In June 2016, South Africa became the first country in Africa to introduce oral pre-exposure prophylaxis (PrEP), a daily antiretroviral pill taken to help prevent HIV, in June 2016. The National Department of Health (NDoH) is using a phased approach for rollout of oral PrEP, which began at facilities providing services to sex workers and was expanded in 2017 to facilities providing services to men who have sex with men (MSM). The phased approach to rollout allows for a dynamic learn-and-adapt process to implementation leading to scale-up.

Operations research is key to this process, generating rapid evidence about oral PrEP uptake and use. To support the NDoH’s rollout of oral PrEP, the OPTIONS Consortium, the HIV Prevention Market Manager (PMM) project, and the NDoH collaborated to carry out operations research under the ACCESS study (Advancing PrEP: Comprehensive and Combined Evaluation of Services for Sex workers and MSM). This research examined factors influencing uptake and continuation, as well as client and provider experiences with oral PrEP services. The findings have informed further strengthening and rollout of PrEP services in South Africa and could provide insights for other countries as they expand access to oral PrEP.

The ACCESS Study

The ACCESS study was conducted at nine facilities in South Africa from May to December 2017. The goal of this cross-sectional operations research study was to identify barriers and enablers to oral PrEP uptake, continuation, and discontinuation in South Africa. The objectives are as follows:

1. Examine factors affecting client’s decision to initiation, continue and/or stop PrEP.
2. Assess service provider knowledge, attitudes and practised behaviours around oral PrEP delivery.
3. Examine the effectiveness of oral PrEP information, education and communication (IEC) materials.

Site Selection: Of the 16 facilities that were providing oral PrEP when the ACCESS study began, nine (six sex worker (SW)- and three MSM-focused) sites were selected. These sites had been implementing PrEP for at least three months and represented a range of delivery sites.

![Figure 1. ACCESS study sample selection for survey and IDIs](image-url)
participants said having multiple partners was their reason for starting oral PrEP, suggesting that perceived risk associated with sexual activity drove uptake. IDIs reinforced this finding as participants reinforced that risk of HIV infection influenced their decision to use PrEP. Additionally in IDIs participants described their behaviours and relationships putting them at risk for HIV, including not knowing partner's HIV status or not trusting them, having multiple partners, doing sex work or having a partner living with HIV.

When asked for more detail about reasons for initiating oral PrEP during IDIs, respondents most often said that they had received information about oral PrEP or encouragement to try it from health care providers, family members, peers, or partners. Several stated that their providers gave them the information they needed to initiate PrEP, and some providers described giving additional counselling or outreach to help them overcome challenges with taking PrEP when they first started.

Many also described initiating oral PrEP because they wanted additional protection against HIV beyond their current HIV prevention practices, and because they experienced issues using condoms alone, such as partner resistance to condom use and condom breaking was another reason. “The other sister of mine, she explaining me, you see this job is risking. The condom gonna burst and some people they're gonna force you...So, it's better to take PrEP” [...] I start to drink until now, I don't have any problem...and when I'm working, I don't have stresse, because I know that I'm preventing.” — FSW, current user, 23 yrs.

Sex and HIV Risk: Drivers to Continue Oral PrEP

Current users were asked why they continue using PrEP and were allowed to select more than one response. About half of clients at SW sites and 53% of clients at MSM sites said they continued to use oral PrEP because they were sexually active. Further, 35% of clients at SW sites said having clients they believe are HIV positive as a reason for continued use.

In IDIs, current oral PrEP users most often described a sense of motivation and determination to protect their health and remain HIV-negative as their main reason for continuing to use it. Participants talked about having motivation to “protect themselves”, “stay healthy”, “keep my status”, “cover the bases”. Some were motivated by fear or worry, knowing that discontinuing oral PrEP would “put my life at risk” or they “might be infected”. “It's all about willpower. And don't fail for peer pressure. It can make you stop without any good reason for yourself […] Remember I told you about my ex-fiancé? He was [HIV] positive…I'm still negative even today because of PrEP, and I have this fear that if I leave it, I might be infected. What helps me is that anything I do, I do wholeheartedly.” — FSW, current user, 30 yrs.

Participants described that relationships and behaviours that they felt put them at risk of HIV acquisition, also motivated them to start and continue using oral PrEP.

Missed Opportunities to Provide Oral PrEP

Of 125 clients who had never used oral PrEP, 31% (n=39) had never heard of oral PrEP and 69% (n=86) had heard of oral PrEP. Among the 86 clients who had heard of oral PrEP, not being offered oral PrEP was the main reason for lack of uptake, representing critical missed opportunities for HIV prevention. Among those who had never used oral PrEP, 39% of clients at SW sites and 77% of clients at MSM sites had never been offered it. Many (23 out of 44) clients who had never been offered oral PrEP perceived themselves to be at risk of HIV. Only 35% of clients who had never used oral PrEP had heard about it at the clinics. Among those who had been offered oral PrEP but declined to use it, concerns about side effects were the main reason for declining, cited by 13 of 29 clients at SW sites and two of five clients at MSM sites.

