

REVIEW ARTICLE

The Promise and Peril of Pre-Exposure Prophylaxis (PrEP): Using Social Science to Inform PrEP Interventions among Female Sex Workers

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Abstract

Advances in biomedical interventions to prevent HIV offer great promise in reducing the number of new infections across sub-Saharan Africa, particularly among vulnerable populations such as female sex workers. Several recent trials testing pre-exposure prophylaxis (PrEP) have demonstrated efficacy, although others have been stopped early for futility. Given the importance and complexities of social and behavioural factors that influence biomedical approaches to prevention, we discuss several key areas of consideration moving forward, including trial participation, adherence strategies, social relationships, and the structural factors that shape PrEP interest, use, and potential effectiveness among female sex workers in sub-Saharan Africa. Our review highlights the importance of involving social scientists in clinical and community-based research on PrEP. We advocate for a shift away from a singular “re-medicalization” of the HIV epidemic to that of a “reintegration” of interdisciplinary approaches to prevention that could benefit female sex workers and other key populations at risk of acquiring HIV. (*Afr J Reprod Health* 2014; 18[3]: 74-83)

Keywords (3-6): biomedical interventions, social science, qualitative and ethnographic research, sub-Saharan Africa

Résumé

Les progrès dans les interventions biomédicales de la prévention du VIH sont très prometteurs pour réduire le nombre de nouvelles infections en Afrique sub-saharienne, surtout parmi les populations vulnérables comme les prostituées. Plusieurs tests d'essais récents de la prophylaxie de la pré-exposition (PPrE) ont démontré l'efficacité, bien que d'autres ont été arrêtés tôt pour la futilité. Étant donné l'importance et la complexité des facteurs sociaux et comportementaux qui influent sur les approches biomédicales de la prévention, nous discutons plusieurs secteurs clés d'évaluation allant de l'avant, y compris la participation aux essais, les stratégies d'adhésion, les relations sociales, et les facteurs structurels qui forment l'intérêt PPrE, l'utilisation et le potentiel efficacité chez les prostituées en Afrique sub-saharienne. Notre étude fait ressortir l'importance de la participation des spécialistes des sciences sociales dans la recherche clinique et communautaire sur la PPrE. Nous plaidons pour un passage d'une seule «ré-médicalisation» de l'épidémie du VIH à celle d'une «réintégration» des approches interdisciplinaires à la prévention qui pourraient bénéficier aux prostituées et aux autres populations clés à risque de contracter le VIH. (*Afr J Reprod Health* 2014; 18[3]: 74-83)

Mots-clés: Interventions biomédicales, sciences sociales, recherche qualitative et ethnographique, Afrique sub-saharienne

Introduction

Globally, female sex workers experience an extraordinary high risk of acquiring HIV. A disproportionate burden of infection is

concentrated in sub-Saharan Africa, where an estimated 29.3% of sex workers are living with HIV¹. Sex work, or the exchange of sex for money, material items, or other forms of support, comprises a continuum of practices and is often

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anchored in poverty, gender-power imbalances, victimization, and lack of opportunities²⁻⁵. The types of venues, clients, and relationships that are formed in sex work contexts vary considerably, carrying important implications for HIV acquisition and prevention^{6,7}. Moreover, broader sociocultural and political economic factors including criminalization, stigma, discrimination, poverty, migration, and limited access to healthcare heighten sex workers' vulnerability to HIV infection, while simultaneously reducing the reach and effectiveness of prevention interventions⁸⁻¹¹.

Biomedical interventions to reduce women's risk of HIV infection have garnered much recent attention. In particular, antiretroviral pre-exposure prophylaxis (PrEP) has been praised as a means of empowering vulnerable individuals to protect themselves¹². PrEP refers to the use of antiretroviral medications by HIV-negative individuals to reduce their risk of acquiring HIV. PrEP may be administered orally (e.g., formulations of tenofovir alone or in combination with emtricitabine) or topically (e.g., tenofovir-based gels applied vaginally or rectally), and additional methods of administration are undergoing development and testing (e.g., injectables). Theoretically, PrEP could help sex workers protect themselves in contexts where condom use is difficult to negotiate. Unfortunately, mixed results from recent PrEP trials involving heterosexual, at-risk women highlight several challenges. While CAPRISA 004¹³, Partners PrEP¹⁴, and the Botswana TDF2 trials¹⁵ reported protective effects of gel and oral formulations ranging from 39–72% efficacy, FEM-PrEP (assessing daily oral dosing)¹⁶, and VOICE (testing gel and oral formulations)¹⁷, were stopped early for lack of efficacy likely due to suboptimal product adherence¹⁶. These mixed results and the dose-response relationship between efficacy and adherence underscores the need for an enhanced understanding of social and behavioural influences on PrEP use^{18,19}. Ultimately, to improve effectiveness in real-world settings, more research is needed on the contextual factors surrounding women's personal experiences with PrEP²⁰. Such efforts will be particularly important in contexts of

vulnerability and social marginalization, which often drive and are reinforced by sex work.

