Awareness and Acceptability of Pre-Exposure Prophylaxis (PrEP) Among Men Who Have Sex with Men in Kazakhstan: A Mixed Methods Study

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Objectives: Oral pre-exposure prophylaxis (PrEP) is an antiretroviral method of HIV prevention recommended to men who have sex with men (MSM) at high risk of infection. In Kazakhstan, which has one of the fastest growing HIV epidemics globally, PrEP is not currently available. The aim of this study is to explore the possibilities for PrEP initiatives in Kazakhstan by investigating awareness and acceptability of this prevention method among MSM. **Methods:** This mixed-methods study employs an online survey and qualitative interviews to describe PrEP awareness and acceptability. **Results:** Less than half (39.8%) of survey participants had heard of PrEP. However, a majority (85.2%) of MSM would possibly or definitely use PrEP if it was available. Awareness of PrEP was positively associated with willingness to use PrEP. The main reason to be interested in PrEP was an increased feeling of protection, whereas barriers were related to the idea of taking daily medication and the potential for side effects. **Conclusion:** PrEP is an essential component of HIV combination prevention. Our findings suggest potential for PrEP programmes among MSM in Kazakhstan and possibly in other Central Asian nations, when taking into account burdens of taking PrEP as well as more structural health policy issues.

Keywords: Pre-Exposure Prophylaxis, HIV Infections, Sexual and Gender Minorities, Health Policy, Kazakhstan

Introduction

The global HIV/AIDS epidemic remains a major public health issue: in 2015, an estimated 36.7 million people worldwide were living with HIV [1]. Despite global progress, the incidence of HIV continues to grow in some regions, with one of the most rapidly

accelerating epidemics taking place in Eastern Europe and Central Asia (EECA). New HIV infections in EECA rose by 57% between 2010 and 2015, and 1.5 million people are currently living with HIV [1]. Although access to antiretroviral treatment has expanded in the region, there are still large groups of people who are not being treated, especially among the key affected

populations [1]. It is increasingly recognised that universal access to testing and treatment alone will not stop the epidemic and that the HIV/AIDS response in the region requires effective primary prevention. However, traditional prevention methods have been found to be of limited effectiveness [2].

PrEP is a daily pill consisting of a combination of tenofovir/ emtricitabine, two anti-retroviral drugs. It is branded by Gilead Sciences as Truvada and was first approved for prevention in 2012 in the United States. The advantage of PrEP over existing methods is that it separates the act of prevention from the sexual encounter and that it can be used without sexual partners knowing [3]. PrEP is very effective when taken consistently [4-6]. Use of Truvada is associated with minor side effects such as nausea and in rare cases with effects on bone mineral density and kidney functioning [7]. PrEP is not intended as a stand-alone intervention, but as part of a multi-faceted strategy involving the use of condoms and regular medical follow-ups [8].

The World Health Organization recommends that PrEP should be offered as a choice to key populations (KP) affected by HIV such as sex workers, men who have sex with men (MSM), and injecting drug users, as well as to anyone else at substantial risk of HIV infection [9]. Given the evidence and WHO recommendations, piloting and eventual rolling out of PrEP programmes might be a significant step in controlling the epidemic in EECA. However, PrEP is currently only available in a handful of countries, none of which are in this region.

As the largest and most developed nation in Central Asia, it seems Kazakhstan would be best equipped to act as a frontrunner in providing PrEP. Until 1991, Kazakhstan was part of the Union of Soviet Socialist Republics (USSR). As an independent state, Kazakhstan has transitioned to an upper middle income country [10]. Despite wanting to be progressive, Kazakhstan still lags behind regarding human rights [11]. Moreover, the country has inherited from the Soviet era a highly centralised healthcare system with a neglect of primary care, a weak integration of services, and a shortage of healthcare staff [12]. Funding for healthcare comes from general taxation as well as from significant out-of-pocket payments, which led to 7.4% of the population not being able to afford health services in 2008 [12]. The country is currently planning healthcare reforms needed to improve health system performance [13].

In Kazakhstan, the HIV prevalence rate among adults aged 15 to 49 is 0.2% [14]. Kazakhstan is among the ten countries

in the world with the fastest growing HIV incidence rates [15]. Similar to other countries in the region, the epidemic in Kazakhstan particularly affects KP including MSM. The prevalence of HIV among MSM in Kazakhstan has been estimated between 3-20% [16-17]. Prevention efforts among MSM have been hampered by poor surveillance, and by the stigma against gay people in Kazakhstan.

In order to inform HIV prevention policy in Kazakhstan, there is a need to understand the current environment for potential implementation of PrEP. The theoretical basis for PrEP uptake has been captured by Kelley et al. [18] in the 'PrEP continuum of care'. The authors found a step-wise progression towards protection from HIV infection: progressing from at-risk people who are aware of PrEP and willing to use it, to those who are able to access healthcare, receive a PrEP prescription, and take it as prescribed. According to Kelley et al. [18], "awareness of PrEP and subsequent willingness to initiate PrEP among those at highest risk for HIV infection is the necessary first step to PrEP uptake" (emphasis added). Therefore, the focus of this study was on the principle step in the model (awareness/acceptability) in order to determine whether there is a demand for PrEP at all.

