.62), among those 25 to 34 years of age (27.2%) (PR: 1.43; 95%CI: 1.32-1.55); participants from foreign countries such as Brazil (28.8%) (PR:1.39, 95%CI: 1.28-1.50) or other European countries (27.6%) (PR: 1.32; 95%CI: 1.19-1.47) when compared to those born in Portugal . The association between education and the knowledge of PEP showed that participants with a professional training degree (46.0%) (PR: 3.94; 95%CI: 3.57-4.36) had more knowledge than those with basic or less education level. Participants who have self-identified as gay (49.7%) (PR:4.35 95%CI: 4.20-4.77) have higher proportion of knowledge of PEP than heterosexual (11.1%); of the 3 key groups that are of main concern in our study and compared to not having been identified as any of them, MSM only were approximately 5 times more likely to know about PEP (PR: 4.76 95% CI: 4.36-5.20), migrants who reported to be MSM were also 5 times more likely to know about PEP (PR: 4.96 95% CI:4.50-5.46) and those who are MSM, migrants and sex workers had 5 times higher knowledge (PR: 5.03; 95%CI: 4.18-6.06). Those who were migrants only were less likely to know about PEP (7.0%) (PR:0.71; 95%CI: 0.62-0.81).

Association between sociodemographic characteristics and the uptake of PEP

Among participants who knew about PEP, 2865 answered the question “have you ever used PEP” (332 missing’s), of those 289 (10.1%) have used PEP in their lifetime. In table 2. Males (n=241) were more likely to have used PEP (11.3%) than trans individuals (7.1%) and females (6.6%). There is a relatively close percentage across all age groups who have used PEP; participants

who are between 25 and 34 (11.8%) were more likely to have used PEP (PR: 1.70; 95% CI: 1.25-2.31); followed by those who are 35 and 44 years of age (11.6%). Participants from foreign countries, in this case Brazil, demonstrated an increased use of PEP, 2.7 times more (95%CI: 2.11-3.45) than those born in Portugal; participants with secondary education have used PEP at least once more frequently (PR: 1.37; 95%CI: 1.02-1.83) than those with basic or less education. Gay men were 2 times more likely to use PEP (PR: 2.26; 95% CI:1.70-3.01) than heterosexual. Observing the 3 key groups, the uptake of PEP has been more frequent among MSM only (8.2%), followed by migrants only (7.7%) and SW only (7.1%). In addition among participants in this study who are categorized in one or more groups higher use was found among MSM, migrants and SW (22.2%; PR: 7.48; 95% CI 3.74-14.94), followed by MSM and migrants (19.7; PR: 6.63; 95% CI:3.85-11.42), migrants and SW (12.8%) and MSM who are SW (7.5%).

Discussion

A low proportion of knowledge and usage of PEP was found. Only 20% of the participants in our study knew about PEP and only 10% of the participants used PEP. Being gay male, having between 25 to 34 years of age, having higher levels of education was associated with more knowledge and the utilization of PEP. Findings in our study revealed higher knowledge among those participants who are classified into one or more groups. Due to vulnerability, highest proportion of knowledge was found among those that were MSM, migrants and SW, lower knowledge was observed only among migrants and only among SW. Those key groups with higher knowledge have higher uptake of PEP therefore, reinforcing rationale in accessing PEP will increase knowledge and uptake of PEP among users in our screening network.

Knowledge and uptake in our study was lower than the findings from a study conducted in London among 179 MSM individuals whose purpose was to examine the awareness and use of PEP. Results from this study revealed an 88.3% of respondents have heard about PEP and 27.4% have used it.¹⁶ In addition, the use of PEP was also higher among those MSM participants from the PROUD study revealing that 34% out 184 have used within the that 12 months and 71 (13%) have used PEP more than once¹⁷ As well, comparing our results with a study conducted in Italy the results show that there was higher knowledge about PEP and treatment as prevention (TasP) in heterosexual participants and people living with HIV/AIDS (PLWHA) than the MSM group, however this results still surpasses the findings from our study.¹⁸

There have been a few studies conducted on the use of PEP in non-occupational users. This study has presented low knowledge of PEP in all population groups especially in SW and Migrants. Moreover, our results underscore the importance of raising/initiating educational campaigns for all key population groups. Despite the fact that the knowledge and utilization of PEP is low in Portugal, this study has highlighted the importance of providing counseling to targeted population groups to discuss information about the advantages and risk-reduction methods PEP may offer to users. The incrementation of new approaches to vulnerable populations should be established by the health system and health care workers to address beneficial outcomes for services for HIV. At one point, those individuals who tend to fall into repeatedly in high risk behaviors should be the main focus to access services immediately.¹⁹

Considering that Portugal was one of the countries in Europe with more new infections yearly, even though over the past 10 years the curve has decreased from 2167 HIV infections in 2007 to 1030 HIV infections in 2016.⁷ The health system in Portugal provides a free health care services for all those who reside in Portugal through the National Health System. Providing adequate HIV testing from professional and risk reduction counseling to determine the factors of such behaviors can result as a positive impact on public health. Mainly, the overall purpose is to understand why PEP is being accessed in certain situations but yet, still being underutilized within populations who are most at risk. Stressing the importance of the correct use of PEP can enhance the effectiveness of the approach of this pharmacological prevention.

