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Views of policymakers, healthcare workers and NGOs on oral and parenteral HIV preexposure prophylaxis (PrEP): implications for implementation

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ABSTRACT

Objectives: To examine policymakers and providers' views on PrEP, and their willingness to support its introduction, to inform policy and practice in this emerging field.

Design: Semi-structured qualitative interview study.

Setting: Peru, Ukraine, India, Kenya, Uganda, Botswana, and South Africa.
Participants: 35 policymakers, 35 healthcare workers, and 21 NGO representatives involved in HIV prevention.

Results: Six themes emerged from the data. (i) perceived HIV prevention landscape: prevention initiatives needed to be improved and expanded; (ii) PrEP awareness: 50 participants had heard of PrEP and 41 had not; (iii) benefits of PrEP: one component of the combination prevention arsenal that could help prioritise HIV prevention, empower key populations, and result in economic gains; (iv) challenges of PrEP: regimen complexity, cost and cost-efectiveness, risk compensation, efficacy and effectiveness, stigmatisation and criminalisation, information and training, and healthcare system capacity; (v) programmatic considerations: user eligibility, communication strategy, cost, distribution, medication and HIV testing compliance; and (vi) early vs. late implementation: participants were divided as to whether they would support an early introduction of PrEP in their country or would prefer to wait until it has been successfully implemented in other countries, with around half of those we spoke to supporting each option. Very few said they would not support PrEP at all.

Conclusions: Despite the multiple challenges identified, there was general willingness to support the introduction of PrEP. Yet, strengthening existing HIV prevention efforts was also deemed necessary. Our results suggest that an effective PrEP programme would be delivered in healthcare facilities, but also involve NGOs and the community, and consider the needs of mobile populations. Comprehensive information packages and training for users and providers would be critical. The cost of PrEP would be affordable and possibly segmented. Extensive counselling and innovative monitoring measures ought to be considered.

ARTICLE SUMMARY

Article focus

Understanding the attitudes, perceptions and preferences of key stakeholders towards PrEP, to identify important programmatic aspects that may enhance or hinder its effectiveness.

Key messages

- Policymakers, healthcare workers, and NGOs, particularly from Sub Saharan Africa, would be willing to support PrEP if proven cost-effective.
- PrEP was envisaged as part of a combination prevention strategy deeply rooted in and driven by its beneficiaries.
- To effectively tackle the HIV epidemic, reducing stigmatisation against those at higher risk of infection and strengthening existing prevention programmes is as critical as introducing new ones.

Strengths and limitations of this study

- This is the first international study on key stakeholders' preferences and concerns regarding PrEP and how best to address these at a policy and service level.
- Data collection was standardised, which facilitates data comparability, and relevant participants were recruited.
- Limitations include the largely hypothetical nature of the addressed PrEP characteristics, potential social desirability bias, and purposive recruitment – mainly in urban areas.

INTRODUCTION

HIV incidence is stabilising and beginning to decline in many countries with generalised epidemics. Further efforts should now focus on consolidating this trend[1]. New prevention approaches are being considered that might, in combination with existing ones, help achieve this goal. Following both successful and futile results in recent clinical trials[2-7], the use of anti-retrovirals to prevent HIV transmission (ART) or acquisition (preexposure prophylaxis or PrEP) has become a focus of HIV/AIDS policy discussions. Although further clinical evidence will be needed to determine optimal regimens and delivery mechanisms[8], multi-disciplinary preparatory work needs to be undertaken to identify where existing and potential modalities may fit best within an integrated HIV prevention package.

Previous work on the implications of a future PrEP implementation has highlighted the importance of engaging relevant stakeholders in a consultation process designed to strengthen, legitimise, and ultimately enhance its sustainability and effectiveness[9-11]. Understanding the preferences and concerns of policymakers and providers towards PrEP, drawing on their experience in designing and delivering comparable programmes, is therefore paramount to the success of this prevention approach[12-14].

This article reports on qualitative research exploring policymakers, healthcare workers, and non-governmental organisations' (NGOs) perspectives on oral and parenteral PrEP in seven countries: Peru, Ukraine, India, Kenya, Uganda, Botswana, and South Africa. The research presented here complements a study on attitudes and acceptance of PrEP among potential users reported elsewhere[15]. Our aim is to inform priority setting, programme design, and implementation, should PrEP prove cost-effective.

METHODS

A qualitative approach is most appropriate in an exploratory, in-depth study of this sort[16]. Face-to-face individual interviews were therefore conducted between November 2010 and March 2011 with purposively selected policymakers, healthcare workers, and NGO representatives responsible for or involved in HIV prevention in seven countries with diverse HIV epidemics: Peru, Ukraine, India, Kenya, Uganda, Botswana, and South Africa.

Ipsos MORI, an international social research company, coordinated the data collection. Interviews were conducted by experienced local senior researchers. Interviewers were trained face-to-face by both our team and/or Ipsos MORI. They were also provided with a comprehensive interview manual, which contained background on PrEP research, frequently asked questions, information on participant eligibility, detailed interview instructions, and a consent form in countries where local ethical approvals required this. Interviews took place in a private office at the participants' work place and lasted between 45 and 60 minutes. Interview guides and materials were translated into Spanish (Peru) and Russian (Ukraine) by the local research team, and checked in London by professional translators for consistency and quality. In India and Sub Saharan African countries interviews were conducted in English.

We used a semi-structured and probing interview guide constructed through expert consultations and a literature review. Before commencing, participants were informed that their answers would be anonymised and treated with strict confidentiality. Participants were first asked about their role, involvement with HIV prevention, perceptions of their countries' HIV prevention efforts, and awareness of PrEP. Then they were asked about their awareness and understanding of PrEP. Subsequently, interviewers read a description of hypothetical and real PrEP attributes, including: its ineffectiveness against other sexually transmitted diseases; its route of delivery: as a daily and before-and-after-sex pill, and eventually as a monthly and bi-monthly injection; its mild temporary side effects including: tiredness, headaches, and gassiness; its partial protective efficacy against HIV, especially if not taken as directed; and the need for frequent HIV testing. It was stressed that PrEP was undergoing clinical trials and its characteristics remained uncertain. Participants were then asked

to rank their concerns in order of importance. They were also asked to identify the benefits of PrEP, if any. Subsequently, they were asked to describe what an effective PrEP programme would look like in their countries. Participants were finally asked whether they would support PrEP being introduced at an early, a later stage or not at all.

All interviews were digitally recorded, transcribed and translated into English by professional translators where necessary, and were analysed independently by AW, GBG and AE to ascertain inter-rater coding reliability[17]. Using thematic analysis[18 19], an initial categorising system was developed based on the study objectives and the interview guides. We identified new themes and sub-themes emerging from the data analysis, which were included when consensus was reached regarding their relevance. A final thematic index was produced to code all data.

RESULTS

We conducted a total of 91 interviews (13 per country) including 35 policymakers, 35 healthcare workers, and 21 NGO representatives. Fifty-one participants were male and 42 were female. Participants' eligibility criteria are described in Table 1. We present our findings across countries and job roles, highlighting areas of convergence and divergence around six themes: perceived HIV prevention landscape, PrEP awareness, perceived benefits of PrEP, perceived challenges of PrEP, programmatic considerations, and early vs. late implementation.

Perceived HIV prevention landscape

Peruvian participants mentioned that their HIV epidemic had reached a plateau with a significant reduction in mortality. Men who have sex with men (MSM), especially transsexuals, were identified as the most affected group. Stigma, low self-esteem, and substance abuse were frequently referred to as underlying determinants of high HIV incidence among MSM. Cultural and religious barriers, insufficient resources, and the recent decentralisation of Peru's healthcare system, which had led to inefficiencies in the provision of services, were raised as the main reasons behind the current HIV prevention deficiencies. A mismatch between treatment and prevention expenditure and the comparatively low HIV incidence among the beneficiaries of prevention programmes were mentioned as main causes for concern.

Most Ukrainian participants agreed that HIV prevention had recently become a priority on their government's agenda. Nonetheless, they raised concerns regarding the accuracy of the official HIV incidence data, and the pervasive criminalisation and stigmatisation of key populations (Injecting drug users (IDUs), female sex workers (FSWs), and MSM), which in turn hindered their access to prevention programmes. Participants felt that reducing Ukraine's dependency on international donors, increasing and optimising public resources for HIV prevention, as well as involving communities in the design of prevention programmes, strengthening advocacy work and raising awareness, was urgently needed to increase the impact and sustainability of prevention efforts.

Similarly, Indian participants felt that their country's HIV prevention efforts were insufficient and identified sex workers, MSM, truck drivers, serodiscordant couples, and IDUs as populations at higher risk of infection. Key HIV prevention challenges included: lack of access to condoms and difficulty negotiating condom use, stigmatisation – often from healthcare workers – and unknown HIV status. Like in Peru, most noted that investment in prevention programmes was often inversely proportional to the risk of the populations they targeted and some suggested that the available HIV incidence and prevalence figures were underreported.

