**How can we support the use of oral PrEP among young women who sell sex? A PrEP cascade analysis**

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**Introduction**

Adolescent girls and young women aged 15-24 account for ~26% of new HIV infections in eastern and southern Africa.1 Among this population, young women who sell sex (YWSS) are at particularly high risk of HIV, reporting higher numbers of partners and less condom use than their peers not involved in sex work, and having poorer access to health services than older female sex workers (FSW).2–4 Reducing HIV incidence among YWSS requires combination prevention that is responsive to their needs and addresses barriers to their service use.5

Oral pre-exposure prophylaxis (PrEP) is efficacious when taken as prescribed.6,7 As YWSS often struggle to negotiate condom use, PrEP offers women more choice and control over their sexual health.8 For PrEP to be effective at population-levels, individuals must have high demand, PrEP services need to be available, accessible and acceptable, and those who initiate PrEP must adhere during periods of use. To maximise the potential impact of PrEP, cascades and continuums have been used to identify gaps in delivery and use,9 and target programmes to support initiation, and optimise adherence and continued use.10

In Zimbabwe, YWSS were among the target population for the DREAMS initiative, which sought to reduce HIV incidence by 40% among adolescent girls and young women in 10 African countries.11,12 In districts where DREAMS funding was available, PrEP availability was a key service for YWSS combined with efforts to increase demand and support use. We previously showed that, while it is plausible that DREAMS may have contributed to reduced HIV risk among YWSS, it did not achieve 40% reduction in HIV incidence.13 We also showed that new HIV infections did not differ by ever-reporting PrEP use in 2019. To inform efforts to support PrEP use among YWSS, we constructed a PrEP cascade to investigate and understand reasons for gaps in PrEP use, and explored whether factors likely to influence demand for and opportunities to access PrEP were associated with uptake.

**Methods**

**Study location & population**

Data were collected from YWSS aged 18-24 residing in two Zimbabwean cities selected for the DREAMS Partnership interventions. In each city, the national FSW HIV prevention programme, ‘*Sisters with a Voice’* (Sisters), offered HIV testing, condom promotion and distribution, community mobilisation and referral to legal advice through static clinics. At Sisters, YWSS were offered referrals to other DREAMS partners offering additional HIV prevention services, including oral PrEP and social protection.14

**Data collection**

Respondent driven sampling (RDS) was used to recruit YWSS to the DREAMS impact evaluation.15 Described elsewhere, the evaluation estimated the impact of DREAMS on HIV incidence among women recruited through RDS and followed-up 24-months post-enrolment. Prior to RDS, YWSS identified through mapping and representative of the typology of sex work in each city were invited to act as “seeds”.15,16 To initiate RDS, these “seed” participants were given two vouchers to recruit YWSS, whom they knew and knew sold sex. Eligible participants were given two vouchers to recruit a further two women. This process continued over six recruitment waves.15 YWSS aged 18-24 who sold sex were eligible, defined as sex in exchange for material goods/money where the sex wouldn’t happen in the absence of the exchange.

**Behavioural survey**

Consenting women completed an interviewer-administered questionnaire and offered HIV-testing services.15 All women received the result of their HIV test. Women were followed up 12- and 24-months post-enrolment (2018 and 2019, respectively), asked to complete the same questionnaire and offered HIV-testing as at enrolment. The questionnaire elicited women’s demographics, history of selling sex, sexual behaviours, access to HIV prevention services and engagement with the broader package of services available through DREAMS.

**Qualitative interviews**

Between September 2017-November 2019, 43 DREAMS participants from among the women recruited through RDS were purposively selected for interview. Women were selected for diversity in age and levels of participation across the range of DREAMS services. Interviews were conducted 12- and 24-months post-enrolment, and explored motivations for engaging with DREAMS services and any challenges encountered during participation in DREAMS. A shorter version of the interview topic guide was piloted prior to RDS. We interviewed 19 YWSS selected as “seeds” for the RDS and explored feasibility of asking about their sexual relationships, involvement in selling sex, engagement with care, barriers to accessing HIV prevention and treatment, and interest in activities to be offered under DREAMS. Interview guides were subsequently expanded to elicit perceptions and experiences and explore if and how involvement in DREAMS affected their health, behaviour and well-being. Sixteen respondents were interviewed >1-time to understand changing experiences and perceptions. Two female social scientists conducted interviews, which lasted 30-60 minutes and were audio-recorded, in Shona or Ndebele.

