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“AIDS Impact Special Issue” – High PrEP acceptability and need for tailored implementation in Cambodian key populations: results from a qualitative assessment

Camilla Oliveri^{a*}, Rothmony Eang^{b*}, Olivier Ségéral^c, Marion Mora^a, Lerksmey Puth^b, Sengrith Prom^b, Emilie Mosnier^{a,d}, Vichea Ouk^e, Bruno Spire^a, Vonthanak Saphonn^b and Marion Fiorentino^a

^aAix Marseille Univ, IRD, Inserm, SESSTIM, Sciences Economiques & Sociales de la Santé & Traitement de l'Information Médicale, ISSPAM, Marseille, France; ^bUniversity of Health Sciences, Phnom Penh, Cambodia; ^cHIV Unit, Infectious Diseases Department, Geneva University Hospital, Geneva, Switzerland; ^dGrant Management Office, University of Health Sciences, Phnom Penh, Cambodia; French Agency for Research on AIDS, Viral Hepatitis and Emerging Infectious diseases (ANRS-MIE), Phnom Penh, Cambodia; ^eNational Center for HIV/AIDS, Dermatology and STD, Phnom Penh, Cambodia

ABSTRACT

The HIV epidemics in Cambodia is concentrated in key populations (KPs). Pre-exposure prophylaxis (PrEP) has been officially approved in the country since 2019. However, its use may still be controversial after a PrEP clinical trial was interrupted in Cambodia after being deemed unethical in 2004. In this context, it was necessary to evaluate PrEP acceptability and administration preferences of KPs in Cambodia, with a view to increasing roll-out and uptake. We conducted a qualitative study in 2022 comprising six focus groups and four semi-structured individual interviews with transgender women, men who have sex with men, male entertainment workers, venue-based female entertainment workers (FEW), street-based FEW, and PrEP users who participated in a PrEP pilot study that started in 2019. Overall, KPs positively perceived PrEP, with some reservations. They preferred daily, community-based PrEP to event-driven, hospital-based PrEP, and highlighted that injectable PrEP would be a potential option if it became available in Cambodia. We recommend (i) proposing different PrEP regimens and PrEP delivery-models to broaden PrEP acceptability and adherence in Cambodia (ii) increasing the number of community-based organisations and improving the services they offer, (iii) rolling out injectable PrEP when it becomes officially available, and (iv) improving PrEP side effects information.

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Introduction

Cambodia has almost achieved the UNAIDS 90–90–90 goals in its general population (86%, 86%, 84%) and HIV prevalence in the country is 0.5%. However, among key populations (KP), prevalence is still very high: 4.9% for female entertainment workers (FEW), 4% for men who have sex with men (MSM), and 9.6% for transgender women (TGW) (UNAIDS, 2022). Young MSM and TGW are highly affected by new HIV infections accountable for 42.6% (UNAIDS, 2023).

Pre-exposure prophylaxis (PrEP) is a validated tool to prevent HIV infection recommended by the World Health Organisation. It combines tenofovir and emtricitabine in pill form, and is taken either daily or for individual sexual encounters (“event-driven” hereafter)

(Spinner et al., 2016). In MSM, oral PrEP is estimated to reduce HIV acquisition by 75% (Murchu et al., 2022). In 2021, injectable PrEP (which is based on cabotegravir and administered once every 2 months) was first approved in the United States (Office of the Commissioner, 2021).

Given the high HIV prevalence and incidence rates in KPs in Cambodia, making PrEP available could be very beneficial. However, ethical concerns and protests from KPs communities regarding PrEP clinical trials have emerged in Nigeria, Cameroon and Cambodia throughout the first decade of the twenty-first century (Mack et al., 2010; Peterson & Folayan, 2019). An HIV prevention clinical trial, which aimed to test the efficacy and safety of tenofovir among HIV-negative Cambodian

CONTACT Camilla Oliveri  camilla.oliveri@inserm.fr  Aix Marseille Univ, IRD, Inserm, SESSTIM, Sciences Economiques & Sociales de la Santé & Traitement de l'Information Médicale, ISSPAM, Marseille, France

*These authors contributed equally to this work

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entertainment workers (EW, i.e., who practices commercial sex), was halted in 2004 after community EW organisations condemned what they saw as exploitation of EW by pharmaceutical companies and populations from developed countries (Grant, 2016; Mills et al., 2005). Thus, controversy may still surround this antiviral medicine in Cambodia, because of the political and media-based fall-out after the interruption of this trial.