The perceptions of participants from Sub-Saharan Africa were comparable. Most agreed that HIV incidence was highest among young people, especially women, and stable couples. However, MSM (including prisoners), FSWs, fishermen, and truck drivers were also mentioned among those at higher risk of infection. Participants acknowledged their countries' efforts to reduce HIV incidence, yet they

felt these remained sub-optimal. Key prevention challenges included: lack of resources and competing priorities – specifically HIV treatment –, stigma and criminalisation of groups at higher risk – which frequently impeded their access to HIV services –, inadequate communication strategies – often mono-lingual (English) and focused on certain groups –, overreliance on the ABC approach (abstinence, being faithful, and using condoms), prevalence of multiple concurrent partnerships, women's vulnerability and inability to negotiate the use of condoms, and donors' silo approach and often divergent agendas.

PrEP awareness

Participants' degree of awareness about PrEP varied across countries and job role, as reported in Table 4. Fifty participants were aware of PrEP and 41 were not.

Perceived benefits of PrEP

There was general consensus across countries and job roles regarding the benefits of PrEP, as reported in Table 2 and illustrated in Box 1. Most participants emphasised that PrEP was an additional prevention tool for those most at risk of infection, which would complement and possibly enhance existing methods. They also felt that implementing PrEP as part of a combination prevention strategy could result in a much needed increase in public resources devoted to HIV prevention. PrEP was widely perceived as an empowering mechanism that could enhance users' wellbeing, reduce the burden of the disease, and have a positive impact on countries' economies.

Box 1 PrEP benefits: important topics

Combination prevention

"Consider you are a truck driver... at high risk and eligible for PrEP, so we test you, you are negative, you are not circumcised, so we circumcise you. Then as you leave, we give you PrEP and we give you a month supply of condoms... We would have examined to see if you have any STDs... You'll be asked to come back after one month for a supply of PrEP and condoms... The entry point for this truck driver was PrEP. He was eligible for PrEP but we tested him and testing is a very critical tool, we circumcised him, we screened him of STDs, we gave him condoms... this person has accessed more than PrEP. We hope that this will happen as well." (K03, national policymaker)

"Taking into account the fact that there are no effective vaccines or effective prophylaxis, all prophylactic measures which could be used simultaneously or consecutively, raise the safety of potential victims of the virus" (Uk11, supranational NGO).

Prioritising HIV prevention

"We need to treat [HIV positives], reduce their viral load, improve their CD4 count and then that way we reduce the transmissibility levels. Also, it is good for us to protect the ones who are HIV negative... we need to weigh the two and see how we can balance [them] so that we don't lean on one side". (K05, local policymaker)

"...I do hope that with a plan, with all these discussions we really come back with a determination to revolutionize prevention and I think this tool would be one of the things that will help us." (SA10, VCT counsellor)

Empowering key populations

"We have had a snag around the ABC strategy because it does not work for women. Because their rights are abused, even if she abstains, someone will rape her. There are social factors that glorify male infidelity, however faithful you are as a woman, your husband is having sex with other women and that is ok in Ugandan society. Condom use can only work if you negotiate for sex. In our context it's mostly men who have the power to decide how and when to have sex with women." (Ug12, NGO representative)

"...if you are a female sex worker or a transgender, you may have a partner who is not willing to use a condom... In such scenarios, where condom negotiation is low, then PrEP works."(I11, NGO representative)

Financial gains

"...[HIV negative] people do not stop working and that means... economic gain on a domestic and national level." (P09, doctor – HIV clinic)

"...the maternal death rate will drop. Neonatal death rate will drop. The rate of [hospital] admissions will drop. There will be no orphans. And... we won't have to pay more money for grants for those kids." (SA01, national policymaker)

Perceived challenges of PrEP

The identified challenges of PrEP were largely comparable. Yet, there were differences in frequency and ranking order, particularly across countries, as reported in Table 3 and illustrated in Box two.

Most participants pointed out that the PrEP regimen would be difficult to follow. Identified barriers to uptake included: side effects, particularly in Ukraine and Peru; adherence, predominantly in South Africa; and the emergence of resistance, mainly in Botswana, Kenya, and Uganda. With the exception of India, the cost and cost-effectiveness of PrEP were also frequently mentioned as key concerns. An increase in risk behaviours (i.e. decrease in condom use, increase in sexual activity, and number of different partners) was a relevant issue among Indian, South African, and Batswana participants. With the exception of Kenya and Uganda, a high PrEP efficacy and/or effectiveness was generally deemed critical for making the case for allocating public funds to this initiative. In India, it was frequently stressed that effectiveness data should be generated by local clinical trials. Some participants felt that reaching key populations would pose significant challenges due to the stigmatisation and criminalisation of certain sexual practices, which could in turn have an impact on governments' willingness to introduce PrEP. This held particularly true in Peru and to a lesser extent in Ukraine, India and Uganda. The provision of adequate information and training to healthcare providers and users was also deemed challenging, particularly in Ukraine, Uganda and South Africa. Some participants mentioned their health systems were overloaded and raised concerns regarding their capacity to offer PrEP. Participants from Southern Africa felt their healthcare workforce was already overstretched, whereas Indian participants' concerns revolved around logistics and continuity of supply.

Box 2 PrEP challenges: important topics

Regimen

"Antiretroviral medication is quite hard to take. The patients who are involved in ARV therapy, which is a life-long therapy, undergo special preparation... They are taught how they should take it, how often, they are told about the side effects, what they are allowed to do and what they aren't allowed to do." (Uk08, doctor – HIV cinic)

"...a major concern for me is adherence... we are having challenges with people adhering to anti-retroviralsanti-retrovirals... monthly injection, that will be better." (SA02, national policymaker)

Cost and cost-effectiveness

"...the cost of the whole service... the drug itself... we need to be able to know: is your liver functioning, is your kidney functioning? ...all those basic tests we need to do. Who's going to bear the cost for that?" (K04, local policymaker).

"Uganda in particular doesn't have enough ARVs, even for [HIV positive] people who urgently need them..." (Ug10, VCT counsellor)

"I would support [PrEP] if there is evidence that it works. My benchmark would be what I invest in treatment, because one would assume that prophylaxis has to help me spend less than what I spend on treatment." (P04, national policymaker)

Risk compensation

"...there are concerns about disinhibition with medical male circumcision, where people might believe they are now completely immune to HIV when they're not. I suspect the same would apply to PrEP." (SA05, local policymaker)

"The more we convince people that PrEP might protect you, the more they will relax about using condoms. Also, some are not scared of possibly dying in 10 years" (I12, NGO representative).

Efficacy and effectiveness

"...if you have a drug of the desired efficacy, then we might begin to have a substantial reduction of new infections, assuming the adherence is right..." (B09, doctor – ARV clinic)

"[PrEP] will require huge backup, especially if its efficacy is a grey area. It would require emphasizing that anybody who is using it is not 100% protected and make sure that they use condom or get themselves tested." (I03, national policymaker)

Stigmatisation and criminalisation

"…[PrEP implementation] will also depend on whether the next government is more conservative or more open to sexuality, regardless of if there is scientific evidence…" (P01, national policymaker)

"Our system doesn't take care of high risk groups at all. There is a lot of stigma; [healthcare workers] are not sensitized to deal with these groups." (I04, local policymaker)

"…our parliament is thinking of ways of criminalizing HIV infection… I don't think we should go towards criminalizing HIV infection because we are going to punish innocent people…" (Ug10, NGO representative)

Information and training

"...we have to make sure the population understands the full ramifications of the intervention... the fact that it's only effective if you take it constantly, the detail, not the fact that there's a pill that can prevent HIV, that's totally ineffective... I would want the message to be well nuanced, which is a play-off, because you also want it to be impactful, so it's difficult, honest, but impactful." (SA04, local policymaker)

"An effective program would be one that includes community awareness and education for all levels and different targeted groups... for instance the messages to the youth may not be the same [as those] to married couples, to fishmongers, to semi-illiterate communities... medical workers will also have to be trained" (Ug03, national policymaker)

Healthcare system capacity

"...my main concern is around the question of logistics. How do you go about controlling the process?" (I02, national policy maker)

"...[PrEP] will be an additional burden and most health systems can't afford to employ more people." (Ug08, doctor – HIV clinic)

Programmatic considerations

There were many commonalities in participants' views and recommendations on what an eventual PrEP programme should look like. An overview of key sub-themes is provided below.

User eligibility

Participants from countries with concentrated epidemics (Peru, Ukraine, and India) felt that prioritising key populations would be a cost-effective approach. Yet, concerns were raised regarding the ability of IDUs and mobile populations to comply with a PrEP regimen. A confidential and tactful approach was perceived as critical to prevent further stigmatisation and avoid jeopardising demand among those at higher risk of HIV infection. Offering PrEP to sex workers' clients was also suggested.

Most participants from countries with generalised epidemics (Sub Saharan Africa) would offer PrEP to young people and serodiscordant couples first. Other priority populations included sex workers, MSM, truck drivers, and fishermen. However, most felt that due to the characteristics of their epidemics, prioritisation would be challenging.