**Outcomes and explanatory variables**

The cascade used in this analysis was informed by the framework proposed by Schaefer et al,10 which conceptualises that demand for, access to and use of/adherence to an HIV prevention product is influenced by individual- and structural-level factors. Self-reported outcomes of interest for the PrEP cascade included ever: having heard of, being offered, and using PrEP, and current PrEP use. For women followed-up in 2018 and/or 2019, women were defined as having heard of, ever being offered or ever using PrEP by 2019 if they reported these outcomes at any point during the study. A further outcome of interest was HIV seroconversion.

To understand gaps across the PrEP cascade, we described domains (measured in 2019) thought to influence each step. For having heard of PrEP, measures included: knowledge of other prevention measures (sex with one HIV negative partner, consistent condom use and medical male circumcision). For this step, we also explored perceptions of other YWSS’ willingness to take PrEP and whether PrEP was thought to make it easy for YWSS to protect themselves from HIV. Measures for potential reasons for gaps in ever being offered PrEP included: attending a Sisters clinic and testing for HIV in the past 6-months. Measures explored as underlying gaps in ever and current use of PrEP included: perceived support for PrEP use from friends/peers, family and sexual partners, condomless sex with regular partners and clients in the past month, and self-perceived risk of HIV in the next 12-months.

Explanatory variables explored for association with PrEP use included those likely to influence decisions and opportunities to initiate PrEP.17,18 These variables, measured at enrolment, included: age, marital status, educational attainment, being at risk of common mental health disorders (CMD) measured using the Shona Symptom Questionnaire,19 whether women self-identified as FSW, age at which women started and duration of selling sex, client numbers in the past month, self-perceived HIV risk in the next 12-months, knowledge of other HIV prevention measures, perceived support for PrEP use and attendance at a Sisters clinic in the 12-months prior to enrolment. Additionally, we explored whether ever being offered PrEP by 2019 and women’s identification as a FSW between 2017-2019 were associated with PrEP use.

**Data analysis**

We restricted analyses to women testing HIV negative at enrolment. First, we described enrolment characteristics and behaviours of all women and of those retained in the 2019 follow-up survey. Among these, we described the number and proportion of new HIV infections by PrEP use, and explored whether steps in the cascade were associated with sero-conversion.

Second, using data from all three surveys, we constructed PrEP cascades for 2017 and 2019. Using the framework proposed by Schaefer et al10, we estimated levels of: having heard of, ever offered, ever and current use of PrEP at enrolment (2017) and by 2019. For each step, we described potential reasons for gaps, as described, and, adjusting for age and site, explored whether these factors differed within each step. To further understand gaps in the cascade, we conducted thematic content analysis of qualitative interviews with the specific aim of interrogating each stage of the prevention cascade as perceived and experienced by women participating in DREAMS. This involved re-coding transcripts into broad codes relevant to each step of the cascade . Data were transcribed and translated into English and imported into NVIVO-12. Thematic analysis was achieved by re-reading transcripts to identify emerging themes and reconciliation of codes after iterative discussions. We present data on women's understanding of PrEP, where they accessed services, and narratives around choosing to initiate PrEP and subsequent (dis)continuation.

In our third step, we used logistic regression to explore the association between the explanatory variables described and PrEP use by 2019. Our crude models adjusted for age at enrolment and included a fixed effect for site. All variables were explored in adjusted analyses, in which we adjusted for variables associated with PrEP use at p<0.10-level in crude analyses. Adjustment followed the distal-proximal framework used in an analysis of enrolment data,2 as such, we did not adjust for variables considered proximal to the outcome relative to the variable of interest. As our analysis used data at follow-up and half the women were not retained, we did not RDS-weight the data. This aligns with our analysis of the primary outcome.13

**Ethics**

The Medical Research Council Zimbabwe (MRCZ/A/2085) and London School of Hygiene & Tropical Medicine (11835) approved the study. Written informed consent was obtained from all women prior to participation.