In this context, there is a need to know Cambodian KPs' current perception or acceptability of PrEP, or indeed their preferences for its administration and PrEP delivery-models (i.e., daily, event-driven, oral, injectable, medical-based, community-based).

With a view to understanding whether it would be possible to implement PrEP in Cambodia, we investigated two main topics: PrEP, and the HIV/STI context in KPs. Specifically, for the first topic, we explored PrEP acceptability, perceived benefits and drawbacks, and preferences regarding regimen type and delivery-model. For the second topic, we examined awareness of HIV and STI infection risks, perceived risk factors, access to information about preventive methods, and use of these methods.

We formulated four hypotheses: (i) PrEP awareness and acceptability is low in KPs in Cambodia, as this is the case in other South-East Asian countries (Yi et al., 2017), (ii) the Cambodian context might be especially unfavourable to PrEP given the above-mentioned controversy, (iii) community organisations can play a critical role in providing PrEP information, initiation and counselling, as KPs are difficult to reach in health facilities in Cambodia, and (iv) community organisations may lack the financial, logistical and skill capacities to adequately deliver PrEP.

Methods

This study was conducted from March to May 2022 in Phnom Penh. We used a qualitative, community-based approach comprising six focus groups and four semi-structured individual interviews. Focus groups provided the opportunity to observe the process of constructing knowledge, which allows access to collective representation and construction of meanings (Kitzinger, 1994; Kitzinger et al., 2004). The semi-structured individual interviews aimed to capture the point of views of representatives of some KPs.

The interview guide was prepared by MF, MM, RE, and OS. It addresses these topics both in the focus groups and in the semi-structured individual interviews: (i) HIV risk perception, (ii) experience with medical facilities and community organisations, (iii) perception

of and satisfaction with available HIV prevention strategies (i.e., condoms), (iv) expectations and needs regarding innovative HIV prevention strategies (oral and injectable PrEP), and (v) beliefs and representations about PrEP and its perceived efficiency. The interview guide was tailored to the interviewees. The guide included information about PrEP to be provided to participants in the TGW, MSM, MEW, venue-based and street-based FEW focus groups.

Three community-based organisations were involved in the research design process and in the recruitment of participants (Men's Health Cambodia (MHC) and Men's Health Social Service (MHSS)), which both support MSM and TGW, and Cambodian Women for Peace and Development (CWPD), which supports FEW. The objective was to recruit approximately half of participants from the CBOs networks, and half from outside the CBOs networks.

The 10-member six focus groups comprised 10 TGW, 10 cisgender venue-based FEW (i.e., working in entertainment establishment such as karaoke, bars, beer gardens, massage parlours), 10 cisgender street-based FEW (i.e., self-employed, working on the street or in parks), 10 cisgender male entertainment workers (MEW), 10 cisgender MSM, and 9 PrEP users (of whom 6 were cisgender MSM and 3 TGW). The latter had participated in a pilot study of medical PrEP delivery called "Khmer-PrEP" who started in 2019.

For the four semi-structured individual interviews, we interviewed a TGW and a cisgender FEW key influencer, both of whom were leading figures within their respective communities. We also interviewed a cisgender MSM who was a former participant in the Khmer-PrEP pilot programme and had stopped using PrEP, as well as an upper-class hidden cisgender MSM.

Eligibility criteria for study participation (i.e., focus groups and interviews) were (i) for MSM: being sexually active and have had anal sex with at least one male or TGW partner in the previous 12 months, (ii) for TGW: being biologically male at birth and self-identifying as a woman or non-binary gender and having had anal sex with at least one male in the previous 12 months, (iii) and for EW: having had sexual intercourse at least once in exchange for money during the previous month.

The language of the focus groups and interviews was in Khmer. The facilitator was RE and he performed both the focus groups and the semi-structured individual interviews. To avoid bias, the facilitator first asked interviewees about their prior knowledge of PrEP before presenting them with information on the subject. The information provided remained impartial as it exclusively focused on PrEP purpose. The interview guide was

adhered to. However, at times, it was adapted based on the flow of the conversation, such as delving into specific issues raised by the participants. The focus groups lasted between 1 and 2 h while the semi-structured individual interviews lasted between 30 min and 1 h.