Communication strategy

An effective communication strategy would involve Ministries of Health, relevant HIV services, and civil society. Peer educators, community leaders and social networks were regarded as crucial components of a PrEP communication campaign, albeit complemented with targeted mass media advertising, as they would provide access to and colloquial information exchange with key populations.

Participants noted that training PrEP providers and those involved in a communication campaign was critical. For example, a Ukrainian nurse working at an HIV clinic pointed out: "We should teach our staff how to approach people, how to present PrEP to them to prevent them from saying it's nonsense and they don't believe in it". (Uk08).

A PrEP communication campaign was also perceived as a potential vehicle of messages against stigma and prejudice, contributing to address these fundamental barriers. Some suggested that a consultation process would be essential to meet communities' needs and tackle any concerns from the outset.

Cost

Most participants agreed that PrEP should be free or heavily subsidised. Some, however, felt that a cost-segmented strategy was a more sustainable approach. It was noted that asking users to pay an affordable amount for the medication and associated services could improve adherence, as illustrated by a Ukrainian national policymaker: "...people should pay at least for some percentage of the medicine cost ... If they pay this money they will naturally keep in mind the necessity to take this pill... because they have bought it at their own expense. They had to work to buy PrEP ...I mean, the attitude is completely different in this case. It's not a freebie" (Uk02).

Distribution

There was widely held support for PrEP to be managed by the Ministries of Health and distributed through existing public and NGO-based healthcare services. It was stressed that PrEP distribution channels had to comply with strict privacy and confidentiality codes of practice. For example, an Indian local policy maker stressed: "If everyone takes PrEP, then there will be no stigma. But if you will start with certain groups [there will be]... so confidentiality has to be taken care of when you are giving such medicines" (I04).

Distributing PrEP in ART centres was not favoured, as users may worry about being associated with HIV patients. Some participants felt that distributing PrEP through pharmacies would reduce transportation costs and facilitate uptake. Yet, most agreed that other essential PrEP services (i.e. counselling, HIV testing) had to be delivered at a healthcare setting. Providing PrEP to highly mobile populations such as sex workers and truck drivers was raised as an important hurdle. This was illustrated by a Kenyan doctor working at an HIV clinic: "...we will have to force them to start going to a facility regularly, not just for the test but for the drug, for the test they can go anywhere but to get a drug ...you have to register somewhere and go there regularly ...I think that may discourage them because some of them are highly mobile groups." (K08)

Medication and HIV testing compliance

People's willingness and ability to take long term prophylactic medication and to frequently get tested for HIV was raised as a major challenge. Those who raised this considered offering tailored information and counselling, devising a contractual agreement between the provider and the user, subject to regimen compliance, and developing a tight monitoring system, including electronic reminders and frequent follow up, to be fundamental in order to enhance compliance to treatment and testing. As suggested by a VCT counsellor in Botswana:

Participant: "...the individual can be told when to come for the next supply and when they come that's when they get tested."
Interviewer: "Who would keep the card, is it the patient or would it remain at the clinic?"

Participant: “The patient would have to keep the card so that he can get it in any facilities so that you don't restrict that person to one health facility. The patient will be free to go to Marina, to go to Tlokweng and get the treatment when it’s due.” (B10)

Most agreed that the PrEP route of administration would play an important role onlevels of adherence: an injection once or every two months was preferred over a daily or a before-and-after-sex pill, although a considerable minority felt that offering different modalities to match users’ needs would be a desirable option. For example, an Indian community health worker pointed out: “It depends on a person’s sexual interaction. If a person has sex once a month, then he can go for a before-and-after pill. Those who do it regularly would want to go for the injection” (I06).

Early vs. late implementation

43 participants would support PrEP being implemented early in their countries: three in Peru, five in Ukraine, three in India, seven in Kenya, six in Uganda, eight in Botswana, and 11 in South Africa. A Ugandan doctor working in a reproductive health clinic illustrates this tendency: “...we needed PrEP yesterday, I mean, what about the people who will contract HIV after it is found to have worked, that would have been a missed opportunity” (Ug07). 44 participants, however, would only support the introduction of PrEP in their countries after proven safe and cost-effective elsewhere. A Ukrainian national policymaker exemplifies this position: “PrEP should pass all the clinical trials. If its effectiveness is proved, then why not?” (Uk03). Only two participants from India, one from Uganda, and one from Botswana would not support PrEP at all.

DISCUSSION

This is the first study to explore policymakers and providers’ views on oral and parenteral PrEP. We found many commonalities between participants’ opinions on HIV prevention in general, and PrEP in particular, both across job roles and countries. However, local differences in the perceived benefits and constraints of PrEP were also observed, a reflection of particular epidemiological, socioeconomic, and political contexts. These differences should not be overlooked in the planning of an eventual PrEP implementation.

Most participants felt that HIV prevention needed to be enhanced to effectively tackle their epidemic. Introducing new HIV prevention modalities as part of a combination prevention strategy was not only deemed necessary to decrease HIV incidence, but was also perceived as an opportunity to expand and strengthen existing prevention efforts.

Although most participants easily identified the benefits of PrEP, were able to envisage how it would fit into existing services, and were supportive of introducing it in their countries, they also expressed numerous concerns. The complexity of implementing PrEP, its cost/cost-effectiveness, partial efficacy, , the ability of key populations to access, understand and comply with it, and potential perverse effects such as increased risk behaviours and STIs, and the emergence of resistance, were important challenges which deserved consideration.

Strengths and limitations of this study

Our research builds on previous qualitative work on topical PrEP, and our results are comparable to previous studies exploring attitudes of policymakers and implementers towards microbicide gels. Hoffman et al compared data from the U.S and South Africa and found several commonalities across job roles and settings, and overall enthusiasm about this method, yet balanced with concerns analogous to those found in our study[20]. Similarly, Orner et al found that participants’ considerable support for microbicides was tempered by concerns regarding effectiveness, cost, increase in risk behaviour and challenges related to education and distribution[21]. Our results also resonate with the views of Piot et al, who urge governments, communities and scientists to adopt HIV prevention as a

national cause and ensure its funding, to work together to build demand for HIV prevention and to implement combination prevention programmes against HIV, including PrEP[22].

This research was conducted while PrEP attributes and effectiveness are still uncertain and only sixty percent of interviewees were aware of PrEP. In light of recent trial results and the worldwide attention these have received, we expect that awareness relating to this technology might be higher. However, many of the opinions expressed here are based on previous experience and knowledge of the local epidemic.

Although interviews were conducted in an open and non-judgmental manner, and participants were made aware that all data would be anonymised once it had been analysed by our research team, given the sensitive nature of this study, participants may at times have felt compelled to give "desirable" answers. Of similar importance, purposively recruiting participants may have an effect on the generalisability of our results. Nonetheless, the many commonalities in participants' opinions are encouraging, suggesting that it may be possible to devise standardised PrEP programmes which could be subsequently shaped to meet local needs.

Future research

Qualitative research undertaken using purposive sampling enables a wide range of experiences and opinions to emerge, but further quantitative work, particularly among providers, is needed to determine the true prevalence of our findings. Moreover, as clinical trials continue to shed light on PrEP effectiveness among different key populations, research on policymakers and providers' views on PrEP considering new findings, in other countries and rural settings is likely to provide different, rich accounts. Future research on the preferences and concerns of communities' opinion leaders and peer educators towards PrEP would also be of considerable value.

Impact on policy and practice

The critical question from a policy perspective is whether countries are willing and prepared to introduce PrEP. We have learnt from our previous study that key populations would be willing to use PrEP[15]. The work reported here demonstrates that, despite multiple concerns, policymakers and implementers, particularly from Sub Saharan African countries, would also be willing to support PrEP once it proves cost-effective.

We found that the identified barriers to PrEP were largely comparable to the perceived HIV prevention challenges. This suggests that current prevention shortfalls may have a bigger impact on an eventual PrEP implementation than vice versa. Significantly reducing HIV incidence, therefore, would require countries not only to incorporate new prevention methods, but also to strengthen, redirect and integrate existing prevention programmes[23]. The emergence of a Combination Prevention Secretariat, a joint collaboration of the Bill and Melinda Gates Foundation, PEPFAR, UNAIDS and the World Bank, reflects the importance of this approach for donors[24]. The sustainability of such integrated strategies, however, depends on the availability of international and local resources as much as it does on societal and political will.

Due to the significant challenges to implementing PrEP, including a desire to wait for successful programs to begin in other countries, it may be advisable to identify early adopters to initiate feasibility studies and demonstration projects with PrEP as a component of combination prevention.

Because some key stakeholders are still unaware of PrEP, an important aspect of initial work will be to provide information about PrEP, including its rationale, benefits and drawbacks. Comprehensive training programmes for providers and users, and targeted communication strategies, which encompass wider issues related to stigma and the specific needs of those most at risk of HIV infection, ought to be developed and tested before introducing PrEP.