**Results**

**Enrolment characteristics and retention**

Among 963 HIV negative women enrolled into the study, 20.5% (n=197) were aged 18, >50% considered themselves FSW (66.5%, n=633) and reported ≥3 clients in the past month (57.2%, n=551). The majority considered their risk of HIV in the next 12-months to be low/small (62.8%, n=501). Half had knowledge of other HIV prevention measures (48.3%; n=465). Over half the women were retained in the study in 2018 (54.4%; n=524) and 2019 (55.9%; n=538). Retention in 2019 was higher among women who, at enrolment, reported selling sex for ≥4 years and started selling sex aged 10-14 years (Table 1).

By 2019, 5.8% (n=31) of women seroconverted, among whom 38.7% (n=12) reported ever using PrEP between 2017-2019. Adjusting for age and site, there was little evidence for an association between steps in the cascade and HIV sero-conversion (Suppl Table 1).

**Cascade Step 1: Ever heard of PrEP**

Over time, all domains of the cascade increased (Figure). By 2019, most women had heard of PrEP (95.7%; n=514) compared to half (50.3%; n=481) in 2017. Never having heard of PrEP was higher among women who disagreed (22.7%; n=5/22) that PrEP would make it easier for women to protect themselves from HIV than among women agreeing with the statement (5.1% n=16/316) of (Table 2). In qualitative interviews (Table 3), women described how they heard of and informed their friends about PrEP:

*I know about it, when you go to Sisters [Clinic] they always talk about it [PrEP] and it feels like a song (chuckles). I was supposed to go collect it [PrEP] on Wednesday but I did not go…. I did not have bus fare(22-years)* *BYOLN03R3*

**Cascade Step 2: Ever offered PrEP**

In 2017, few women had been offered PrEP (11.7%, n=112); by 2019, 54.9% (n=294) reported ever being offered PrEP. *Never* being actively offered PrEP was lower among women who had been to a Sisters clinic (40.1% vs never: 64.0%) and had tested for HIV in the last six months (41.8% vs not-tested 56.5%) (Table 2). The cost and opportunity cost of accessing PrEP, including missing school, limited women’s ability to go to clinics where PrEP was available:

*I was referred for PrEP in town but time does not permit...I do [want to take PrEP] but time won’t allow me…Please bring some for me if you can. Because I really want it. (22-years) BYOCS25R1*

Some women had been to the clinic, but then were asked to come back the following day:

*The first time I wanted to go and get PrEP I did not have the time to go there because of school. When I had the time and wanted PrEP I was told to come the following day and never went back again. (23-years) MTRCS30R2*

**Cascade Step 3: Ever taken PrEP**

In 2017, 6.9% (n=66) of women reported ever taking PrEP, increasing to 33.6% (n=181) by 2019. There was little difference in PrEP use by perceived support for PrEP use and condomless sex in the last month (Table 2). PrEP use was strongly associated with ever being offered PrEP (60.5% vs 1.2%). In risk factor analyses (Table 4), ever using PrEP by 2019 was higher among women who, at enrolment, reported 10+ clients in the past month (44.5% vs 26.5% for 1-3 clients; adjOR=1.71 95%CI 1.06, 2.76) and had been to a Sisters clinic in the past 12-months (54.5% vs 26.7%, adjOR=2.92 95%CI 1.91, 4.46), with weaker evidence that use was higher among women who were ever/currently married (42.9% vs 29.1%, adjOR=1.51 95%CI 0.98, 2.32).

PrEP use was lower among women who, at enrolment, reported selling sex for <2-years (24.3% vs 2-3-years: 37.7%, adjOR=0.51 95%CI 0.32, 0.83), and who disagreed that friend/peers would support their PrEP use (24.2% vs 36.9%; adjOR=0.54 95%CI 0.31, 0.95). Half the women identified as FSW throughout the study (48.1%, n=255). There was borderline evidence that PrEP use was associated with self-identification: use was lowest among women who never identified as FSW (26.7%, n=28/105) and who identified as FSW at enrolment but not follow-up (25.0%, n=27/109) . In qualitative interviews, women revealed a willingness to take PrEP but concerns that it would disclose their sex work.