The data collected were transcribed verbatim and directly translated into English by the Cambodian team. Interactions, participants' emotions, and the aspects of non-verbal communication were enclosed within brackets and were taken into account during the thematic content analysis. CO performed data analysis with NVivo using a thematic approach. To obtain the final codebook, the coding process followed two steps: (i) the development of a large detailed codebook and (ii) the clustering of the most significant codes, which are further subdivided into subcodes related to each KP. In focus groups, the process of construction of meanings emerged from participants' responses, as they evoked what others had previously stated and personalised their responses with their own viewpoints and experiences. To secure the rigour of the study, the research teams strictly collaborated during the data collection and analysis. MF and MM regularly supervised the coding process. The results were discussed collectively and were compared with the scientific literature. The citations included here have been slightly modified to improve clarity.

This study received ethical approval from the Cambodian National Ethics Committee for Health Research on the 23rd of October 2020 (n°264 NECHR).

Results

The study included 63 participants (4 in interviews and 59 in focus groups), aged between 18 and 43 years old. Eighteen of the focus groups participants came from Phnom Penh, 13 from Siem Reap, 8 from Kampong Som, 10 from Kandal, 4 from Banteay Manthey, 4 from Battambang, and 2 from Sihanoukville. Participants' characteristics are described in Table 1.

Perceived risk factors for contracting HIV: promiscuity, alcohol use, and not using condoms

All the participants were aware of the risk of HIV infection. They perceived uncertainty about a sexual partner's HIV status (including steady partners) and promiscuity as risk factors for contracting HIV:

We cannot trust our partner, we cannot see HIV, so we need to be careful. No matter how much we trust, we must protect ourselves to avoid the risk of HIV infection. (FG, street-based FEW)

Table 1. Characteristics of the key populations who participated in the study's six focus groups and four semi-structured interviews.

Self-identification	Focus groups		
	Number of participants	Gender	Age range (years)
Transgender women (TGW)	10	10 transgender women	22–36
Venue-based female entertainment workers	10	10 cisgender women	24–38
Street-based female entertainment workers	10	10 cisgender women	23–43
Male entertainment workers	10	10 cisgender men	19–36
Men who have sex with men (MSM)	10	10 cisgender men	18–35
PrEP users (6 MSM and 3 TGW)	9	6 cisgender men 3 transgender women	21–36
Semi-structured interviews			
TGW, key influencer	1	Transgender woman	27
Entertainment worker key influencer	1	Cisgender woman	41
MSM ex-PrEP user	1	Cisgender man	42
Upper-class hidden MSM	1	Cisgender man	30
Total number of participants	63		

Other perceived risk factors were the disinhibiting effect of alcohol and drug use during sex, poor hygiene, anal sex, and group sex. Moreover, with regard to HIV prevention, not using PrEP (in respondents who were already aware of it), and especially the misuse (e.g., leading to breakage) and non-use of condoms were considered risk factors. Barriers to condom use were drunkenness, client refusal, lack of availability (supply or money), and trust in stable partners:

With our husband, we cannot let him use condoms. When he uses a condom [because we ask him to], he suspects that we do not trust him that why we ask him to use condom. So, if we use this medicine [PrEP], we are not afraid of getting infected by our husbands. (FG, venue-based FEW)

Perceived benefits of oral PrEP: good alternative to condoms, efficient HIV protection, and access to free health check-ups

A majority of participants positively perceived oral PrEP because of the following participant-reported benefits: it protects people from HIV, it avoids risks related to condom misuse and it replaces the need for condoms. In addition, participants underlined that PrEP uses means access to free kidney and liver health check-up as well as free access to STI screening, that it increases trust during sex and in partners, and lessens discrimination of sexual partners living with HIV:

When we use PrEP, the change is that it can help reduce discrimination, as we know that using PrEP, we can have sex with HIV-positive people. So today, HIV-positive people still have the opportunity to have sex as normal and those who love HIV-positive people dare to open more than before. Before, no one dared to love HIV-positive people because they were very worried, so this is a good change. (FG, PrEP user)

In the PrEP user focus group, two other benefits were underlined: PrEP was provided free of charge in Cambodia and was easy to administer.