The results of this study have implications for PrEP feasibility and demonstration projects. Our data indicate that PrEP should be offered to key populations in the first instance, although reaching some of these groups[25 26] and prioritising specific populations in settings with generalised epidemics, is likely to be challenging. PrEP should be coordinated by the Ministries of Health and involve relevant NGOs and community representatives. Effective and affordable information channels should include existing healthcare services, peer educators, community leaders, social networks, and targeted mass media advertising. PrEP should mainly be offered in public and NGO-based healthcare services as part of a combination prevention package, and be decoupled from specialised ART services to avoid stigmatisation. An integrated service which would allow mobile populations to access PrEP in different areas should be considered. The ongoing decentralization of HIV services towards primary care, promoted by funders, is a step in the right direction[27]. PrEP should be affordable and its price could be segmented. All available PrEP routes of administration should be offered, although parenteral PrEP, when and if becomes available, would be easier to adhere to. Counselling and frequent monitoring, as well as introducing innovative measures to increase regimen adherence, such as contractual agreements between providers and users, and the use of mobile technology, may limit the emergence of resistance to anti-retrovirals and increase PrEP effectiveness.

More profound societal and legislative changes, aimed at tackling widespread stigma, may be necessary for new HIV prevention approaches in general, and particularly those directed at stigmatised populations, to be fully successful. The enthusiasm and debate surrounding scientific breakthroughs like PrEP have the potential to become a catalyst for change.

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Contributions
AW, AE, GBG, EG, MRD and PKP agree with the manuscript's results and conclusions. AE and AW designed the measures/the study with the support of EG and PKP. AW, GBG and AE reviewed available data and literature, and performed the analyses. All authors contributed to the interpretation of results and write up. MRD and PKP were principal investigators for the grant at Imperial College London.

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Ethical approval
This study was approved by the Ethics Committee of Imperial College London, the Universidad Peruana Cayetano Heredia in Peru, the Sociological Association of Ukraine (SAU), the Independent Ethics Committee Consultants (IEC) in India, the Institutional Review Board of the Kenya Medical Research Institute (KEMRI), the Director General Health Services of the Ministry of Health in Uganda, the Health Research and Development Division of the Ministry of Health in Botswana and the Human Research Ethics Committee (Medical) of the University of Witwatersrand in South Africa.

Table 1: Participant eligibility criteria

JOB ROLE	ELIGIBILITY CRITERIA
Policymakers (5 per country)	
National policymakers (3)	• Senior officials • Portfolio includes HIV prevention
Local policymakers (2)*	• Working in local authorities outside the capital city • One local authority is at the forefront of HIV prevention • Portfolio includes HIV prevention
Frontline healthcare workers (5 per country)	
Community health worker (1)	• Involved in HIV prevention
Healthcare professionals working in a reproductive health clinic (1)	• Doctor or registered nurse • Involved in HIV prevention
Healthcare professionals working in an HIV clinic (2)	• At least one doctor • Involved in HIV prevention
HIV/AIDS Voluntary Counselling and Testing (VCT) counsellor	• Lay counsellor, trained counsellor or registered nurse who is a counsellor
NGOs (3 per country)	
Staff of supranational NGO (1)	• Senior staff • Involved in HIV prevention
Staff of NGOs who work with vulnerable populations (2)	• Senior staff • National or regional influence • One is supportive of HIV prevention

*In Peru we only interviewed national policymakers due to the centralised nature of its HIV policy making process.

Table 2: PrEP benefits

	Policymakers	Healthcare workers	NGOs
Peru	• Prevention tool for most at risk • Additional prevention strategy	• Additional prevention strategy • Tool for high risk groups • Potential economic gains • Opportunity to make prevention a Priority	• Empowering prevention tool • Additional prevention strategy • Opportunity to increase investment in prevention
Ukraine	• Additional prevention strategy • Increased well being • Empowerment of most at risk	• Alternative prevention strategy • Potential economic gains • Reduce HIV incidence	• Additional prevention strategy
India	• Alternative prevention strategy serodiscordant couples • Not gender specific	• Additional prevention tool • Potential economic gains • For serodiscordant couples	• Additional prevention strategy
Kenya	• Alternative prevention strategy • Potential economic gains • May benefit most at risk • Empowering most at risk	• Alternative prevention strategy • Potential economic gains • May benefit most at risk	• Additional prevention strategy • May benefit most at risk
Uganda	• Reduce HIV incidence • Potential economic gains • May benefit most at risk • For those who cannot negotiate condom use	• Alternative prevention strategy • For those who cannot negotiate condom use • Potential economic gains	• Reduce HIV incidence • May benefit most at risk
Botswana	• Reduce HIV incidence • Reduce cost of treatment and care • HIV-free newborns • Protect HWs • May benefit most at risk	• Reduce HIV incidence • Help avoid family breakups • HIV-free newborns • Potential economic gains	• Alternative prevention strategy • For those who cannot negotiate condom use • For high risk periods
South Africa	• Reduce HIV incidence • May help achieve Millennium Goals[†] • For those who cannot negotiate condom use	• Alternative prevention strategy • For those who cannot negotiate condom use • May help prevent other illnesses[¥] • May help to fight stigma	• Alternative and empowering prevention strategy for most at risk

NGO: non-governmental organisation. *In descending order from most recurrent. [†]HIV-related, maternal and child health, and gender equality. [¥]Associated with AIDS (i.e. cervical cancer and tuberculosis).

Table 3: PrEP challenges[†]

	Policymakers	Healthcare workers	NGOs
Peru	***Risk compensation, effectiveness, side effects	***Low educational level, cost-effectiveness, access to key groups	***Stigma, religious and political barriers, access to key groups
	**Religious and political barriers, adherence, training providers and users	**Adherence, stigma, side effects	**Side effects, risk compensation, adherence
	*Demand (lack or excess), access to key groups	*Training providers and users, risk compensation	*Resistance, government support
Ukraine	***Cost-effectiveness, side effects, increase in STIs	***Adherence, side effects, training providers	***Government willingness, adherence, training providers
	**Adherence, access to key groups, black market	**Cost, supply, government support	**Side effects, HIV testing, cost
	*Implementation, government support	*Religious barriers, risk compensation	*Resistance, black market
India	***Efficacy, need for local trials, risk compensation	***Risk compensation, stigma, lack of awareness	***Risk compensation, efficacy, need for local trials
	**Users mistrust, adherence, supply	**Adherence, HIV testing, users' accessibility	**Supply, adherence, access to key groups
	*Resistance, side effects	*Resistance, side effects	*Stigma, religious and political barriers
Kenya	***Supply, programme complexity, HIV testing	***Risk compensation, cost, adherence	***Cost, training users, resistance
	**Resistance, limited ART coverage, HW workload	**Access to key groups, misconceptions and rumours, limited ART coverage	**Limited ART coverage, supply, adherence
	*Black market, side effects	*Supply, HW workload	*Access to key groups, programme complexity
Uganda	***Cost, limited ART coverage, adherence	***Cost, limited ART coverage, resistance	***Cost, limited ART coverage, user acceptability
	**Risk compensation, sustainability, government support	**Adherence, criminalisation & stigma, risk compensation	**Risk compensation, adherence, sustainability
	*Information and training, HW training and workload	*Side effects, information and training	*Resistance, information and training
Botswana	***Risk compensation, HIV status disclosure, side effects	***Adherence**,* cost, resistance	***Cost-effectiveness, risk compensation, implementation
	**Adherence, resistance, religious barriers	**Efficacy, increase in STIs, information and training	**Resistance, criminalisation & stigma, limited ART coverage
	*Cost-effectiveness, long-term regimen	*Risk compensation**,** HWs workload and levels	*Adherence, side effects
South Africa	***Cost-effectiveness, adherence, cost	***Adherence, healthcare system overload, risk compensation	***Risk compensation, adherence, cost
	**Sustainability, side effects, risk compensation	**Information and training, cost, limited ART coverage	**Government support, side effects, information and training
	*Resistance, defining eligibility criteria	*Side effects, effectiveness	*Effectiveness, healthcare system overload

[†]In descending order from most important and recurrent. ***High priority; **medium priority; *low priority. ART: anti-retroviral therapy; PrEP: pre-exposure prophylaxis; STI: sexually transmitted infections; HWs: health workers; NGOs: non-governmental organisations.

Table 4: PrEP awareness

		Peru	Ukraine	India	Kenya	Uganda	Botswana	South Africa
Ps	Y	2 (national)	2 (national) 1 (local)	3 (national) 1 (local)	2 (local)	0	2 (local)	1 (local)
	N	3 (national)	1 (national)	1 (local)	3 (national)	5 (all)	3 (national)	3 (national) 1 (local)
HWs	Y	5	1	1	2	3	2	5
	N		4	4	3	2	3	
NGOs	Y	1 (supra) 1 (local)	1 (supra)	3 (all)	3 (all)	1 (supra) 1 (local)	2 (local)	1 (local)
	N	1 (local)	2 (local)			1 (local)	1 (supra)	1 (supra) 1 (national)

Ps: policymakers (national and local); HWs: healthcare workers; NGOs; non-governmental organisations (national and supranational). Y: aware; N: unaware.

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Views of policymakers, healthcare workers and NGOs on HIV preexposure prophylaxis (PrEP): a multinational qualitative study

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ABSTRACT

Objectives: To examine policymakers and providers' views on PrEP, and their willingness to support its introduction, to inform policy and practice in this emerging field.