In addition, public and private national organizations whose purpose is to screen for detection of HIV have also assisted with the prevention, detection and treatment for this virus. These organizations have served the general population and for those who are considered as key population groups. The launching of the Community Screening Network not only has become the pioneer of data collection but also the first study in Portugal to evaluate rapid screening test for HIV and sexual transmitted infections among key population groups. It has been driven to establish awareness movements to provide detailed information about the efficacy of time and usage on pharmacological prevention methods such as PEP among users. Our results clarify there is 80% lack of knowledge of PEP and 90% of individuals not using PEP. We can conclude from this study regarding accuracy and level of knowledge on what PEP, or why aren't individuals not seeking proper prevention methods to reduce HIV after being exposed to an HIV positive person which is a limitation from this study

Other several limitations in this study have been identified. Participants not willing to complete all questionnaires at baseline raise the problem of information bias. Although IDU is one of the key groups at the screening network, for this study we did not take this group in consideration because of the low number of participants. Understanding and combining questions from one cohort to the merged project data set has been difficult; understanding that the questions were not established at the same time and one cohort had a concentration only in the MSM population.

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Table 1: Sociodemographic characteristics of participants from the Community Screening Network in Portugal, 2016-2018

	Participants	
	N	%
Total	16301	100.0
Age		
18-24	4277	26.2
25-34	4743	29.1
35-44	3202	19.6
45-54	2101	12.9
55-65	1279	7.8
>65	698	4.3
<i>missing</i>	1	
Gender		
Male	9487	58.2
Female	6710	41.2
Trans	104	0.6
<i>missing</i>	0	
Country/region of birth		
Portugal	9833	60.5
Other European countries	1025	6.3
African countries	2839	17.5
Other American countries	244	1.5
Brazil	2165	13.3
Asia /Middle East /Oceania	156	1.0
<i>missing</i>	39	
Education		
Basic education or less	6201	38.8
Secondary education	4824	30.2
Professional training	881	5.5
Post-secondary	164	1.0
Bachelor	2862	17.9
Masters or doctorate	959	6.0
No response/others	105	0.7
<i>missing</i>	305	
Sexual orientation		
Gay	3210	20.1
Heterosexual	11038	69.0
Bisexual/other	1754	11.0
<i>missing</i>	299	
Key population (MSM or Migrant or Sex worker)		
Not MSM or Migrant or SW	6071	39.9
Only MSM	2414	15.9
Only Migrant	3849	25.3
Only SW	556	3.7
MSM Migrant	1129	7.4
MSM SW	95	0.6
Migrant SW	950	6.3
MSM Migrant SW	135	0.9
<i>missing</i>	1102	

Table 2: Association between sociodemographic characteristics and the knowledge and uptake about PEP from participants from the Community Screening Network in Portugal, 2016-2018