In addition to all these benefits, participants positively perceived PrEP because Cambodian health authorities had approved it and because it was already being used by other members of their specific community:

The question is whether to believe in PrEP or not. I say I believe, because it comes from the Ministry of Health of Cambodia! I believe. (FG, TGW)

Perceived drawbacks to PrEP: absence of protection towards STIs, fear of side effects, and difficulties of adherence

The first drawback to PrEP was the lack of protection against STI other than HIV (and for participating FEW, against unwanted pregnancies):

So between this medicine and condoms, I choose condoms. They have already recommended it [PrEP] to me, but I do not care. Because they said it can only prevent HIV, I can still get pregnant and STIs. Instead, using condoms can prevent STIs, HIV and pregnancy. (FG, venue-based FEW)

The second drawback was the fear of PrEP-related side effects like vomiting, dizziness, headache, sleepiness, and weight gain. Experiencing side effects was one reason why some of the participants who were ex-PrEP users had stopped using it. These same participants (i.e., ex-PrEP users) also mentioned the lack of protection against other STIs, mental load, not having sexual relations, and distrust between partners. With regard to the latter point, some felt that if they were to use PrEP, it would suggest a lack of trust in their partner. Because of this possible perception (i.e., lack of trust), they did not want to use it.

The third drawback reported by participants was the difficulty in adhering to the PrEP regimen caused by drunkenness, travelling, an irregular lifestyle, mental load, and HIV-related stigma. The latter arose from the fear of being considered HIV-positive, especially as PrEP pills are physically similar to antiretroviral therapy pills. Accordingly, some participants would take the pills secretly and live in constant fear of being discovered:

I'm afraid that if I put it in my bag or in my bedroom, I would be afraid of the people around me, or that my family would know that I was taking it. I would feel ashamed, for me personally. For other people, I do not know. Yes, that's it. (FG, TGW)

Preferences for type of PrEP regimen and delivery-model: daily PrEP and community-based PrEP

Most participants preferred daily to event-driven PrEP because (i) the intake schedule was less complicated, (ii) planning for sex was difficult, and (iii) the risk of forgetting to take one's pills was lower. In contrast, TGW preferred event-driven PrEP because of their (i) fear of side effects, (ii) perceived negative interaction with hormonal therapy, (iii) and not wanting to feel like a patient:

If there was an on-demand option before sex, I would use that option. If I had to take the pill daily, it could interact with the hormones I take every day. That's how I see it! Because I take hormone pills daily. If I got PrEP, and I administered it daily, then I would be afraid of having drug reactions. For me, I'd choose the on-demand before sex, sir! (FG, TGW)

Most participants preferred community-based PrEP; however, the upper-class hidden MSM we interviewed said that some high class patients preferred private hospital-based PrEP service because it was faster and more confidential. The barriers to positively perceiving hospital-based PrEP service were (i) a lack of explanation about PrEP intake, (ii) the fear of discrimination, and (iii) feeling embarrassed in front of a doctor:

They [CBO workers] are very friendly. They advise us and we follow; then, we are cured. They pay lots of attention. Their working team explained to us about protecting yourself, we understand, we take the pill and we are cured. (Semi-structured interview, cisgender FEW key influencer)

The barriers to positively perceiving community-based PrEP were the (i) distance and related transportation fees from a structure, (ii) lack of medical expertise and explanations, (iii) long waiting times, (iv) lack of confidentiality, (v) fear to meeting people they knew, (vi) absence of free HIV and kidney/liver check-ups, and finally, (vii) uncertainty about long-term availability of PrEP:

I think the obstacle that we would face when getting the medicine from the community is that we are too friendly with each other, and we play a lot with each other. We do not trust each other; there would be no secrecy that I was taking this pill and having so many partners! That's an obstacle. And secondly, the CBO ... err ... the community-based organization. Is there

any training or clear consultation? Well, under these conditions they [CBO] have to learn about PrEP, they should receive clear training and demonstrate professionalism like a doctor. (FG, TGW)

Perceived benefits of injectable PrEP: reduction of adherence risk

Street-based FEW did not find injectable PrEP a useful option because they believed that the 2-month gap between administrations was too long a time interval and that they would forget their appointment. Other KP positively perceived injectable PrEP because (i) it removed the pill intake burden, (ii) worked faster and lasted longer than oral PrEP, and (iii) reduced the participant-perceived risks of non-adherence, side effects, and the risk of being seen taking it, and therefore potential HIV-related stigma and discrimination:

If we use the injection service, it will be good for me because sometimes when I sleep with clients, I'm drunk ... some other times, I forget ... to use condoms or to use any other medicine; but if we get the injection service, it will be good. And secondly, if we use the oral form, we will be afraid that other people might see the medicine label or capsules. But if we use the injection, we can hide it from them. (FG TGW)

Discussion

This study is novel in that it is the first to investigate PrEP acceptability and administration preferences in Cambodian KPs (including MSM, TGW, MEW, FEW) and key influencer coming from different Cambodian regions.