Design: Semi-structured qualitative interview study.

Setting: Peru, Ukraine, India, Kenya, Uganda, Botswana, and South Africa.
Participants: 35 policymakers, 35 healthcare workers, and 21 NGO representatives involved in HIV prevention.

Results: Six themes emerged from the data. (i) perceived HIV prevention landscape: prevention initiatives needed to be improved and expanded; (ii) PrEP awareness: 50 participants had heard of PrEP and 41 had not; (iii) benefits of PrEP: one component of the combination prevention arsenal that could help prioritise HIV prevention, empower key populations, and result in economic gains; (iv) challenges of PrEP: regimen complexity, cost and cost-efectiveness, risk compensation, efficacy and effectiveness, stigmatisation and criminalisation, information and training, and healthcare system capacity; (v) programmatic considerations: user eligibility, communication strategy, cost, distribution, medication and HIV testing compliance; and (vi) early vs. late implementation: participants were divided as to whether they would support an early introduction of PrEP in their country or would prefer to wait until it has been successfully implemented in other countries, with around half of those we spoke to supporting each option. Very few said they would not support PrEP at all.

Conclusions: Despite the multiple challenges identified, there was general willingness to support the introduction of PrEP. Yet, strengthening existing HIV prevention efforts was also deemed necessary. Our results suggest that an effective PrEP programme would be delivered in healthcare facilities, but also involve NGOs and the community, and consider the needs of mobile populations. Comprehensive information packages and training for users and providers would be critical. The cost of PrEP would be affordable and possibly segmented. Extensive counselling and innovative monitoring measures ought to be considered.

ARTICLE SUMMARY

Article focus

Understanding the attitudes, perceptions and preferences of key stakeholders towards PrEP, to identify important programmatic aspects that may enhance or hinder its effectiveness.

Key messages

- Policymakers, healthcare workers, and NGOs, particularly from Sub Saharan Africa, would be willing to support PrEP if proven cost-effective.
- PrEP was envisaged as part of a combination prevention strategy deeply rooted in and driven by its beneficiaries.
- To effectively tackle the HIV epidemic, reducing stigmatisation against those at higher risk of infection and strengthening existing prevention programmes is as critical as introducing new ones.

Strengths and limitations of this study

- This is the first international study on key stakeholders' preferences and concerns regarding PrEP and how best to address these at a policy and service level.
- The interview guides and local interviewers' training were standardised, which facilitated data comparability.
- Relevant PrEP stakeholders were recruited.
- Limitations include the largely hypothetical nature of the addressed PrEP characteristics, potential social desirability bias, and purposive recruitment – mainly in urban areas.

INTRODUCTION

HIV incidence is stabilising and beginning to decline in many countries with generalised epidemics. Further efforts should now focus on consolidating this trend[1]. New prevention approaches are being considered that might, in combination with existing ones, help achieve this goal. Following both successful and futile results in recent clinical trials[2-8], the use of anti-retrovirals to prevent HIV transmission (ART) or acquisition (preexposure prophylaxis or PrEP) has become a focus of HIV/AIDS policy discussions. Although further clinical evidence will be needed to determine optimal regimens and delivery mechanisms[9], multi-disciplinary preparatory work needs to be undertaken to identify where existing and potential modalities may fit best within an integrated HIV prevention package.

Previous work on the implications of a future PrEP implementation has highlighted the importance of engaging relevant stakeholders in a consultation process designed to strengthen, legitimise, and ultimately enhance its sustainability and effectiveness[10-12]. Understanding the preferences and concerns of policymakers and providers towards PrEP, drawing on their experience in designing and delivering comparable programmes, is therefore paramount to the success of this prevention approach[13-15].

This article reports on qualitative research exploring policymakers, healthcare workers, and non-governmental organisations' (NGOs) perspectives on oral and parenteral PrEP in seven countries: Peru, Ukraine, India, Kenya, Uganda, Botswana, and South Africa. The research presented here complements a study on attitudes and acceptance of PrEP among potential users reported elsewhere[16]. Our aim is to inform priority setting, programme design, and implementation, should PrEP prove cost-effective.

METHODS

A qualitative approach is most appropriate in an exploratory, in-depth study of this sort[17]. Face-to-face individual interviews were therefore conducted between November 2010 and March 2011 with policymakers, healthcare workers, and NGO representatives responsible for or involved in HIV prevention in major cities of seven countries with diverse HIV epidemics: Peru, Ukraine, India, Kenya, Uganda, Botswana, and South Africa. Participants were purposively selected using a combination of criterion and snowball sampling.

Ipsos MORI, an international social research company, coordinated the data collection. Interviews were conducted by experienced local senior researchers. Interviewers were trained face-to-face by both our team and/or Ipsos MORI. They were also provided with a comprehensive interview manual, which contained background on PrEP research, frequently asked questions, information on participant eligibility, detailed interview instructions, and a consent form in countries where local ethical approval required written consent. All participants provided verbal consent. Interviews took place in a private office at the participants' work place and lasted between 45 and 60 minutes. Interview guides and materials were translated into Spanish (Peru) and Russian (Ukraine) by the local research team, and checked in London by professional translators for consistency and quality. In India and Sub Saharan African countries interviews were conducted in English.

We used a semi-structured and probing interview guide constructed through expert consultations and a literature review. Before commencing, participants were informed that their answers would be anonymised and treated with strict confidentiality. Participants were first asked about their role, involvement with HIV prevention, perceptions of their countries' HIV prevention efforts, and awareness of PrEP. To provide all participants with a minimum level of background knowledge, interviewers subsequently read a description of hypothetical and real PrEP attributes, including: its ineffectiveness against other sexually transmitted diseases; its route of delivery: as a daily and before-and-after-sex pill, and eventually as a monthly and bi-monthly injection; its mild temporary side

effects including: tiredness, headaches, and gassiness; its partial protective efficacy against HIV, especially if not taken as directed; and the need for frequent HIV testing. It was stressed that PrEP was undergoing clinical trials and its characteristics remained uncertain. Participants were then asked to rank their concerns in order of importance. They were also asked to identify the benefits of PrEP, if any. Subsequently, they were asked to describe what an effective PrEP programme would look like in their countries. Participants were finally asked whether they would support PrEP being introduced at an early, a later stage or not at all.

All interviews were digitally recorded, transcribed and translated into English by professional translators where necessary, and were analysed independently by AW, GBG and AE to ascertain inter-rater coding reliability[18]. Using thematic analysis[19 20], an initial categorising system was developed based on the study objectives and the interview guides. We identified new themes and sub-themes emerging from the data analysis, which were included when consensus was reached regarding their relevance. A final thematic index was produced to code all data.

RESULTS

We conducted a total of 91 interviews (13 per country) including 35 policymakers, 35 healthcare workers, and 21 NGO representatives. Fifty-one participants were male and 42 were female. Participants' eligibility criteria are described in Table 1. We present our findings across countries and job roles, highlighting areas of convergence and divergence around six themes: perceived HIV prevention landscape, PrEP awareness, perceived benefits of PrEP, perceived challenges of PrEP, programmatic considerations, and early vs. late implementation.

Perceived HIV prevention landscape

Peruvian participants mentioned that their HIV epidemic had reached a plateau with a significant reduction in mortality. Men who have sex with men (MSM), especially transsexuals, were identified as the most affected group. Stigma, low self-esteem, and substance abuse were frequently referred to as underlying determinants of high HIV incidence among MSM. Cultural and religious barriers, insufficient resources, and the recent decentralisation of Peru's healthcare system, which had led to inefficiencies in the provision of services, were raised as the main reasons behind the current HIV prevention deficiencies. A mismatch between treatment and prevention expenditure and the comparatively low HIV incidence among the beneficiaries of prevention programmes were mentioned as main causes for concern.

Most Ukrainian participants agreed that HIV prevention had recently become a priority on their government's agenda. Nonetheless, they raised concerns regarding the accuracy of the official HIV incidence data, and the pervasive criminalisation and stigmatisation of key populations (Injecting drug users (IDUs), female sex workers (FSWs), and MSM), which in turn hindered their access to prevention programmes. Participants felt that reducing Ukraine's dependency on international donors, increasing and optimising public resources for HIV prevention, as well as involving communities in the design of prevention programmes, strengthening advocacy work and raising awareness, was urgently needed to increase the impact and sustainability of prevention efforts.

Similarly, Indian participants felt that their country's HIV prevention efforts were insufficient and identified sex workers, MSM, truck drivers, serodiscordant couples, and IDUs as populations at higher risk of infection. Key HIV prevention challenges included: lack of access to condoms and difficulty negotiating condom use, stigmatisation – often from healthcare workers – and unknown HIV status. Like in Peru, most noted that investment in prevention programmes was often inversely proportional to the risk of the populations they targeted and some suggested that the available HIV incidence and prevalence figures were underreported.