*Ok I did not want it because if I get it [PrEP] and take it home, my family would like to know why I have PrEP and what it is for, exposing my business [sex work] (22-years) BYOLN06R1*

Initiating PrEP was hindered by broader structural factors such as stigma, lack of support for PrEP use, alongside financial and opportunity costs of travelling to the clinic, and related to how PrEP was offered and needs to be taken:

*…I wanted to take PrEP but the processes are too tedious and long for me, I fear that I may also forget to take the tablets [PrEP]. Another thing that got me worried is that when I told him [boyfriend] that PrEP protects me from HIV he asked me where the HIV would be coming from and he asked why I wanted to take it alone and exclude him. So I got scared. (20-years) BYOCS33R2*

**Cascade Step 4: Currently taking PrEP**

In 2019, current PrEP use remained low at 11.5% (n=62). Among women not currently using PrEP, a higher percentage (strongly) disagreed that they would receive support for PrEP use from family (Table 2). Reasons for discontinuing PrEP use were varied (Table 3), and included side effects and, as with PrEP use, reflected broader structural factors:

*When my brother found the pills [PrEP] he got very cross, he yelled and beat me up. He asked me why I had not disclosed my [HIV] status to him. This was because he was not educated on PrEP [assumed she was HIV positive]. My grandmother, however, knew that I was taking PrEP ... She was fine with it. The way my brother was shouting attracted everyone’s attention and the neighbors heard all his insults about him saying I am sick. That made me suicidal and I also decided to stop taking it. (24-years) BYOLN02R2*

Discontinuation of PrEP was also driven by perceived low HIV risk behaviours and recognising the need to adhere to taking PrEP daily, leading some women to prefer condoms:

*I thought it is better to use condoms instead of the pills because I feared that I could not adhere to them. (18-years) BYOCS26R1*

One woman described many reasons for discontinuing PrEP, and later tested HIV positive:

*When I tested HIV negative, they told me about the PrEP ... So I got my PrEP for three months and then I stopped. I stopped taking the pills for many reasons. First, it was cumbersome and burdensome to take the pills every day and when I wasn’t ill. Secondly, I felt more hungry than before, and lastly my brother was suspecting that I was on ART for HIV … so I was increasingly embarrassed about taking them [PrEP] ... after stopping I tested HIV positive .... (19-years) MTRCS20R1*

**Discussion**

Following introduction of PrEP in the two DREAMS sites, just over half the women in our study reported ever being offered PrEP by 2019 and one-third ever used PrEP. Use was higher among women reporting an active offer of PrEP, and was associated with factors likely to influence HIV risk, including being married/cohabiting, numbers of years selling sex and reporting higher numbers of clients. Our mixed method analysis revealed that lack of support for use, costs and opportunity cost to travel to the clinic, side effects and daily pill taking as reasons for observed gaps in the PrEP cascade.

Our study is subject to limitations. Data on an offer of PrEP, use and current PrEP use were self-reported and therefore subject to error.20 Almost half the women recruited were lost to follow-up. Our outcomes are subject to bias if PrEP knowledge and use differ by follow-up. Our risk factor analysis may be subject to bias if PrEP use is differentially misreported by the variables explored. However, as our explanatory variables were measured at enrolment and most women had not yet used PrEP, we consider the risk of bias low. Despite limitations, we recruited and followed-up over 500 YWSS, who are underrepresented in research on FSW. Furthermore, we used data from two time points, with our explanatory variables measured prior to most PrEP use.

Reported non-PrEP use was strongly associated with not having been offered it. In Kenya, Were et al21 found that, in the first two years of PrEP roll-out (2017-2019), low provider screening for PrEP eligibility was among the most common missed opportunities for delivering PrEP to adolescent girls and young women. In South Africa, a study among FSW and men who have sex with men found that 57% of individuals who had never used PrEP had never been proactively offered it.18 Fear of side effects was the primary reason for declining use.18 Similar to findings from our qualitative analysis, Emmanuel et al(2020)22 found that costs and frequency of HIV testing were barriers to PrEP uptake among FSW in Nigeria. Using qualitative data collected during the SEARCH trial in Kenya and Uganda, Camlin et al(2020) found daily pill taking was considered a bigger burden than HIV risk.23 Integrating PrEP into family planning, sexual and reproductive health and targeted services is critical to increase opportunities to offer PrEP.24 With growing evidence of injectable PrEP efficacy,25 longer-acting PrEP may remove some supply-side barriers and those related to confusion between PrEP/ART.