Social science bridges clinical and 'real world' dimensions of human experience. Defined here as anthropology, sociology, and other critical approaches, social science draws on a unique armamentarium of theoretical and methodological tools to understand how structural and socio-cultural factors become physically embodied as health disparities among marginalized groups. Early in the HIV epidemic, social scientists conducting ethnographic observations played a vital role in revealing the behavioural and social dimensions of sexual and drug-related HIV risk practices²¹⁻²³. Others have traced the structural factors underlying the massive spread of HIV across sub-Saharan Africa²⁴.

Recent success with PrEP, however, has emboldened HIV prevention efforts into a new era of "re-medicalization" in which technological solutions are favoured over considerations of entrenched historical, social, political and economic disadvantages that shape individuals' vulnerability to HIV²⁵. Rather than contribute to a polarity of approaches, we join other researchers and policy makers who are calling for a reintegration of social science perspectives into biomedical HIV prevention research²⁶⁻²⁹. Fortunately, several recent biomedical trials have integrated qualitative components into their procedures, illustrating the value of mixed methods approaches³⁰⁻³³.

This paper discusses four salient issues in biomedical HIV prevention research to which social science can contribute: clinical trial participation, product adherence, social relationships and risk, and structural factors that shape health and vulnerability. Situated within an "HIV risk environment" framework that advances an understating of the epidemic at multiple, intersecting socio-structural and micro-levels of experience³⁴, we focus on social science contributions to clinical PrEP research in these four keys areas. We include studies on oral and microbicide gel formulations of PrEP because researchers are still assessing efficacy and acceptability of different formulations and dosing schedules. Although few PrEP trials have

explicitly included female sex workers, we primarily highlight studies with heterosexual women that carry significance for reducing HIV acquisition among sex workers in sub-Saharan Africa. We conclude with suggestions for prevention research and practice with this heterogeneous population of women at high risk of HIV.

Inclusion in PrEP trials

Although female sex workers in sub-Saharan Africa experience heightened risk for HIV, few PrEP trials have specifically recruited from this population. In the Fem-PrEP trial, 12.6% of women reported recently exchanging sex³⁵. For unspecified reasons, an exploratory study of adherence to intermittent PrEP dosing in Kenya that included 67 men who have sex with men only included 5 female sex workers³⁶. Given the fluid boundaries of sex work in many African contexts, including formal sex work, transactional sex, and other informal types of exchange, researchers should consider expanding recruitment and eligibility terminology. Thus, a greater diversity of women could be reached, ultimately informing science on the range of sexual partnerships and practices in the context of PrEP use.

Studies suggest that many female sex workers are interested in using PrEP³⁷⁻³⁹. While much of this work has been survey research, Robertson et al. (2013) integrated survey data with qualitative interviews with female sex workers and their non-commercial male partners in Northern Mexico in an iterative investigation of potential interest in PrEP use and trial participation. This work revealed the tension in positive and negative aspects of microbicide gel use, including its potential to alter intimate relationships dynamics by creating suspicion of infidelity and contributing to conflict. Findings suggest that researchers should consider the subjective meanings that sex workers ascribe to their intimate relationships rather than framing PrEP trial participation solely around constructs of risk and disease³⁸.

Once women are enrolled in trials, mixed methods approaches can elucidate experiences of participation. Within one large microbicide trial in South Africa, Stadler and Saethre (2010) used in-depth interviews with female participants and their

partners, focus groups with community members, and participant observation in clinics to understand perceptions surrounding cash payments and reasons for collecting blood samples⁴⁰. Through data triangulation, this work revealed a complex picture of how conflicting understandings of the nature and intent of research differentially reflect power relations among participants, local communities, and foreign researchers⁴⁰.