The perceptions of participants from Sub-Saharan Africa were comparable. Most agreed that HIV incidence was highest among young people, especially women, and stable couples. However, MSM (including prisoners), FSWs, fishermen, and truck drivers were also mentioned among those at higher risk of infection. Participants acknowledged their countries' efforts to reduce HIV incidence, yet they felt these remained sub-optimal. Key prevention challenges included: lack of resources and competing priorities – specifically HIV treatment –, stigma and criminalisation of groups at higher risk – which frequently impeded their access to HIV services –, inadequate communication strategies – often mono-lingual (English) and focused on certain groups –, overreliance on the ABC approach (abstinence, being faithful, and using condoms), prevalence of multiple concurrent partnerships, women's vulnerability and inability to negotiate the use of condoms, and donors' silo approach and often divergent agendas.

PrEP awareness

Participants' degree of awareness about PrEP varied across countries and job role, as reported in Table 4. Fifty participants were aware of PrEP before the interview took place and 41 were not.

Perceived benefits of PrEP

There was general consensus across countries and job roles regarding the benefits of PrEP, as reported in Table 2 and illustrated in Box 1. Most participants emphasised that PrEP was an additional prevention tool for those most at risk of infection, which would complement and possibly enhance existing methods. They also felt that implementing PrEP as part of a combination prevention strategy could result in a much needed increase in public resources devoted to HIV prevention. PrEP was widely perceived as an empowering mechanism that could enhance users' wellbeing, reduce the burden of the disease, and have a positive impact on countries' economies.

Box 1 PrEP benefits: important topics

Combination prevention

"Consider you are a truck driver... at high risk and eligible for PrEP, so we test you, you are negative, you are not circumcised, so we circumcise you. Then as you leave, we give you PrEP and we give you a month supply of condoms... We would have examined to see if you have any STDs... You'll be asked to come back after one month for a supply of PrEP and condoms... The entry point for this truck driver was PrEP. He was eligible for PrEP but we tested him and testing is a very critical tool, we circumcised him, we screened him of STDs, we gave him condoms... this person has accessed more than PrEP. We hope that this will happen as well." (K03, national policymaker)

"Taking into account the fact that there are no effective vaccines or effective prophylaxis, all prophylactic measures which could be used simultaneously or consecutively, raise the safety of potential victims of the virus" (Uk11, supranational NGO).

Prioritising HIV prevention

"We need to treat [HIV positives], reduce their viral load, improve their CD4 count and then that way we reduce the transmissibility levels. Also, it is good for us to protect the ones who are HIV negative... we need to weigh the two and see how we can balance [them] so that we don't lean on one side". (K05, local policymaker)

"...I do hope that with a plan, with all these discussions we really come back with a determination to revolutionize prevention and I think this tool would be one of the things that will help us." (SA10, VCT counsellor)

Empowering key populations

"We have had a snag around the ABC strategy because it does not work for women. Because their rights are abused, even if she abstains, someone will rape her. There are social factors that glorify male infidelity, however faithful you are as a woman, your husband is having sex with other women and that is ok in Ugandan society. Condom use can only work if you negotiate for sex. In our context it's mostly men who have the

power to decide how and when to have sex with women." (Ug12, NGO representative)

"...if you are a female sex worker or a transgender, you may have a partner who is not willing to use a condom... In such scenarios, where condom negotiation is low, then PrEP works."(I11, NGO representative)

Financial gains

"...[HIV negative] people do not stop working and that means... economic gain on a domestic and national level." (P09, doctor – HIV clinic)

"...the maternal death rate will drop. Neonatal death rate will drop. The rate of [hospital] admissions will drop. There will be no orphans. And... we won't have to pay more money for grants for those kids." (SA01, national policymaker)

Perceived challenges of PrEP

The identified challenges of PrEP were largely comparable. Yet, there were differences in frequency and ranking order, particularly across countries, as reported in Table 3 and illustrated in Box two.

Most participants pointed out that the PrEP regimen would be difficult to follow. Identified barriers to uptake included: side effects, particularly in Ukraine and Peru; adherence, predominantly in South Africa; and the emergence of resistance, mainly in Botswana, Kenya, and Uganda. With the exception of India, the cost and cost-effectiveness of PrEP were also frequently mentioned as key concerns. An increase in risk behaviours (i.e. decrease in condom use, increase in sexual activity, and number of different partners) was a relevant issue among Indian, South African, and Batswana participants. With the exception of Kenya and Uganda, a high PrEP efficacy and/or effectiveness was generally deemed critical for making the case for allocating public funds to this initiative. In India, it was frequently stressed that effectiveness data should be generated by local clinical trials. Some participants felt that reaching key populations would pose significant challenges due to the stigmatisation and criminalisation of certain sexual practices, which could in turn have an impact on governments' willingness to introduce PrEP. This held particularly true in Peru and to a lesser extent in Ukraine, India and Uganda. The provision of adequate information and training to healthcare providers and users was also deemed challenging, particularly in Ukraine, Uganda and South Africa. Some participants mentioned their health systems were overloaded and raised concerns regarding their capacity to offer PrEP. Participants from Southern Africa felt their healthcare workforce was already overstretched, whereas Indian participants' concerns revolved around logistics and continuity of supply.

Box 2 PrEP challenges: important topics

Regimen

"Antiretroviral medication is quite hard to take. The patients who are involved in ARV therapy, which is a life-long therapy, undergo special preparation... They are taught how they should take it, how often, they are told about the side effects, what they are allowed to do and what they aren't allowed to do." (Uk08, doctor – HIV clinic)

"...a major concern for me is adherence... we are having challenges with people adhering to anti-retroviralsanti-retrovirals... monthly injection, that will be better." (SA02, national policymaker)

Cost and cost-effectiveness

"...the cost of the whole service... the drug itself... we need to be able to know: is your liver functioning, is your kidney functioning? ...all those basic tests we need to do. Who's going to bear the cost for that?" (K04, local policymaker).

"Uganda in particular doesn't have enough ARVs, even for [HIV positive] people who urgently need them..." (Ug10, VCT counsellor)

"I would support [PrEP] if there is evidence that it works. My benchmark would be what I invest in treatment, because one would assume that prophylaxis has to help me spend less than what I spend on treatment." (P04,

national policymaker)

Risk compensation

"...there are concerns about disinhibition with medical male circumcision, where people might believe they are now completely immune to HIV when they're not. I suspect the same would apply to PrEP." (SA05, local policymaker)

"The more we convince people that PrEP might protect you, the more they will relax about using condoms. Also, some are not scared of possibly dying in 10 years" (I12, NGO representative).

Efficacy and effectiveness

"...if you have a drug of the desired efficacy, then we might begin to have a substantial reduction of new infections, assuming the adherence is right..." (B09, doctor – ARV clinic)

"[PrEP] will require huge backup, especially if its efficacy is a grey area. It would require emphasizing that anybody who is using it is not 100% protected and make sure that they use condom or get themselves tested." (I03, national policymaker)

Stigmatisation and criminalisation

"…[PrEP implementation] will also depend on whether the next government is more conservative or more open to sexuality, regardless of if there is scientific evidence…" (P01, national policymaker)

"Our system doesn't take care of high risk groups at all. There is a lot of stigma; [healthcare workers] are not sensitized to deal with these groups." (I04, local policymaker)

"…our parliament is thinking of ways of criminalizing HIV infection… I don't think we should go towards criminalizing HIV infection because we are going to punish innocent people…" (Ug10, NGO representative)

Information and training

"...we have to make sure the population understands the full ramifications of the intervention... the fact that it's only effective if you take it constantly, the detail, not the fact that there's a pill that can prevent HIV, that's totally ineffective... I would want the message to be well nuanced, which is a play-off, because you also want it to be impactful, so it's difficult, honest, but impactful." (SA04, local policymaker)

"An effective program would be one that includes community awareness and education for all levels and different targeted groups... for instance the messages to the youth may not be the same [as those] to married couples, to fishmongers, to semi-illiterate communities... medical workers will also have to be trained" (Ug03, national policymaker)

Healthcare system capacity

"...my main concern is around the question of logistics. How do you go about controlling the process?" (I02, national policy maker)

"...[PrEP] will be an additional burden and most health systems can't afford to employ more people." (Ug08, doctor – HIV clinic)

Programmatic considerations

There were many commonalities in participants' views and recommendations on what an eventual PrEP programme should look like. An overview of key sub-themes is provided below.

User eligibility

Participants from countries with concentrated epidemics (Peru, Ukraine, and India) felt that prioritising key populations would be a cost-effective approach. Yet, concerns were raised regarding the ability of IDUs and mobile populations to comply with a PrEP regimen. A confidential and tactful approach was perceived as critical to prevent further stigmatisation and avoid jeopardising demand among those at higher risk of HIV infection. Offering PrEP to sex workers' clients was also suggested.

Most participants from countries with generalised epidemics (Sub Saharan Africa) would offer PrEP to young people and serodiscordant couples first. Other priority populations included sex workers, MSM, truck drivers, and fishermen. However, most felt that due to the characteristics of their epidemics, prioritisation would be challenging.