It is currently unknown whether MSM in Kazakhstan are aware of the existence of PrEP, and whether it would be regarded as an acceptable HIV prevention method, which would be essential for effective future implementation. In other regions of the world, studies have shown that PrEP is seen as an acceptable method of HIV prevention among MSM [19]. However, until now, no studies have been published about PrEP in any Central Asian country. Therefore, this pilot study has the following aim: to explore the possibilities for future PrEP initiatives in Kazakhstan by investigating the awareness and acceptability of this prevention method among MSM.

Materials and Methods

This study employed a mixed methods design, by concurrently conducting a cross-sectional survey and semi-structured interviews. This amounts to between-methods triangulation that reduces the uncertainty in data interpretation. The rationale for using a mixed-methods design was that it provides a more complete understanding of the issue, by enabling explanation of the quantitative results through qualitative analysis.



Survey data

A descriptive cross-sectional survey was conducted in April 2017. The study population consisted of adult (≥18 years old) MSM residing in Kazakhstan. HIV-positive MSM were not excluded since doing so could have significantly decreased the sample size, which was already expected to be small considering the known difficulties with including MSM in research [20]. The guestionnaire included a comment for HIV-positive MSM to fill out the survey as they would have before they contracted HIV. A convenience sample of respondents was recruited through a number of different LGBT-specific media channels (e.g. private Facebook groups) and with the help of local LGBT activists and experts. Sample size was calculated for a desired 95% confidence interval of $\pm 10\%$ using the most conservative prestudy estimates of awareness and acceptability percentages [21]. This yielded a required sample size of N = 96. The final sample was deemed sufficiently large: a total of 108 MSM participated in the survey.

The survey instrument was an anonymous 12-item self-administered online questionnaire, created using Qualtrics software. Participants needed to confirm that they were ≥18 years and give consent to this study to be able to participate. The major content section consisted of an explanation of PrEP and questions to assess awareness and acceptability. Questions concerning knowledge and attitudes were taken from the validated Flash! PrEP in Europe survey, a joint European research project coordinated by the community-based organisations AIDES and Coalition PLUS, as well as the University of Amsterdam [22].

However, several questions from that survey were excluded because a lengthy survey could have negatively affected response rates [23]. For instance, questions on sexual risk-behaviour were not included in our survey, which focused solely on the concepts of PrEP awareness and acceptability. PrEP awareness was assessed by asking whether participants knew what PrEP was and by asking them to select the best description of PrEP from a list of options. The question used to assess PrEP acceptability ("are you interested in using PrEP?") was rephrased to make it more specific (to "would you use PrEP if it were available in Kazakhstan?"). Acceptability was further explored through 5-point Likert scale questions covering the reasons (not) to be interested in taking PrEP. Socio-demographic questions were located at the end of the survey, to avoid respondents losing interest. The questionnaire was translated by a local NGO

(AFEW Kazakhstan) and checked for wording and content from a Kazakhstani perspective.

Qualitative data

Semi-structured interviews were the preferred method to qualitatively investigate this complex and potentially sensitive topic [24]. Interviews were held during April — May 2017. The study population consisted of adult (\geq 18 years old) MSM living in Almaty. HIV-positive individuals were included as well, since it was difficult to gauge their HIV status prior to the interview and because participants might not have wanted to disclose it. Since data saturation generally occurs within the first ten interviews, the proposed sample size for this qualitative part was 10 MSM, which was achieved (n = 10) [25]. Interview candidates were found through snowball sampling and with the help of local LGBT experts.

Prior to the start of the interview, oral informed consent was sought and permission was asked to audio record the interview. We chose not to obtain consent in writing, in order to protect participants' privacy. The right to anonymity in the reporting of study findings and the choice to withdraw from the study at any time was emphasised. During the interview, PrEP was described using verbal explanation and a visual aid adapted from Young et al. [26]. Despite the use of a visual aid, qualitative research into complex phenomena such as PrEP is often limited by participants' ability to "recall, analyse, and communicate effectively" [27]. Therefore, a participatory tool known as card sorting was used [27]. Following a methodology described by Herrington & Coogan, participants were asked to make a hierarchical ordering of reasons for and against PrEP use, while the interviewer asked probing questions [28]. In total, the interviews lasted between thirty minutes and one hour. A Russian interpreter was present during the interviews and interview materials were translated into Russian by AFEW Kazakhstan.

Data analysis

Quantitative and qualitative data was analysed concurrently. Survey data were used to calculate descriptive statistics, and bivariate analyses were performed to compare differences in demographic characteristics and PrEP awareness between MSM willing and unwilling to use PrEP. These associations were investigated using Pearson's chi-square test or Fisher's Exact ProbabilityTest when expected frequencies were low. Only factors

found to be significantly associated (p<0.05) with willingness to use PrEP in the bivariate analysis were purposely selected and further explored with the help of a logistic regression model. Odds ratios and 95% confidence intervals were calculated for the selected variables. All statistical analyses were performed using SPSS version 25.0 (IBM Corp).