Such work reminds us of the importance of the historical and social contexts in which Western clinical research has been viewed as exploitative in developing nations. Researchers should be particularly sensitive to such issues while recruiting vulnerable groups, including sex workers, whose exploitation has been well documented. Earlier controversies include the 2004 shutdown of a PrEP trial by sex workers in Cambodia over lack of community involvement in trial planning, drug safety concerns, and confusion over rights to treatment. Shortly afterwards, a trial targeting at-risk women in Cameroon was also closed due to concerns over treatment for women who seroconverted (they were to be referred to an already overburdened clinic) and rumours that the investigators wanted to inject HIV into subjects (see⁴¹ for an excellent discussion of PrEP trial ethics, including these cases). Rather than viewing such activism around ethical issues as impeding scientific progress²⁵, these cases serve as stark reminders to include the ongoing perspectives and concerns of communities in PrEP research. Long-term ethnographic engagement is needed from the outset of clinical research, including efforts to build trust and transparency, share study results with affected communities, and promote participatory efforts in translating PrEP into an effective and available intervention in diverse communities. We advocate for genuine participation of communities using a human rights-focused approach anchored in a “Nothing About Us Without Us” framework^{42,43}.

Adherence to Biomedical Interventions

As described above, the efficacy of PrEP is strongly linked to product adherence^{35,44}. Although participants in several studies have self-reported high levels of adherence, researchers using mixed methods to assess adherence have found these

reports to be problematic. Pool and colleagues (2010) triangulated data from coital diaries, in-depth interviews, focus group discussions, collection of used gel applicators, and ethnography to conclude that the primary study outcome (structured, self-reported case records) was the least reliable method in assessing sexual activity, condom use, and gel adherence. Although not deliberate deception on the part of participants, recall bias, interviewee and interviewer errors, and differential interpretations of measures highlighted inconsistencies that qualitative and ethnographic methods uncovered³¹.

While adherence assessment presents challenges moving forward, researchers are developing new strategies to promote PrEP adherence^{26,45,46}. In the CAPRISA microbicide trial, adherence promotion was designed to assist women with a coital dosing schedule (inserting the gel 12 hours before and after sexual activity). This adherence plan evolved during the course of the study from educational and assessment strategies to a motivationally-based counselling plan and a separation of clinical staff from those who collected and documented evidence of product use to reduce social desirability in adherence reporting⁴⁷. In a recent review of PrEP adherence strategies, all studies employed approaches based on motivational interviewing and individualized assessment plans to mitigate personal barriers⁴⁵, which while important, minimally addresses broader social and structural factors.

The complex issues that shape adherence extend beyond individual motivation to include relationship factors, disclosure of PrEP use (concerns around being perceived as HIV-positive), research fatigue, and structural issues such as stigma, homelessness, substance abuse, migration, and other life challenges. Additionally, as a backdrop to these important factors, the extreme poverty and material insecurity that typically drives sex work in sub-Saharan Africa may render HIV prevention and PrEP adherence a lower priority than meeting basic needs (e.g., food, shelter) for many women. As such, individual adherence counselling may inadvertently place the onus of responsibility on individuals to overcome barriers outside of their immediate control. Social scientists are well-positioned to explore the often

contraindicated experiences, perceptions, and desires of participants who are uncritically expected to acquiesce into the role of a “compliant” research subject.

Fortunately, some trials have incorporated ethnographic and qualitative methods into their study designs to better understand participants’ experiences. A qualitative sub-study nested within the VOICE trial²⁶ examined adherence issues through focus groups and repeated ethnographic interviews with women. The researchers documented women’s complex and often contradictory experiences of trial participation, including concerns about managing their health and relationships and the differential ways they perceived and valued the research compared with investigators and study staff. In particular, repeated interviews enabled women to open up and reveal information they did not initially disclose to other VOICE interviewers or clinical staff²⁶, attesting to the importance of ethnographic engagement in building trust and rapport to elicit higher quality data.

Similarly, focus groups on experiences with PrEP among men who have sex with men and female sex workers in Kenya found that while the acceptability of oral PrEP was high, concerns around the social costs of PrEP (e.g., stigma, gossip, rumours) were pervasive. In addition to work responsibilities, mobility, and alcohol use, sex work presented additional challenges including a fear of losing clients that led some women to use PrEP secretly or lie about it to avoid being viewed as HIV+⁴⁶. Taken together, these studies highlight the multiple challenges of PrEP adherence, leading social scientists to advocate for broadening the scope of adherence promotion in future trials⁴⁸.

Social Relationships

Biomedicine must also attend to the social contexts surrounding PrEP, including the role of intimate relationships in acceptability and use. Concerns have been raised over how women’s intimate partners react to PrEP trial participation and use, how PrEP might impact relationships, and the very idea that these methods are woman-controlled when male partner approval is often necessary or desired⁴⁹⁻⁵¹. Analysis of HPTN-035

results found that women with new partners used the microbicide gel less consistently and had a higher HIV incidence than women who did not report changing partners⁵². These issues may be further complicated for female sex workers who engage in sexual relationships with intimate partners and clients, as emotional meanings and ability to negotiate safer sex vary by partner type⁷.