Communication strategy

An effective communication strategy would involve Ministries of Health, relevant HIV services, and civil society. Peer educators, community leaders and social networks were regarded as crucial components of a PrEP communication campaign, albeit complemented with targeted mass media advertising, as they would provide access to and colloquial information exchange with key populations.

Participants noted that training PrEP providers and those involved in a communication campaign was critical. For example, a Ukrainian nurse working at an HIV clinic pointed out: "We should teach our staff how to approach people, how to present PrEP to them to prevent them from saying it's nonsense and they don't believe in it". (Uk08).

A PrEP communication campaign was also perceived as a potential vehicle of messages against stigma and prejudice, contributing to address these fundamental barriers. Some suggested that a consultation process would be essential to meet communities' needs and tackle any concerns from the outset.

Cost

Most participants agreed that PrEP should be free or heavily subsidised. Some, however, felt that a cost-segmented strategy was a more sustainable approach. It was noted that asking users to pay an affordable amount for the medication and associated services could improve adherence, as illustrated by a Ukrainian national policymaker: "...people should pay at least for some percentage of the medicine cost ... If they pay this money they will naturally keep in mind the necessity to take this pill... because they have bought it at their own expense. They had to work to buy PrEP ...I mean, the attitude is completely different in this case. It's not a freebie" (Uk02).

Distribution

There was widely held support for PrEP to be managed by the Ministries of Health and distributed through existing public and NGO-based healthcare services. It was stressed that PrEP distribution channels had to comply with strict privacy and confidentiality codes of practice. For example, an Indian local policy maker stressed: "If everyone takes PrEP, then there will be no stigma. But if you will start with certain groups [there will be]... so confidentiality has to be taken care of when you are giving such medicines" (I04).

Distributing PrEP in ART centres was not favoured, as users may worry about being associated with HIV patients. Some participants felt that distributing PrEP through pharmacies would reduce transportation costs and facilitate uptake. Yet, most agreed that other essential PrEP services (i.e. counselling, HIV testing) had to be delivered at a healthcare setting. Providing PrEP to highly mobile populations such as sex workers and truck drivers was raised as an important hurdle. This was illustrated by a Kenyan doctor working at an HIV clinic: "...we will have to force them to start going to a facility regularly, not just for the test but for the drug, for the test they can go anywhere but to get a drug ...you have to register somewhere and go there regularly ...I think that may discourage them because some of them are highly mobile groups." (K08)

Medication and HIV testing compliance

People's willingness and ability to take long term prophylactic medication and to frequently get tested for HIV was raised as a major challenge. Those who raised this considered offering tailored information and counselling, devising a contractual agreement between the provider and the user, subject to regimen compliance, and developing a tight monitoring system, including electronic

reminders and frequent follow up, to be fundamental in order to enhance compliance to treatment and testing. As suggested by a VCT counsellor in Botswana:

Participant: "...the individual can be told when to come for the next supply and when they come that's when they get tested."
Interviewer: "Who would keep the card, is it the patient or would it remain at the clinic?"
Participant: "The patient would have to keep the card so that he can get it in any facilities so that you don't restrict that person to one health facility. The patient will be free to go to Marina, to go to Tlokweng and get the treatment when it's due." (B10)

Most agreed that the PrEP route of administration would play an important role onlevels of adherence: an injection once or every two months was preferred over a daily or a before-and-after-sex pill, although a considerable minority felt that offering different modalities to match users' needs would be a desirable option. For example, an Indian community health worker pointed out: "It depends on a person's sexual interaction. If a person has sex once a month, then he can go for a before-and-after pill. Those who do it regularly would want to go for the injection" (I06).

Early vs. late implementation

43 participants would support PrEP being implemented early in their countries: three in Peru, five in Ukraine, three in India, seven in Kenya, six in Uganda, eight in Botswana, and 11 in South Africa. A Ugandan doctor working in a reproductive health clinic illustrates this tendency: "...we needed PrEP yesterday, I mean, what about the people who will contract HIV after it is found to have worked, that would have been a missed opportunity" (Ug07). 44 participants, however, would only support the introduction of PrEP in their countries after proven safe and cost-effective elsewhere. A Ukrainian national policymaker exemplifies this position: "PrEP should pass all the clinical trials. If its effectiveness is proved, then why not?" (Uk03). Only two participants from India, one from Uganda, and one from Botswana would not support PrEP at all.

DISCUSSION

This is the first study to explore policymakers and providers' views on oral and parenteral PrEP. We found many commonalities between participants' opinions on HIV prevention in general, and PrEP in particular. Interestingly, participants' views were not significantly influenced by their job role, yet policymakers and healthcare workers were better at detailing the benefits of PrEP than NGO representatives. On the other hand, we observed local differences in both the perceived benefits and constraints of PrEP, a reflection of particular epidemiological, socioeconomic, and political contexts. These differences should not be overlooked in the planning of an eventual PrEP implementation.

Most participants felt that HIV prevention needed to be enhanced to effectively tackle their epidemic. Introducing new HIV prevention modalities as part of a combination prevention strategy was not only deemed necessary to decrease HIV incidence, but was also perceived as an opportunity to expand and strengthen existing prevention efforts.

Although most participants easily identified the benefits of PrEP, were able to envisage how it would fit into existing services, and were supportive of introducing it in their countries, they also expressed numerous concerns. The complexity of implementing PrEP, its cost/cost-effectiveness, partial efficacy, the ability of key populations to access, understand and comply with it, and potential perverse effects such as increased risk behaviours and STIs, and the emergence of resistance, were important challenges which deserved consideration.

Strengths and limitations of this study

Our research builds on previous qualitative work on topical PrEP, and our results are comparable to previous studies exploring attitudes of policymakers and implementers towards microbicide gels. Hoffman et al compared data from the U.S and South Africa and found several commonalities across job roles and settings, and overall enthusiasm about this method, yet balanced with concerns analogous to those found in our study[21]. Similarly, Orner et al found that participants' considerable support for microbicides was tempered by concerns regarding effectiveness, cost, increase in risk behaviour and challenges related to education and distribution[22]. Our results also resonate with the views of Piot et al, who urge governments, communities and scientists to adopt HIV prevention as a national cause and ensure its funding, to work together to build demand for HIV prevention and to implement combination prevention programmes against HIV, including PrEP[23].

This research was conducted while PrEP attributes and effectiveness are still uncertain and only sixty percent of interviewees were aware of PrEP. In light of recent trial results and the worldwide attention these have received, we expect that awareness relating to this technology might be higher. However, many of the opinions expressed here are based on previous experience and knowledge of the local epidemic.

Although interviews were conducted in an open and non-judgmental manner, and participants were made aware that all data would be anonymised once it had been analysed by our research team, given the sensitive nature of this study, participants may at times have felt compelled to give "desirable" answers. Of similar importance, purposively recruiting participants may have an effect on the generalisability of our results. Nonetheless, the many commonalities in participants' opinions are encouraging, suggesting that it may be possible to devise standardised PrEP programmes which could be subsequently shaped to meet local needs.

Future research

Qualitative research undertaken using purposive sampling enables a wide range of experiences and opinions to emerge, but further quantitative work, particularly among providers, is needed to determine the true prevalence of our findings. Moreover, as clinical trials continue to shed light on PrEP effectiveness among different key populations, research on policymakers and providers' views on PrEP considering new findings, in other countries and rural settings is likely to provide different, rich accounts. Future research on the preferences and concerns of communities' opinion leaders and peer educators towards PrEP would also be of considerable value.

Impact on policy and practice

The critical question from a policy perspective is whether countries are willing and prepared to introduce PrEP. We have learnt from our previous study that key populations would be willing to use PrEP[16]. The work reported here demonstrates that, despite multiple concerns, policymakers and implementers, particularly from Sub Saharan African countries, would also be willing to support PrEP once it proves cost-effective.

We found that the identified barriers to PrEP were largely comparable to the perceived HIV prevention challenges. This suggests that current prevention shortfalls may have a bigger impact on an eventual PrEP implementation than vice versa. Significantly reducing HIV incidence, therefore, would require countries not only to incorporate new prevention methods, but also to strengthen, redirect and integrate existing prevention programmes[24]. The emergence of a Combination Prevention Secretariat, a joint collaboration of the Bill and Melinda Gates Foundation, PEPFAR, UNAIDS and the World Bank, reflects the importance of this approach for donors[25]. The sustainability of such integrated strategies, however, depends on the availability of international and local resources as much as it does on societal and political will.

Due to the significant challenges to implementing PrEP, including a desire to wait for successful programs to begin in other countries, it may be advisable to identify early adopters to initiate feasibility studies and demonstration projects with PrEP as a component of combination prevention.

Because some key stakeholders are still unaware of PrEP, an important aspect of initial work will be to provide information about PrEP, including its rationale, benefits and drawbacks. Comprehensive training programmes for providers and users, and targeted communication strategies, which encompass wider issues related to stigma and the specific needs of those most at risk of HIV infection, ought to be developed and tested before introducing PrEP.