Audio recordings from the interviews were transcribed to facilitate qualitative data analysis. Study participants were given a unique study identifier which was de-linked from their name. A password-protected document with participants' names and e-mail addresses was kept in order to share the study results with participants, and was subsequently deleted. Recording data

Table 1. Survey sample characteristics and willingness to use PrEP

Variables	Total (n = 108)	Willing to use PrEP $(n = 92)$	Unwilling to use PrEP (n = 16)	χ^2	р
Age					
18-25	38 (35.9%)	33 (35.9%)	5 (31.3%)	0.91	0.890
26-35	49 (46.2%)	41 (34.6%)	8 (50.0%)		
36-45	18 (17%)	16 (17.4%)	2 (12.5%)		
46+	1 (0.9%)	1 (1.1%)	0 (0.0%)		
Education level					
Finished primary or secondary education	14 (13%)	13 (14.1%)	1 (6.3%)	0.75	0.47
Finished higher education	94 (87%)	79 (85.9%)	15 (93.8%)		
Financial situation					
Poor	13 (12%)	13 (14.1%)	0 (0.0%)	2.70	0.27
All right	70 (64.8%)	59 (64.1%)	11 (68.8%)		
Good or excellent	25 (23.2%)	20 (21.7%)	5 (31.3%)		
Region of residence					
Almaty (city)	53 (49.1%)	46 (50.0%)	7 (43.8%)	3.53	0.19
Astana (city)	17 (15.7%)	12 (13.0%)	5 (31.3%)		
Other region	38 (35.2%)	34 (37.0%)	4 (25.0%)		
Relationship status					
Single	46 (42.6%)	38 (41.3%)	8 (50.0%)	3.79	0.28
Having dates	30 (27.8%)	27 (29.3%)	3 (18.8%)		
In a relationship	18 (16.7%)	17 (18.5%)	1 (6.3%)		
In an open relationship	14 (13%)	10 (10.9%)	4 (25.0%)		
Sexual orientation					
Gay	73 (67.6%)	65 (70.7%)	8 (50.0%)	6.84	0.05
Bisexual	31 (28.7%)	25 (27.2%)	6 (37.5%)		
Straight	3 (2.8%)	1 (1.1%)	2 (12.5%)		
Other	1 (0.9%)	1 (1.1%)	0 (0.0%)		
HIV status					
HIV-positive	10 (9.3%)	9 (9.8%)	1 (6.3%)	3.40	0.31
HIV-negative	71 (65.7%)	58 (63.0%)	13 (81.3%)		
Does not know	15 (13.9%)	15 (16.3%)	0 (0.0%)		
Does not want to tell	12 (11.1%)	10 (10.9%)	2 (12.5%)		
PrEP awareness					
Has heard of PrEP	43 (39.8%)	41 (44.6%)	2 (12.5%)	5.85	0.01
Has not heard of PrEP	65 (60.2%)	51 (55.4%)	14 (87.5%)		

^a p-value < 0.05

and transcripts will be retained for a maximum of five years. Thematic analysis of the interview transcripts was conducted using the Framework approach to organise data according to key themes [29]. This approach consisted of two stages. First, codes were generated from the data through inductive ("open") coding. Second, these codes were categorised according to a theoretical framework of acceptability developed by Sekhon et al. [30].

In studies investigating the potential of PrEP, acceptability is generally assessed by measuring likelihood or willingness to use. However, in order to understand the underlying reasons for accepting or not accepting PrEP, such results should be supplemented with an analysis of the various components that can act as barriers or facilitators. Following a systematic review, Sekhon et al. distinguished seven components of acceptability of health interventions: affective attitude, burden, ethicality, intervention coherence, opportunity costs, perceived effectiveness, and self-efficacy [30]. These components were used to facilitate qualitative data analysis and to guide the development of our coding scheme (see Supplementary Material). Coding was done by the first author and checked by co-authors.

Results

Participant characteristics

The characteristics of the survey sample (n=108) are shown in Table 1. From demographic characteristics such as education level it seems that the sample mostly represents the higher socio-economic classes, and most were drawn from the country's two largest cities. While several participants stated to be heterosexual, those were not excluded, because many MSM in Kazakhstan are closeted and may identify as straight.

Semi-structured interviews were conducted with MSM (n = 10) who resided in Almaty. The mean age of the interviewees was 31 years (range 19–43, SD = 6.9). The majority (n = 9) identified as gay, one as bisexual. Most (n = 8) were HIV-negative while a minority (n = 2) were positive. Half of the participants were working in a medical or HIV/AIDS related field or were involved with LGBT activism.

Awareness of PrEP

A slim minority (39.8%) of survey participants had previously

heard of PrEP (Table 1, see also Table 2). Of the MSM that were interviewed about PrEP, most were already aware of its existence. However, qualitative analysis suggested that PrEP awareness was linked to being active in social networks and being more "internationally oriented", i.e. able to read English and having travelled abroad.