Partner disclosure and risk communication are key features of PrEP acceptability and adherence. In CAPRISA, exit surveys indicated that 67% of women disclosed gel use to their most recent sexual partner, which had a small but statistically significant association with adherence but not efficacy. While most women found the conversation to be “easy,” 30% characterized it as “difficult,” and nearly a third did not disclose their PrEP use at all⁵³. While survey data have revealed important information about the occurrence of disclosure, survey measures cannot always capture the social contexts surrounding disclosure decisions.

Qualitative studies have discussed a range of male partner perspectives on PrEP, which in turn shape women’s perceptions and willingness to participate in trials, disclose PrEP use, and adhere to dosing recommendations²⁶. Women’s narratives reveal a tension between the social risks that PrEP use poses (e.g., relationship strain, creating suspicion of infidelity) with the biomedical HIV prevention potential of PrEP. Qualitative studies have identified multiple consequences of PrEP use, highlighting a need to consider how relationship dynamics and power differentials could challenge women’s ability to adopt PrEP as a viable HIV prevention method^{32,38,54}.

Also concerning, social science approaches have identified intimate partner violence as a “hidden harm” of PrEP⁵⁵. Serial in-depth interviews with 150 women enrolled in the VOICE trial in South Africa found that more than half experienced partner violence linked to their participation in the trial. Within the context of everyday violence characterized by male authority over relationships, some women concealed their involvement in the trial and avoided disclosure to protect themselves. Furthermore, the promotion of condoms in the trial protocol, which was conceptualized as an “ethical” prevention measure

because not everyone would be randomized to receive the active ingredient, yielded the unintended consequence of introducing partner suspicion and mistrust. This example raises important questions about the sensitivity of researchers and study staff to the social harms that unfold outside of controlled study settings⁵⁵. Given the high level of violence that many female sex workers face from intimate partners and clients⁵⁶⁻⁵⁸, attention to the social harms linked to trial protocols should be an urgent consideration for ethics committees and priority for future research and practice.

Structural Considerations

Clearly, individuals’ motivations, decisions, and behaviours regarding PrEP use are important in clinical research. However, individual-level factors are shaped by broader contextual characteristics. Understanding higher level structures becomes critical when working with vulnerable groups like sex workers who could benefit greatly but are rarely involved in the design or implementation of prevention policies or programmes.

Social science research has highlighted how structural factors such as economic inequalities, legislation criminalizing sex work, insufficient education and training, social discrimination, gender-based violence, and other inequalities disproportionately render female sex workers vulnerable to HIV^{2,11,59}. In turn, these structural vulnerabilities are embodied by women as mental health issues, substance abuse, violent traumas, and multiple other health harms. For example, studies of alcohol use among sex workers have linked harmful drinking with multiple adverse health indicators, including other drug use, mental health issues, inconsistent condom use, sexual violence, and sexually transmitted infections (STIs)^{60,61}. Moreover, injection drug use is increasingly promoting HIV transmission in sub-Saharan Africa. In Kenya and Tanzania, researchers have documented injection drug use, sex work, and HIV risk behaviours such as syringe sharing and ‘flashblood’ (e.g., intentionally injecting blood from another drug user) among highly vulnerable women^{62,63}. Taken together, this work suggests the potential challenges of adherence to PrEP among sex workers,

underscoring the importance of developing protocols that address macro and micro-level expressions of vulnerability²⁸.

Particularly as PrEP research efforts transition from clinical efficacy to community effectiveness, social scientists can help navigate the complex factors involved in scale-up. In addition to protecting sex workers' human rights and access to health services^{8,10}, community-based HIV prevention programmes offering PrEP for vulnerable women should work with other social service agencies. Promising work has suggested the importance of women's economic empowerment (e.g., through microfinance), while community mobilization efforts among sex workers have increased access to services^{64,65}.

Rather than portioning funds into silos, governments and donor agencies should support combination interventions that conceptualize sex workers' health through a holistic perspective. Such programmes should combine biomedical, behavioural, and structural approaches that are sensitive to local HIV risk environments and involve communities of sex workers themselves. Recent modelling has suggested that adding oral PrEP to other HIV prevention activities in South Africa could reduce HIV incidence among female sex workers and their clients by 40% over 10 years⁶⁶. Such approaches could also combine family planning with PrEP interventions to expand the reach of services for sex workers. Vaginal ring innovations, which have potentially dual microbicide-contraceptive capability, represent one way to bridge the gap⁶⁷. Importantly, identifying the appropriate delivery and mix of health services for sex workers, who comprise a heterogeneous group across diverse socio-cultural contexts throughout Africa, requires additional social science research and long term ethnographic engagement.