The results of this study have implications for PrEP feasibility and demonstration projects. Our data indicate that PrEP should be offered to key populations in the first instance, although reaching some of these groups[26 27] and prioritising specific populations in settings with generalised epidemics, is likely to be challenging. PrEP should be coordinated by the Ministries of Health and involve relevant NGOs and community representatives. Effective and affordable information channels should include existing healthcare services, peer educators, community leaders, social networks, and targeted mass media advertising. PrEP should mainly be offered in public and NGO-based healthcare services as part of a combination prevention package, and be decoupled from specialised ART services to avoid stigmatisation. An integrated service which would allow mobile populations to access PrEP in different areas should be considered. The ongoing decentralization of HIV services towards primary care, promoted by funders, is a step in the right direction[28]. PrEP should be affordable and its price could be segmented. All available PrEP routes of administration should be offered, although parenteral PrEP, when and if becomes available, would be easier to adhere to. Counselling and frequent monitoring, as well as introducing innovative measures to increase regimen adherence, such as contractual agreements between providers and users, and the use of mobile technology, may limit the emergence of resistance to anti-retrovirals and increase PrEP effectiveness.

More profound societal and legislative changes, aimed at tackling widespread stigma, may be necessary for new HIV prevention approaches in general, and particularly those directed at stigmatised populations, to be fully successful. The enthusiasm and debate surrounding scientific breakthroughs like PrEP have the potential to become a catalyst for change.

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Contributions

AW, AE, GBG, EG, MRD and PKP agree with the manuscript's results and conclusions. AE and AW designed the measures/the study with the support of EG and PKP. AW, GBG and AE reviewed the available data and literature, and performed the analyses. All authors contributed to the interpretation of results and write-up. MRD and PKP were principal investigators for the grant at Imperial College London.

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Competing interests

The authors have declared that no competing interests exist.

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Ethical approval

This study was approved by the Ethics Committee of Imperial College London, the Universidad Peruana Cayetano Heredia in Peru, the Sociological Association of Ukraine (SAU), the Independent Ethics Committee Consultants (IEC) in India, the Institutional Review Board of the Kenya Medical Research Institute (KEMRI), the Director General Health Services of the Ministry of Health in Uganda, the Health Research and Development Division of the Ministry of Health in Botswana and the Human Research Ethics Committee (Medical) of the University of Witwatersrand in South Africa.

Table 1: Participant eligibility criteria

JOB ROLE	ELIGIBILITY CRITERIA
Policymakers (5 per country)	
National policymakers (3)	• Senior officials • Portfolio includes HIV prevention
Local policymakers (2)*	• Working in local authorities outside the capital city • One local authority is at the forefront of HIV prevention • Portfolio includes HIV prevention
Frontline healthcare workers (5 per country)**	
Community health worker (1)	• Involved in HIV prevention
Healthcare professionals working in a reproductive health clinic (1)	• Doctor or registered nurse • Involved in HIV prevention
Healthcare professionals working in an HIV clinic (2)	• At least one doctor • Involved in HIV prevention
HIV/AIDS Voluntary Counselling and Testing (VCT) counsellor	• Lay counsellor, trained counsellor or registered nurse who is a counsellor
NGOs (3 per country)	
Staff of supranational NGO (1)	• Senior staff • Involved in HIV prevention
Staff of NGOs who work with vulnerable populations (2)	• Senior staff • National or regional influence • One is supportive of HIV prevention

*In Peru we only interviewed national policymakers due to the centralised nature of its HIV policy making process.
** Working in public, non-profit or private healthcare facilities

Table 2: PrEP benefits

	Policymakers	Healthcare workers	NGOs
Peru	• Prevention tool for most at risk • Additional prevention strategy	• Additional prevention strategy • Tool for high risk groups • Potential economic gains • Opportunity to make prevention a Priority	• Empowering prevention tool • Additional prevention strategy • Opportunity to increase investment in prevention
Ukraine	• Additional prevention strategy • Increased well being • Empowerment of most at risk	• Alternative prevention strategy • Potential economic gains • Reduce HIV incidence	• Additional prevention strategy
India	• Alternative prevention strategy serodiscordant couples • Not gender specific	• Additional prevention tool • Potential economic gains • For serodiscordant couples	• Additional prevention strategy
Kenya	• Alternative prevention strategy • Potential economic gains • May benefit most at risk • Empowering most at risk	• Alternative prevention strategy • Potential economic gains • May benefit most at risk	• Additional prevention strategy • May benefit most at risk
Uganda	• Reduce HIV incidence • Potential economic gains • May benefit most at risk • For those who cannot negotiate condom use	• Alternative prevention strategy • For those who cannot negotiate condom use • Potential economic gains	• Reduce HIV incidence • May benefit most at risk
Botswana	• Reduce HIV incidence • Reduce cost of treatment and care • HIV-free newborns • Protect HWs • May benefit most at risk	• Reduce HIV incidence • Help avoid family breakups • HIV-free newborns • Potential economic gains	• Alternative prevention strategy • For those who cannot negotiate condom use • For high risk periods
South Africa	• Reduce HIV incidence • May help achieve Millennium Goals[†] • For those who cannot negotiate condom use	• Alternative prevention strategy • For those who cannot negotiate condom use • May help prevent other illnesses[¥] • May help to fight stigma	• Alternative and empowering prevention strategy for most at risk

NGO: non-governmental organisation. *In descending order from most recurrent. [†]HIV-related, maternal and child health, and gender equality. [¥]Associated with AIDS (i.e. cervical cancer and tuberculosis).

Table 3: PrEP challenges[†]

	Policymakers	Healthcare workers	NGOs
Peru	***Risk compensation, effectiveness, side effects	***Low educational level, cost-effectiveness, access to key groups	***Stigma, religious and political barriers, access to key groups
	**Religious and political barriers, adherence, training providers and users	**Adherence, stigma, side effects	**Side effects, risk compensation, adherence
	*Demand (lack or excess), access to key groups	*Training providers and users, risk compensation	*Resistance, government support
Ukraine	***Cost-effectiveness, side effects, increase in STIs	***Adherence, side effects, training providers	***Government willingness, adherence, training providers
	**Adherence, access to key groups, black market	**Cost, supply, government support	**Side effects, HIV testing, cost
	*Implementation, government support	*Religious barriers, risk compensation	*Resistance, black market
India	***Efficacy, need for local trials, risk compensation	***Risk compensation, stigma, lack of awareness	***Risk compensation, efficacy, need for local trials
	**Users mistrust, adherence, supply	**Adherence, HIV testing, users' accessibility	**Supply, adherence, access to key groups
	*Resistance, side effects	*Resistance, side effects	*Stigma, religious and political barriers
Kenya	***Supply, programme complexity, HIV testing	***Risk compensation, cost, adherence	***Cost, training users, resistance
	**Resistance, limited ART coverage, HW workload	**Access to key groups, misconceptions and rumours, limited ART coverage	**Limited ART coverage, supply, adherence
	*Black market, side effects	*Supply, HW workload	*Access to key groups, programme complexity
Uganda	***Cost, limited ART coverage, adherence	***Cost, limited ART coverage, resistance	***Cost, limited ART coverage, user acceptability
	**Risk compensation, sustainability, government support	**Adherence, criminalisation & stigma, risk compensation	**Risk compensation, adherence, sustainability
	*Information and training, HW training and workload	*Side effects, information and training	*Resistance, information and training
Botswana	***Risk compensation, HIV status disclosure, side effects	***Adherence**,* cost, resistance	***Cost-effectiveness, risk compensation, implementation
	**Adherence, resistance, religious barriers	**Efficacy, increase in STIs, information and training	**Resistance, criminalisation & stigma, limited ART coverage
	*Cost-effectiveness, long-term regimen	*Risk compensation**,** HWs workload and levels	*Adherence, side effects
South Africa	***Cost-effectiveness, adherence, cost	***Adherence, healthcare system overload, risk compensation	***Risk compensation, adherence, cost
	**Sustainability, side effects, risk compensation	**Information and training, cost, limited ART coverage	**Government support, side effects, information and training
	*Resistance, defining eligibility criteria	*Side effects, effectiveness	*Effectiveness, healthcare system overload

[†]In descending order from most important and recurrent. ***High priority; **medium priority; *low priority. ART: anti-retroviral therapy; PrEP: pre-exposure prophylaxis; STI: sexually transmitted infections; HWs: health workers; NGOs: non-governmental organisations.

Table 4: PrEP awareness

		Peru	Ukraine	India	Kenya	Uganda	Botswana	South Africa
Ps	Y	2 (national)	2 (national) 1 (local)	3 (national) 1 (local)	2 (local)	0	2 (local)	1 (local)
	N	3 (national)	1 (national)	1 (local)	3 (national)	5 (all)	3 (national)	3 (national) 1 (local)
HWs	Y	5	1	1	2	3	2	5
	N		4	4	3	2	3	
NGOs	Y	1 (supra) 1 (local)	1 (supra)	3 (all)	3 (all)	1 (supra) 1 (local)	2 (local)	1 (local)
	N	1 (local)	2 (local)			1 (local)	1 (supra)	1 (supra) 1 (national)

Ps: policymakers (national and local); HWs: healthcare workers; NGOs; non-governmental organisations (national and supranational). Y: aware; N: unaware.