"In some circles, I guess, yes, it is known. Especially among those who can read in English or who tend to learn more about themselves, about LGBT issues. But that is not the majority of LGBT people." (HIV-positive MSM, 26–35 years)

Table 2. Awareness of PrEP and informal use among survey respondents who had already heard of PrEP (n=43)

Knowledge of PrEP	n
Correct knowledge of PrEP	16 (37.2%)
Incorrect knowledge of PrEP	27 (62.8%)
PrEP information sources	n
Medical personnel	4 (9.3%)
NGOs	0 (0.0%)
Friends	2 (4.7%)
HIV-positive persons	3 (7.0%)
Mainstream media	12 (27.9%)
Community media	13 (30.2%)
Social media	13 (30.2%)
Scientific sources	5 (11.6%)
Other	3 (7.0%)
Informal PrEP use	n
Already using PrEP	4 (3.7%)
Not using PrEP	104 (96.3%)

Information sources.

Survey participants had heard about PrEP mostly through media outlets: mainstream (27.9%), community (30.2%) and social (30.2%) media. People also knew PrEP through scientific sources (11.6%), medical personnel (9.3%), HIV-positive persons (7.0%), friends (4.7%), or other sources (7%). In the interviews, it was said that most information provided is in English or Russian, and there is a lack of information about any LGBT-related issues in the Kazakh language.

All interviewees believed it was important to provide information about PrEP. Several participants mentioned social media (Facebook or Instagram) as a means to improve PrEP awareness and to promote PrEP if it were to become available,

and the use of dating apps such as Hornet or Grindr. Also, participants stated that information about PrEP could be provided at gay night clubs in Almaty, or that HIV-positive MSM may help inform the community about PrEP because of their experience.

Knowledge of PrEP

Of those who heard of PrEP prior to the survey, about two thirds had correct knowledge of what it is and how it works. Among survey participants and interviewees with incorrect knowledge the confusion between PrEP and post-exposure prophylaxis (PEP) was most common.

"I believe we actually have a sort of PrEP.We have something that they give if you go to one of the AIDS centres, when you are a medical worker and you have a potential risk of having been infected. I have read that they give you a sort of, I think Truvada, one of the PrEPs." (HIV-negative MSM, 26–35 years)

In the survey, four participants (3.7%) stated that they were already using PrEP. However, none of them displayed correct knowledge about PrEP, so it is possible that they confused PrEP with PEP or antiretroviral therapy. This is especially likely because none of the participants in the qualitative part of this study knew anyone in Kazakhstan who was already obtaining PrEP through informal channels.

Acceptability of PrEP

Around half (48.2%) of the survey participants would probably or definitely use oral PrEP if it was available in Kazakhstan today, whilst about a third (37%) would maybe use PrEP. These combined groups were classified as 'willing to use PrEP'. A minority (14.8%) of MSM stated that they would probably or definitely not use PrEP, and were described as 'unwilling to use PrEP' (Table 1). In the bivariate analysis, no associations were found between demographic or HIV-related factors and willingness to take PrEP. However, having previously heard of PrEP was significantly associated with willingness to use PrEP $(\chi^2=5.85, df=1, p=0.016)$. This variable was further analysed through simple logistic regression which confirmed that those already aware of PrEP were more likely (OR=5.63, 95% CI 1.21–26.19, p=0.028) to be accepting of PrEP (Table 3). Survey participants' reasons for being interested or not in taking PrEP are shown in Figure 1. Attitudes towards PrEP are described in detail in the following sections.

Table 3. The results of logistic regression on willingness to use Pre-Exposure Prophylaxis (PrEP)

PrEP awareness	Willing to use PrEP OR (95% CI)	р
Has heard of PrEP	5.63 (1.21- 26.19)	0.028
Has not heard of PrEP	1.00	

Taking control of HIV prevention.

The most important reason for MSM to feel positive about PrEP was the possibility to be safer and more in control with regard to HIV infection. A large majority of survey participants agreed with the statements that using PrEP would make them: feel more in control (85.9%), feel less anxious (84.8%), feel safer (83.7%) and have a more satisfying sex life (71.7%).

Several interviewees had experiences with condoms rupturing or sexual partners secretly taking off condoms, and they would feel more in control with PrEP. Related to this are the problematic opening hours of the AIDS centres that make it impossible to obtain PEP during the weekend.

"I know that PrEP does not protect 100%, but I would feel much more protected when I would use PrEP. When I have risk sex on Friday, when the condom breaks for example, I can't go to the AIDS centre to take post-exposure prophylaxis." (HIV-negative MSM, 36–45 years)

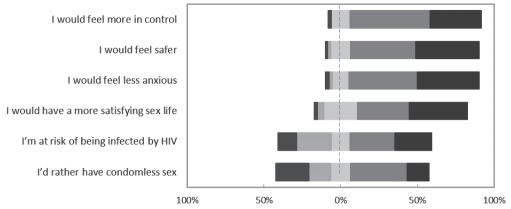
Various interviewees talked about extreme paranoia and anxiety after potential exposure to HIV, which impacted their daily lives by causing insomnia or difficulties with concentrating at work. Most interviewees felt that having PrEP would help decrease these feelings.