Our results disproved the first two of our four hypotheses (see above). Although PrEP knowledge was low amongst participants, PrEP acceptability was high. This suggests that Cambodia constitutes a favourable context to increase PrEP roll-out and uptake, despite the related controversy. The results are in line with the other two hypotheses were proven. Specifically, participants were difficult to reach in health facilities, highlighted the potential important role of community-based organisations in PrEP uptake. Having said that several perceived shortcomings in these organisations were highlighted. Moreover, our results showed that (i) KP participants wanted different PrEP regimen type (daily, event-driven, or injectable PrEP) and delivery-model (hospital-based PrEP or community-based PrEP) depending on the community to whom they belonged, and that (ii) KP participants were willing to take injectable PrEP.

KP participants in this qualitative study in Cambodia perceived they were at high risk of contracting HIV, and that alcohol abuse, promiscuity and not using condoms

were the three main risk factors for contracting HIV. Participants mentioned various obstacles to using condoms including: drunkenness, clients' refusal because condomless sex increased their (i.e., the clients') sexual pleasure, lack of availability (supply or money), and trust in stable partners. The 2019 and 2022 Integrated HIV Bio-Behavioural Surveillance surveys in Cambodia (IBBS) demonstrated that among MSM, TGW and FEW, not using condoms was more likely with non-commercial and regular partners (vs. commercial and casual partners) (NCHADS, 2022a). Specifically, 33% of MSM did not use a condom during their most recent sexual encounter with male regular partners, 24% with male casual partners, 16% with male paid partners and 19% with male paying partners. The respective rates of condom disuse for TGW were 28%, 16%, 11%, and 11% (NCHADS, 2019b). Finally, 45% of FEW did not use a condom during their most recent sexual encounter with regular partners, 15% with casual partners, and 8% with paying partners (NCHADS, 2022a).

In our study, despite the fact that not all the participants were aware of PrEP (especially those living in rural areas), many perceived it positively because it replaced condoms and protected against HIV. Moreover, participants saw other benefits: it increased trust during sex and in partners, and was linked to access to free STI screening and to kidney and liver check-ups. A gap between awareness of PrEP and willingness to use it was highlighted in another study conducted among FEW in Cambodia in 2019. Specifically, 32% of participants were aware of it, while 67% said they would use it if it became available (Garg et al., 2023). It is insightful to note that some participants perceived PrEP as a tool which increased trust during sex and in partner while others feared that it would suggest a lack of trust in their partner. This is a "PrEP ambiguity" as (i) the contrast between being in good health and the necessity of daily pill intake, (ii) taking PrEP as a responsible and irresponsible act, (iii) the sense of being protected against HIV but not against other STIs, (iv) the acceptability of PrEP in preventing HIV juxtaposed with the stigma surrounding sexuality, and (v) the feeling of sexual liberation tempered by the obligation to adhere to a medical treatment. "PrEP ambiguities" may hinder its accessibility and engagement. However, they also serve as drivers, motivating efforts to make PrEP more accessible (Skovdal et al., 2023).

The main three participant-perceived drawbacks to PrEP in our study were the absence of protection against STI other than HIV, the fear of side effects or HIV-related stigma, and difficulty adhering to the regimen. In a recent qualitative study conducted in Vietnam among MSM, the fear of side effects and of stigmatisation, as well as

adherence difficulties were also the main drawbacks to PrEP uptake (Nguyen et al., 2021).

However, it is possible that diversifying the PrEP regimen type (daily, event-driven, or injectable PrEP) and the delivery-model (hospital-based PrEP or community-based PrEP) could solve some of the perceived drawbacks reported in our study if they are adapted to the preferences of each community or individual.