	Knowledge about PEP			Uptake of PEP		
	No	Yes	PR (95% CI)	No	Yes	PR (95% CI)
Total	12815 (80.0%)	3197 (20.0%)		2576 (89.9%)	289 (10.1%)	
Gender						
Male	6974 (74.7%)	2360 (25.3%)	Ref.	1901 (88.7%)	241 (11.3%)	Ref.
Female	5796 (88.1%)	781 (11.9%)	0.47 (0.44; 0.51)	623 (93.4%)	44 (6.6%)	0.59 (0.43; 0.80)
Trans	45 (44.6%)	56 (55.4%)	2.19 (1.84; 2.62)	52 (92.9%)	4 (7.1%)	0.64 (0.25; 1.64)
Age group						
18-24y	3413 (81.0%)	801 (19.0%)	Ref.	686 (93.1%)	51 (6.9%)	Ref.
25-34y	3399 (72.8%)	1267 (27.2%)	1.43 (1.32; 1.55)	1020 (88.2%)	136 (11.8%)	1.70 (1.25; 2.31)
35-44y	2404 (76.8%)	727 (23.2%)	1.22 (1.12; 1.34)	564 (88.4%)	74 (11.6%)	1.68 (1.19; 2.36)
45-54y	1761 (85.4%)	302 (14.6%)	0.77 (0.63; 0.87)	237 (89.8%)	27 (10.2%)	1.48 (0.95; 2.31)
55-65y	1168 (93.1%)	87 (6.9%)	0.36 (0.30; 0.45)	62 (100%)	0 (0%)	-
>65y	669 (98.1%)	13 (1.9%)	0.10 (0.06; 0.17)	7 (87.5%)	1 (12.5%)	1.81 (0.28; 11.52)
Country/Region of birth						
Portugal	7656 (79.2%)	2014 (20.8%)	Ref.	1665 (93.2%)	121 (6.8%)	Ref.
Brazil	1517 (71.2%)	615 (28.8%)	1.39 (1.28; 1.50)	465 (81.7%)	104 (18.3%)	2.70 (2.11; 3.45)
Other European Countries	731 (72.4%)	278 (27.6%)	1.32 (1.19; 1.47)	220 (85.3%)	38 (14.7%)	2.17 (1.55; 3.06)
African Country	2589 (93.2%)	189 (6.8%)	0.33 (0.28; 0.38)	146 (93.0%)	11 (7.0%)	1.03 (0.57; 1.88)
Other American Countries	179 (75.5%)	58 (24.5%)	1.18 (0.94; 1.47)	46 (83.6%)	9 (16.4%)	2.42 (1.30; 4.50)
Asia/Middle East/ Oceania	114 (77.0%)	34 (23.0%)	1.10 (0.82; 1.49)	27 (84.4%)	5 (15.6%)	2.31 (1.01; 5.25)
Educational level						
Basic education or less	5378 (88.3%)	710 (11.7%)	Ref.	600 (91.0%)	59 (9.0%)	Ref.
Secondary education	3688 (77.3%)	1083 (22.7%)	1.95 (1.79; 2.12)	897 (87.8%)	125 (12.2%)	1.37 (1.02; 1.83)
Professional training	473 (54.0%)	403 (46.0%)	3.94 (3.57; 4.36)	350 (88.8%)	44 (11.2%)	1.25 (0.86; 1.81)
Post-secondary	106 (71.1%)	43 (28.9%)	2.47 (1.91; 3.21)	35 (87.5%)	5 (12.5%)	1.40 (0.59; 3.28)
Bachelor	2189 (77.6%)	632 (22.4%)	1.92 (1.74; 2.12)	465 (93.0%)	35 (7.0%)	0.78 (0.52; 1.17)
Masters or Doctorate	653 (68.7%)	298 (31.3%)	2.69 (2.39; 3.02)	213 (92.6%)	17 (7.4%)	0.83 (0.49; 1.39)
Sexual orientation						
Heterosexual	9636 (88.9%)	1205 (11.1%)	Ref.	946 (94.3%)	57 (5.7%)	Ref.
Gay	1600 (50.3%)	1581 (49.7%)	4.35 (4.20; 4.77)	1296 (87.2%)	191 (12.8%)	2.26 (1.70; 3.01)
Bisexual or other	1339 (78.4%)	369 (21.6%)	1.89 (1.75; 2.16)	309 (89.6%)	36 (10.4%)	1.84 (1.23; 2.74)
Key population (MSM or Migrant or Sex worker)						

Not MSM or Migrant or SW	5393 (90.1)	595 (9.9)	Ref.	457 (97.0)	14 (3.0)	Ref.
MSM only	1266 (52.7)	1137 (47.3)	4.76 (4.36; 5.20)	987 (91.8)	88 (8.2)	2.75 (1.58; 4.79)
Migrant only	3510 (93.0)	265 (7.0)	0.71 (0.62; 0.81)	203 (92.3)	17 (7.7)	2.60 (1.31; 5.18)
SW only	409 (76.9)	123 (23.1)	2.33 (1.96; 2.77)	105 (92.9)	8 (7.1)	2.38 (1.02; 5.54)
MSM Migrant	569 (50.8)	552 (49.2)	4.96 (4.50; 5.46)	420 (80.3)	103 (19.7)	6.63 (3.85; 11.42)
MSM SW	53 (56.4)	41 (43.6)	4.39 (3.45; 5.59)	37 (92.5)	3 (7.5)	2.52 (0.76; 8.42)
Migrant SW	703 (75.6)	227 (24.4)	2.46 (2.14; 2.82)	190 (87.2)	28 (12.8)	4.32 (2.32; 8.04)
MSM Migrant SW	67 (50.0)	67 (50.0)	5.03 (4.18; 6.06)	49 (77.8)	14 (22.2)	7.48 (3.74; 14.94)

Conclusion

Despite the availability of obtaining PEP from hospitals and community centers in Portugal, our findings reassure the low knowledge and probably underuse of PEP. PEP for non-occupational exposures demonstrated effectiveness if used correctly. Therefore, strategies to increase knowledge and uptake are needed particularly among females, older individuals, who come from African countries with basic education being heterosexual who are migrants only and those who are SW only. Education programs empowering individuals to make appropriate choices in terms of prevention such as knowing when to use PEP can have a positive impact in reducing new HIV cases.

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