"I mean, about getting infected, it obviously affects your thinking and you just get paranoid all the time. And emotional outbursts. What if I have it? What am I going to do? What am I going to tell my parents?" (HIV-negative MSM, 18–25 years)

Addressing the growing HIV epidemic

Several interviewees mentioned the growing HIV epidemic in Kazakhstan as an important reason why they thought it would be good to introduce PrEP. Most participants thought PrEP should be offered as an additional method to MSM, especially to serodiscordant couples. Two interviewees said that the most important target group should be sex workers. Some participants noted that it is important not to market PrEP as something specifically for gay men, because then it might not be accepted

Reasons for being interested in PrEP (n = 92)



Reasons for not being interested in PrEP (n = 16)

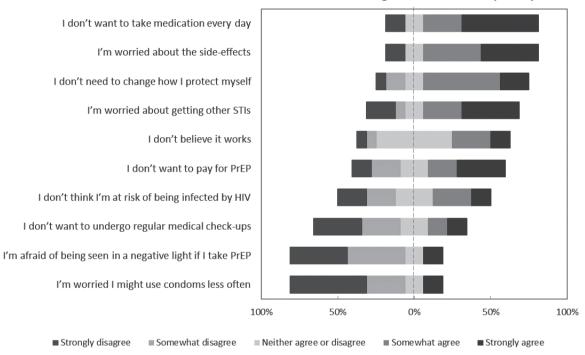


Figure 1. Reasons for being interested or not in taking PrEP if it was available today. Participants who would 'maybe', 'probably' or 'definitely' use PrEP (n = 92) were asked how important several factors were for their interest in taking PrEP. Participants who stated they would not use PrEP (n = 16) were asked about the reasons for not wanting to use it.

by a homophobic society such as Kazakhstan.

"In terms of epidemiology, it would be best to use Truvada as PrEP. It's been a long time coming. If we had incorporated it in the system way back, then we wouldn't have so many cases of HIV." (HIV-negative MSM, 26–35 years)

However, most participants thought it unlikely that Kazakhstan will approve PrEP for HIV prevention. They stated that others (NGOs, scientists) should convince the government

that PrEP needs to be available to address the growing HIV epidemic, essentially by conducting a pilot study locally.

"The research is from Europe, not from Central Asia. If we can show that it works here... We need to have information from a pilot. This difficult programme can only be started after a pilot study. If it is very effective, then it is nice for the government." (HIV-negative MSM, 36–45 years)

Perceived effectiveness

Despite an overall positive attitude towards PrEP, the MSM who took part in this study did have some concerns. In our survey, respectively 37.5% and 50% of those not wanting to take PrEP stated that they did not believe it works, or were unsure of whether it is effective. Qualitative analysis suggested that those who had read about PrEP were more likely to trust its effectiveness.

Two thirds (68.8%) of survey participants not interested in PrEP stated that their current methods were effective enough. Similarly, various interviewees noted that condoms are more effective than PrEP and also prevent against other STIs. However, they were positive about the idea of combining the methods for increased protection.

"Because I am not 100% sure about the effectiveness of this drug and I am sure that condoms protect from other diseases as well, it is much more advantageous to use condoms. But I am really positive about combined usage, both condoms and PrEP." (HIV-negative MSM, 26–35 years)

Side effects

One of the main concerns associated with PrEP, however, was the potential for side effects. Three quarters (75.0%) of survey participants not interested in taking PrEP, worried about this. In the interviews, various participants noted that although they would worry about side effects, these would be acceptable because PrEP prevents an incurable disease and helps to decrease anxiety.

"If it's just nausea and diarrhoea, that is a small part of my worry, the side effects. If it controls my anxiety and makes me feel more in control and safer, I can get over that." (HIV-negative MSM, 26–35 years)

PrEP adherence and dosing schemes

Another major barrier was the need to take PrEP daily. Among survey participants not interested in PrEP, three quarters (75.0%) stated they would not want to take daily medication. It was stated that adherence might be low because there is no visible connection between taking PrEP and being healthy and because MSM in Kazakhstan do not have sex with men on a regular basis, since there is no cruising area and finding sexual partners can be challenging.

"My HIV-positive friend, he says: I have to take these five

pills if I want to live. There is a direct connection. But taking a preventative medicine is like: if I miss it today is it really a big deal?" (HIV-negative MSM, 26–35 years)

The need to take PrEP every day was also seen as a barrier because taking medicine while being healthy is not acceptable to everyone. Even when it comes to treatment, there is a culture in Kazakhstan about not wanting to think about one's health or take medication. It was suggested that "on-demand" dosing of PrEP would be preferable for most MSM.

"I want to be healthy, and if I take medicine every day it seems I am unhealthy. It's psychological." (HIV-negative MSM, 36–45 years)

"But I really don't like the idea of taking a pill every single day, because it is really a lot, so I wonder why is there not a scheme that if you have some plans for the night, you take it and you are protected. [...] People would be less likely to want to take it because it is every day." (HIV-negative MSM, 26–35 years)

Medical checks

Taking PrEP may also be burdensome because of the regular medical follow-up. One quarter (25.0%) of survey respondents stating that they would not take PrEP did so because of the regular check-ups. The main reasons why these are perceived as a burden were the problematic opening hours of medical institutions, as well as the long queues.

"Every time you go to the medical institution, you take about half a day for these check-ups because of the queues. And our medical institutions work from 9 to 6pm. And not on the weekends. It is a problem, because in Almaty people work all the time." (HIV-positive MSM, 36–45 years)

PrEP-related stigma

LGBT discrimination in Kazakhstan is widespread, and most interview participants were not openly gay due to worries of discrimination or physical violence. Many MSM in Kazakhstan are married to women. Some participants thought the stigma is becoming worse because of the growing influence of Islam whereas other remarked that the younger generations are increasingly open-minded.