For instance, TGW in our study believed that taking PrEP daily could cause side effects due to the large number of pills required. Consequently, they preferred on-demand PrEP and injectable PrEP, if the latter becomes available in Cambodia. The fear of interactions between PrEP and gender affirming hormone therapies has been frequently reported in TGW according to a systematic review in the US (Dang et al., 2022), and was reported as a reason to discontinue PrEP use in Thai TGW (Thongsak et al., 2023). Interestingly, our finding (i.e., the preference for event-driven PrEP over daily PrEP in TGW) is inconsistent with a US study where young TGW preferred daily towards on-demand PrEP and did not mention potential interactions with hormone therapy (Macapagal et al., 2021). Consistently with our finding, a qualitative study in India demonstrated that TGW preferred event-driven to daily PrEP, but mainly because of the unpredictability of their schedules (Chakrapani et al., 2020).

Moreover, injectable PrEP was perceived to reduce the threat of HIV-related stigma as it avoided the risk of being seen taking pills. The advantages of injectable PrEP in terms of perceived ease of use, better protection against HIV and stigma reduction have also been demonstrated in other contexts (Reyniers et al., 2023).

Similarly, the community-based delivery mode was preferred because of the perceived non-discriminatory ambience of community-based organisations (i.e., compared to hospitals). In a recent qualitative study conducted in South Africa among cisgender men, the unfriendly staff, the long waits and the lack of privacy were the reasons why the participants preferred community-based PrEP than clinic-based PrEP (Smith et al., 2023). The same trend emerged in Malawi (Lancaster et al., 2020) and in Vietnam (Nguyen et al., 2021).

The difficulties of adhering to PrEP (see above) could be resolved by choosing the PrEP regimen (i.e., daily, event-driven or hypothetically injectable) that best suited one's own needs. Moreover, the extension of community-based organisations' and hospitals' opening hours and implementing an appointment alert system could resolve certain adherence difficulties. In summary, our results showed that proposing different methods and places of administering PrEP would broaden acceptability and adherence.

This study has several limitations. First, our study population was not fully representative of each KP studied. Second, although the protocol planned for male and female researchers to conduct the focus groups and interviews, COVID-19-related logistical problems prevented us from having female researchers present. As the issues investigated could be considered delicate for some KP, it would have been advantageous to have at least one female researcher. Third, it is possible that the respondents' discourses suffered from social acceptability bias, power dynamics and strong voices in focus groups. The welcoming and non-judgmental setting, and the circular seating arrangement of participants, aimed to reduce the impact of power dynamics. Finally, the analysis of verbatims was performed on texts that were translated directly from Khmer to English, which might have induced a translator bias (Abalkhail, 2018).

The study also has several strengths. First, the choice to conduct focus groups and interviews ensured we could record all the aspects of non-verbal communication, and allowed participants to express themselves much more fully compared to using a closed-ended questionnaire. The facilitator ensured that everyone could voice their opinions, and the fact that focus groups consisted of individuals belonging to the same KP helped mitigate potential biases. Second, although the study is not representative of the totality of each KP community, it collected the perceptions of participants from various KPs with different ages, geographical origins, social classes and PrEP experiences. Third, as knowledge of PrEP was poor, it seemed that participants were not previously influenced by messages on PrEP.

Cambodia has officially approved PrEP in 2019 (National Center for HIV/AIDS, Dermatology and STD (NCHADS), 2019a, 2022b). Community-based organisations could play a critical role in PrEP delivery in Cambodia if some programmatic considerations are taken into account. We recommend four actions for community-based organisations in Cambodia: increasing the number of CBO and improving the services they offer through the presence of a doctor, reducing waiting times, increasing privacy protection, and providing STIs screening. Furthermore, to address the main drawbacks in PrEP uptake in Cambodia, we suggest proposing different PrEP regimens and PrEP delivery-models according to the preference of each community, improving promotion of PrEP through social networks (Facebook, Telegram and Instagram) and the communication about PrEP side effects to avoid misinformation, making injectable PrEP available, and better protection against HIV-related stigma.

Finally, a future quantitative assessment of the topics we investigated here would be useful to understand them further and to evaluate PrEP perceptions and acceptability on a large and representative scale.

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Authors' contribution statement

RE, OS, MM, BS, SV, and MF conceived and designed the study. RE, LP, and SP collected the data. CO analysed data and CO, RE, MF, MM, EM, OS, and BS interpreted them. CO drafted the paper and all authors revised it critically for intellectual content. All authors approve the final version to be published and agree to be accountable for all aspects of the work.

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