In our study, a higher percentage of women offered PrEP initiated it than in the SEARCH trial, where 27% of high risk individuals initiated PrEP.17 Our risk factor analysis found no evidence that self-perceived HIV risk at enrolment was associated with PrEP use. However, PrEP use was highest among women who identified as FSW throughout the study, and associated with reporting more clients and selling sex for longer. Similarly, our qualitative findings underscore that women’s decision-making around PrEP includes consideration of risk based on sexual behaviours, including condom use and their perception of different sexual partners, with higher use among married/cohabiting women. These findings are similar to those from a qualitative study among sero-discordant couples in Zimbabwe, which found that risk perception was linked to willingness to take PrEP.26 These findings suggest that women in longer-term, stable relationships – who may find condom negotiation harder or condom use less pleasurable– are seeking alternative prevention measures. Rather than focus on reduced HIV risk and medicalise PrEP, efforts to increase demand should focus on messaging around personal protection, reduced sex-related anxiety and increased sexual pleasure with regular partners.27,28

Sero-conversion after 24-months was similar by whether or not women reported ever using PrEP in and by 2019.13 Although we did not collect adherence data and our measures of ever and current PrEP use were self-reported, some women likely sero-converted due inadequate adherence and/or PrEP discontinuation. A systematic review of 41 studies, representing 22,034 individuals, found high PrEP discontinuation at 1-month.29 Among the women in our study, low continued use of PrEP was likely driven by a combination of supply-side reasons and structural factors, including stigma related to HIV and sex work, association of medication with ART, and lack of social support.

Similar to our findings, qualitative data in the SEARCH trial identified that, in addition to pill burden, PrEP use was discontinued because of HIV/ART-related stigma, relationship dissolution and lack of support for use.23 A Zimbabwean study among FSW living with HIV found that women experienced more stigma related to their sex work than HIV stigma;30 a systematic review of 15 studies from sub-Saharan Africa identified stigma related to sex work and HIV as a barrier to HIV testing.31 Addressing stigma associated with sex work, as well as HIV, may support women’s PrEP use and adherence. Family support emerged during qualitative interviews, and quantitative findings suggest lower PrEP use among women with less support from friends/peers, with similar levels of PrEP use by perceived family support. These findings align with evidence from a scoping review of ART uptake and adherence among FSW, which found that social support facilitated uptake and adherence.32 Again, as PrEP becomes available in alternate and longer-term formulations, these barriers may subside. However, strategies to address HIV/ART-related stigma and increase support for PrEP use remain critical.

**Conclusion**

To date, there is little data on PrEP use over time among YWSS, including young FSW aged <25. As PrEP is scaled-up across southern and eastern Africa, understanding barriers to use among this group of women is critical to support uptake and adherence.3,23 Our study shows that barriers to PrEP initiation and continuation are similar to those among other populations and in other countries. To increase effectiveness among YWSS, proactive offers of PrEP are needed combined with building social support among peers, partners and communities as knowledge and understanding of PrEP increases. Messaging to encourage PrEP use should position PrEP in a way that matches women’s perceptions regarding what places them at risk of HIV.

**Conflicts of Interest:** The authors have no conflicts of interest to declare.

**Authorship:** BH drafted the paper and led the quantitative data analysis. FM and JB led the qualitative analysis. IB, JH, FMC and SF led study design for the DREAMS evaluation. SC and JH contributed to quantitative data analysis and commented on drafts. JH conceived an outline of the discussion. GJ, TC and PM led qualitative data collection. FC was the PI for the DREAMS evaluation in Zimbabwe and helped revise the paper. All authors have read and approved the manuscript.

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