"Many gays live in constant fear and disguise, much like myself. I just pretend to be straight because in my work I cannot be openly saying I am dating a guy. I think this has a



psychological impact on me, because at some point you really get tired of being someone else." (HIV-negative MSM, 26–35 years)

"You need to talk more. If something is happening in the street, if two men are holding hands... If everyone starts to do that, then they need to start accepting it." (HIV-negative MSM, 18–25 years)

In addition to LGBT stigma, there is discrimination associated with HIV/AIDS, which was said to stem from a lack of knowledge on HIV that may cause people who practice risk sex not to take preventive measures or get tested for HIV. This lack of knowledge was thought to be caused by flawed sexual education in Kazakhstan, and by a culture of not talking about sex.

"But when I ask people here, it's almost this 'Of course I'm negative, I'm Kazakh. Of course, it's none of your business'. But when I ask 'Did you ever get tested?' it's like, 'No, why should I get tested?'." (HIV-negative MSM, 26–35 years)

Additionally, there can be stigma associated with the use of PrEP itself. However, in our survey only 12.5% stated they would not take PrEP because of fear to be seen in a negative light. Similarly, all interview participants had a positive image of PrEP users, and believed stigma would not be an issue because they would only talk about PrEP to those people they trusted. One participant believed there might be discrimination if people mistake it for something taken by HIV-positive persons.

"I think nothing negative. I think they are people who care for their health and want to have a long life." (HIV-negative MSM, 26–35 years)

Moreover, some interviewees thought that if PrEP would lead to discrimination, it would be because of the links to being gay or having risk sex. Especially among married MSM, it may be difficult to justify using what participants called "gay-related" things such as condoms or PrEP. On the other hand, one interviewee noted that PrEP is much easier to hide ("just say it's vitamins") than condoms. Here again, improved sexual education was thought to be key in removing these associations.

"And in marriage you will not use condoms because your wife will find the condom. You cannot wear it in your pocket because your wife can find it. That is why people don't want to use condoms and they want to use PrEP." (HIV-negative MSM, 36–45 years)

Preferred place of PrEP provision

Interviewees stated they would not be comfortable discussing PrEP with their general practitioner because of privacy concerns and the homophobic attitudes of some healthcare professionals. However, most MSM would be comfortable discussing PrEP at the AIDS centre, which was regarded as a specialised centre where MSM can be open about their sexuality.

"For gays, I think the best place is the HIV centre, it is a special place and doctors know about the problem. They will be more qualified. What about my family doctor? He knows my name, and my father or my mother." (HIV-negative MSM, 36–45 years)

Nonetheless, there are still barriers associated with visiting AIDS centres. Most importantly, many MSM were afraid of being seen by relatives or friends. Also, two participants worried about privacy even at the AIDS centre, with people walking in during medical checks, and several interviewees said it would be good to also provide PrEP at more anonymous places such as pharmacies or NGOs.

Financing of PrEP

Among survey participants not interested in taking PrEP, half (50.0%) stated that they did not want to pay for it. Interviewees believed that PrEP will be very expensive because of corruption. The majority said they would be willing to pay some money for PrEP. The maximum monthly price that those participants were willing to pay for PrEP ranged from 6,000 to 70,000 KZT (i.e. approximately 20 to 200 EUR). However, it should be noted that many Kazakhstani people will not be able to afford this.

"You know, not everyone can afford this medicine. I can afford it, maybe for my boyfriend or girlfriend. But the minimal salary in Kazakhstan is about 22,000 tenge. It's about 50 dollars at the current exchange rate." (HIV-positive MSM, 36–45 years)

About half of the interviewees believed PrEP should not be paid for out-of-pocket but should be provided for free, especially since Kazakhstan is supporting other innovative things such as green energy and because prevention will be more cost-effective than treatment. However, several others disagreed, either because they believed funding treatment was more important or because they thought the money should rather be invested in providing condoms and sexual education.

"Sex is about pleasure. Why should the government pay for my pleasure? I don't know. But HIV is a big problem, it is about our human future. So in that way, they should pay. Because I work, I can pay for PrEP. What if I lose my work? I don't lose my sexuality. What should I do then? Just stop?" (HIV-negative MSM, 36–45 years)

"This is a preventive thing, this is not something to treat. I think the government should provide HIV medicine for people who actually have HIV, but I don't think PrEP should be part of that. I think it should be affordable but not covered by the government." (HIV-negative MSM, 26–35 years)

Effects of PrEP on condom use

Of survey respondents not interested in PrEP only a small number (12.5%) gave as a reason that they would use condoms less often. In the interviews, around half always used condoms, whereas some occasionally had unprotected sex and a minority believed they would stop using condoms if they took PrEP. It was, however, believed that many MSM in Kazakhstan would not use condoms anymore when taking PrEP. On the other hand, participants suggested that many MSM in Kazakhstan already do not use condoms, and that PrEP would be vital to reducing HIV incidence in this group.