Conclusion: Reintegrating Social Science into Biomedical HIV Prevention

The remarkable promise of biomedical interventions such as PrEP has ushered in a new era of HIV prevention. In particular, vulnerable groups like female sex workers who bear a disproportionate burden of HIV infection could

benefit from such technologies. Clinical trials are the gold standard for assessing the safety and efficacy of new biomedical prevention approaches before implementing them in the real world, where community effectiveness remains to be seen. However, the success of several recent trials should not obscure the contributions that social scientists continue to make toward the development of biomedical, behavioural, structural, and combination prevention approaches²⁵. With the exciting advent of PrEP, the recent "re-medicalization" of the HIV epidemic serves as a reminder that Western biomedicine is itself a cultural system that deserves scrutiny from other disciplinary perspectives as well as from those who are under its purview as research subjects and potential beneficiaries. We draw our discussion to a close by suggesting several key contributions social science can make to biomedical HIV prevention efforts including PrEP use among female sex workers.

The social sciences embrace a non-linear methodological approach to studying humans, recognizing that all data collection involves social interaction and arguing that even "objective" data from clinical studies are artefacts of the cultural lenses through which studies are designed. We are not arguing that it is impossible to generate clinical evidence to inform HIV interventions, but rather that many clinical outcomes (e.g., adherence, incidence) can be better understood by also considering the socio-cultural and political environments in which these data are generated²⁸. Instead of being employed by clinical researchers to foster participant compliance or identify "cultural" factors to be modified to reach trial goals, social scientists can offer improved understandings of how individuals *experience* prevention efforts in the context of their everyday lives and communities. This becomes particularly important when working with vulnerable populations, including sex workers, whose often-neglected voices need to be better incorporated into prevention efforts⁴³. Long-term ethnographic engagement and the involvement of affected communities are critical and should permeate all phases of clinical research, including access to technologies and research results even after studies

conclude.

We applaud the mixed methods studies of PrEP that have more richly contributed to our understanding of prevention efforts^{26,31,32}. However, we caution that careful selection of particular methods should be appropriate to the research questions at hand. For example, focus groups, which are often favoured by clinical researchers for their speed and “efficiency,” are best reserved for understanding group differences and dynamics and are often inappropriate and insufficient for exploring more complex, sensitive sexual health topics that are better explored through repeated individual interactions. Moreover, conducting and presenting qualitative results simply to reflect or “explain” quantitative results may miss the human element that qualitative inquiry is designed to capture. Social scientists are trained to critically evaluate evidence from a holistic perspective and convey a humanizing understanding of the resiliency and challenges that characterize marginalized populations’ experiences, including sex workers in diverse African contexts.

Likewise, ethnographic approaches can help ground PrEP promotion efforts within local contexts by enhancing cross-cultural understanding (including clinical research as a cultural system) and providing fine-grained interpretations of unexpected, incongruent, or complex outcomes. Ultimately, the women who participate in trials are much more than “compliant” or “non-compliant” research subjects: they are mothers, wives, partners, family and community members who may engage in sex work in the face of material insecurity and extraordinary life circumstances. Working directly with these women to understand local prevention needs and effectively communicate these needs to diverse audiences will be critical in scaling up PrEP effectiveness in “real world” settings.

Finally, social science perspectives must continue to draw attention to the broader HIV risk environment in which clinical trials operate and PrEP interventions are enacted and experienced. The financial cost of rolling out PrEP in diverse communities is an important consideration in this work that will require the political will and commitment of governments and donor agencies.

In addition to the economic factors that drive sex work, researchers and policy makers should urgently work toward the decriminalization of sex work and attend to the social marginalization, gender-based power imbalances, substance use, and myriad other health and social harms with which sex workers contend^{10,68}. Ultimately, implementing successful biomedical interventions and creating meaningful change to reduce the burden of HIV in sub-Saharan Africa will require not only clinical and social science perspectives, but those of sex workers themselves.

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Contribution of Authors

JLS conceived of the paper and wrote the initial draft of the manuscript; AMRB, AS, SA, SAS, WMW assisted with writing the manuscript and provided feedback on successive drafts. All authors approved the final version.

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