"I would use condoms less, because of the feeling. Knowing that I am taking this medication, I would feel confident and not always use condoms." (HIV-negative MSM, 18–25 years)

The main reason for not wanting to use condoms was said to be the reduced feeling during sex. Another factor is related to access to condoms: they can be expensive and are less freely available in Almaty than in the past when free condoms were often distributed at gay night clubs. Lastly, several participants mentioned the stigma related to buying condoms or asking sexual partners to wear one. "People don't feel in a position to discuss them, like 'I don't like this' or 'can we discuss safe sex'. When I had sexual contact with Americans or Europeans, that is an easy thing. If someone doesn't like something, he or she says it. Here it is a little bit tricky." (HIV-positive MSM, 26–35 years)

Discussion

This mixed-methods study was the first to investigate awareness and acceptability of PrEP among MSM in any Central Asian country. With this exploratory study we sought to provide a basis for future work on the use of PrEP for HIV prevention among MSM in Kazakhstan.

The results show that PrEP is not widely known: less than half (39.8%) had heard of PrEP prior to taking the survey, and among these only a small majority (62.8%) had correct knowledge about PrEP. Globally, awareness rates increased in the past few years since the publication of the iPrEX trial data [4]. In Kazakhstan, awareness may be low because there is no real MSM community due to the widespread homophobia [11].

It should be noted that the survey sample in this study consisted of mostly well-educated individuals residing in Almaty and Astana. Previous studies have shown that PrEP awareness is linked to living in large cities and higher education [31, 32]. Thus, PrEP awareness may be much lower in rural areas of Kazakhstan. It is crucial that if PrEP programmes are started in the future, special attention is paid to ensuring that all MSM at risk are reached with PrEP messaging. Similar to our findings, a mixed-methods study among MSM in Scotland suggested that online social networks can offer a promising solution to provide PrEP information to those who do not use the commercial gay scene [31].

Even when awareness rates are low, interest in PrEP among HIV-negative MSM is generally relatively high [19]. In the aforementioned study among MSM in Scotland, Frankis et al. [31] found no relation between PrEP acceptability and previous awareness, reinforcing "the notion that information alone is insufficient to support PrEP usage and [underlining] the need for both awareness-raising and support for PrEP use" (p. 12). However, we did find a positive relation between previous awareness and willingness to use PrEP, Thus, it seems that information campaigns about PrEP for HIV prevention could serve as a valuable first step in further enhancing PrEP acceptability among MSM in Kazakhstan.

In our study in Kazakhstan, PrEP acceptability was relatively high with around half (48.2%) of survey participants stating they would probably or definitely use PrEP if it was available, whilst about a third (37%) were still uncertain. Further studies are needed to investigate what socio-demographic and HIV-related factors are statistically associated with willingness to use PrEP since we found no statistically significant associations, potentially due to sample size limitations.

Acceptability levels slightly lower (41%) than in our study have been found among MSM in Thailand, which may be due to PrEP efficacy being defined there as only fifty percent [33]. Although higher PrEP acceptability rates have been found

among MSM in several other Asian countries (67.8% in China and 55.7% in India), those surveys did not have an option to express uncertainty about PrEP interest [34, 35]. If our respondents who answered 'maybe' are classed as interested in PrEP, which we eventually did in order to compare between MSM willing and unwilling to use PrEP, then PrEP acceptability among MSM in Kazakhstan is very high at 85.2%. Future research on awareness and acceptability of any healthcare innovation would benefit from the development of standardised questionnaires to facilitate better comparisons.

The main reasons for Kazakhstani MSM to be interested in PrEP related to increased safety and control of HIV prevention. Interviewees revealed severe anxiety about HIV transmission and were enthusiastic about additional protection, similar to findings from previous qualitative studies in which PrEP was regarded as an option to engage in worry free sex, and as protection that is independent of sexual partners' behaviour [36, 37]. This anticipated empowering effect was confirmed by Collins et al. [38] who showed that PrEP "reduced fear and shame associated with sex and facilitated greater sexual satisfaction and intimacy" (p. 55).

Our study also found several barriers to PrEP acceptability. One of the most highly endorsed barriers was the burden in terms of potential side effects. Currently, an updated version of Truvada that is thought to have fewer side effects, is being investigated by Gilead. Such improved versions of PrEP might prove more acceptable to MSM. Another important barrier was the strain of taking a daily pill, similar to a qualitative study from India [35]. Participants reported preferences for less frequent or "on demand" dosing. The IPERGAY trial was the first study to employ this type of episodic dosing: MSM took two tablets of Truvada two to 24 hours before sexual intercourse and another tablet at both 24 and 48 hours after, which reduced the risk of contracting HIV by 86 percent [6]. This regimen may therefore be a good alternative to daily PrEP for Kazakhstani MSM, who mostly do not have regular sex.

Participants in the qualitative part of this study stated that PrEP would lead to a decrease in condom use. Several studies have reported anticipated increases in risk behaviour due to PrEP, whereas the large iPrEX study did not find any association between PrEP and risk compensation [4, 36, 39]. Further research into this is needed in Kazakhstan and other settings, but in any case PrEP needs to be offered as part of a comprehensive HIV

prevention strategy that includes risk reduction counselling. Moreover, it should be recognised that (due to stigma, lack of knowledge, and limited access to condoms) the percentage of Kazakhstani MSM already engaging in unprotected sex may be as high as 69.0%, and that PrEP could play a crucial role in protecting them from HIV infection [16].

An unexpected finding of this study was related to stigma and discrimination. Despite the intolerance in Kazakhstan towards LGBT people and people living with HIV (PLHIV), and in contrast with other studies [40], specific PrEP-related stigma was not a major barrier to PrEP acceptability. Our qualitative findings suggest that anticipated PrEP stigma is low among MSM in Kazakhstan because of the potential for covert use. MSM approached it pragmatically: when other people do not know that you take PrEP, how could they discriminate you for it? In this way, PrEP may be less stigmatising than condoms and may be preferable to MSM living in more difficult country contexts such as Kazakhstan [41]. MSM in this study also believed discrimination not to be an issue at the specified AIDS centres, where doctors have been trained to work with LGBT people and where attitudes around HIV are different, making these a promising setting for future PrEP provision.

Challenges associated with PrEP introduction extend to structural barriers, including the limited sexual education and the potentially prohibitive cost of PrEP. Medication is costly in Kazakhstan due to a combination of factors, including the country's economic transition and the limited pharmaceutical infrastructure [42]. Although no conclusive data exists for Kazakhstan, in other countries such as India the most at-risk MSM are of lower socio-economic status, which makes the affordability of HIV prevention methods especially important [35]. However, financial planning of PrEP may be difficult because it is unclear how many MSM there are in Kazakhstan and how much PrEP should be procured. Due to the absence of reliable data, the HIV epidemic among MSM is largely hidden and MSM "remain a key population in name only" [20]. Currently, little to no money from national budgets of Central Asian countries is allocated to specific HIV interventions for MSM [43]. Because of the climate of discrimination against LGBT people, the government may be reluctant to introduce PrEP if it is communicated as something specifically for gay men.

Several suggestions for further research have arisen from this study. First of all, it became apparent that the burden of taking

PrEP is an important barrier to its uptake. Thus, there is a need for additional studies investigating alternative PrEP formulations or regimens. Second, this study has provided inconclusive evidence on the potential for decreased condom use as a result of PrEP. Future PrEP studies need to remain alert of this issue, and additional meta-analyses would be warranted. Third, future studies are needed to investigate awareness and acceptability of PrEP among other key populations in Kazakhstan. This would not be relevant only in Kazakhstan: there seems to be a worldwide lack of PrEP acceptability studies among key populations other than MSM. Fourth, research on awareness and acceptability of any healthcare innovation would significantly benefit from the development of standardised questionnaires, in order to facilitate better comparisons.

Limitations of the study

The main strengths of this study are the combination of quantitative and qualitative methods and the relatively successful recruitment of MSM, given the difficulties with accessing this population. However, our findings are subject to several limitations.

Most importantly, the survey results may not be generalizable to all Kazakhstani MSM, due to the small sample sizes and the potential sample bias towards MSM from higher socio-economic classes. Logistic regression analysis was only performed for the variable 'PrEP awareness', since we used the method of purposeful selection to avoid statistical errors [44]. Moreover, the small size of the group unwilling to use PrEP (n=16), enabled only simple logistic regression without adjustments for additional variables. Correcting for additional variables would have violated one of the assumptions for regression analysis, i.e. that a minimum of 10 events are required per independent variable in the model [45]. However, because of the expected sample size limitations and since the survey served only as a preliminary exploration, from the beginning we have been mostly interested in descriptive statistics that could provide an answer to the question whether there is potential for PrEP at all in Kazakhstan. Further studies involving more detailed quantitative analyses, including multivariate logistic regression, are needed to investigate associations between socio-demographic factors and PrEP awareness and acceptability.

Moreover, our survey was limited in length due to worries about 'scaring off' potential participants with a lengthy

questionnaire and intimate questions, especially given the country context. Although the short survey may have positively contributed to participation rates being higher than expected, those planning further studies in Kazakhstan should consider utilising more extensive questionnaires that include questions about sexual behaviour (e.g. condom use).

Finally, an important limitation lies in asking MSM to respond to a hypothetical scenario in which PrEP is available, and doing so based on limited information [46]. However, since PrEP is currently not available, such estimations of anticipated behaviour represent the only means to inform about acceptability of future PrEP programmes.

Conclusions

PrEP is an essential component of HIV combination prevention. In this study, a broad picture was drawn of PrEP awareness and acceptability in Kazakhstan. Our findings suggest that there are only certain groups of MSM that know PrEP, and that future (social media) information campaigns should aim to reach all MSM communities. Raising awareness would also help increase acceptability of PrEP. Nonetheless, the results show that there is already significant interest in PrEP among MSM in Kazakhstan, mainly because of the opportunity for additional and covert protection against HIV, which would empower MSM to take control of HIV prevention in this difficult country context. However, several acceptability barriers as well as more structural issues (such as the country's limited pharmaceutical infrastructure or the attitudes towards LGBT people) should be addressed in order for pilot studies to show the full potential of PrEP in Kazakhstan and possibly in other Central Asian nations.

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