Sex and HIV Risk: Drivers of Oral PrEP Uptake

Being sexually active was the primary reason for initiating oral PrEP, cited by 35% of clients from SW sites and 53% of clients at MSM sites. Of those who responded to this question, about one-quarter of

In this scenario, the majority of past users that experienced side effects discontinued PrEP use within 1 to 5 months of use. Absence was the most common reason for discontinuation.


Among past users, side effects were the main reason for oral PrEP discontinuation. The primary side effects were nausea and vomiting for SW site participants and nausea and headaches for MSM site participants. Discontinuation due to side effects occurred primarily during the first three months of use. Feeling stigmatised was the second most common reason for discontinuation.

Side Effects Affect Daily Life of Past Users More than Current Users

More past users (95%) than current users (59%) had experienced side effects. Among those reporting side effects, 61% of current users considered the side effects tolerable, compared to 15% of past users. More past users than current users reported that side effects of oral PrEP affected daily life.

In IDIs, many current users reported experiencing side effects from oral PrEP, but most said these effects had resolved or had become manageable over time. Some described using specific strategies to

### Results of the Client Survey

#### Client Demographics

The mean age was 31.3 years for clients from SW sites, and 34.6 for clients at MSM sites, which is consistent with the age demographics seen in the national PrEP rollout. Participants were primarily South Africans who were never-married or currently single.

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### Figure 2: Reasons for lack of oral PrEP uptake among never users (n=125)

- **Offered PrEP but never declined**: 31%
- **Offered PrEP but never offered**: 39%
- **Never heard of PrEP**: 2%

### Figure 3: Time of PrEP use for clients who stopped due to side effects

- **SW Sites (n=23)**
- **MSM Sites (n=26)**

The majority of past users that experienced side effects discontinued PrEP use within 1 to 5 months of use.
manage side effects, such as changing the time of day when they took oral PrEP or taking it with a meal:

“When I started taking the pill at 11am I would be stressed, because sometimes I would get nauseous; sometimes you would find that my friends would say I am moody, emotional, and easily pissed off and I didn’t know what was going on ...
... maybe those are the side effects of the pill. So, I told myself, “Okay, (participant name) maybe the issue here is with the time you’re taking the pill – try and change the time and see the results’ [...] when I take the pill at 8pm, there is nothing much to worry about.”

— Current user, MSM, 27 yrs.

A few participants described seeking help by going to the clinic or calling a provider for assistance, but others said they did not need to do so because they had been counselled on side effects or had read the informational materials.

Management of Side Effects Not Well Covered in Counselling Sessions
Clients who had been offered oral PrEP by a provider were asked to recall topics covered during counselling sessions. Most clients remembered being counselled about side effects, but less than half recalled receiving counselling about how to manage side effects.

Combination Prevention among FSWs Using Oral PrEP
Participants who self-identified as female sex workers (n=156) were asked about condom use with main partners, casual partners, and clients. More than 80% of FSWs reported using a condom the last time they had sex with a client; reported use was similar among current, past, and never users of oral PrEP. However, the FSWs who had discontinued using oral PrEP were less likely to report condom use with either casual or main partners compared to current or never users. Overall, condom use at last sex was lower with main partners than it was with casual partners and clients.

Out of 20 FSW who had disclosed oral PrEP use to a main partner, 10 stated condom use remained the same and five stated that condoms were used more frequently. Conversely, four reported they had never used condoms, and one said that condoms were used less frequently.

Oral PrEP Messages Were Well Received and Viewed as Empowering
The ACCESS study also sought feedback from clients on the format and messaging of information, education, and communication (IEC) materials developed to support the rollout of oral PrEP for sex workers and MSM. The main IEC messages were: “We are the generation that will end HIV,” and “I have the right to live HIV free; I have the duty to stop the spread of HIV.”

Materials such as the posters, fact sheet, pocket book, palm card and brochure conveying these messages were posted in health facilities and given to healthcare providers to give to clients. These IEC materials contained standardised information about oral PrEP.

The majority of clients surveyed had seen both messages, and most liked the messages and found them empowering. Feedback from the IDI respondents was also positive. They liked the messages because they provided important and/or useful information. When asked specifically about the messages, respondents said the slogans made them feel happy/hopeful for the future:

“I was very happy, because fighting this virus made me happy. The slogan also made me very excited, because we need to be that generation that fights infection.”

— Current User, FSW

Figure 4: Side effects affect daily life of past users

<table>
<thead>
<tr>
<th></th>
<th>Current users</th>
<th>Past users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experienced side effects (%)</td>
<td>n=54</td>
<td>n=55</td>
</tr>
<tr>
<td>0%</td>
<td>59%</td>
<td>61%</td>
</tr>
<tr>
<td>10%</td>
<td>15%</td>
<td>31%</td>
</tr>
<tr>
<td>20%</td>
<td>83%</td>
<td>83%</td>
</tr>
</tbody>
</table>

Current users stated that they were determined to use PrEP despite side effects and used strategies like seeking help from the clinic or changing time of day they took the pill.

In the IDIs, some clients said the IEC materials gave them the detailed information they needed to make decisions about oral PrEP use:

“They explained to me when I started that you might have side effects and there are pamphlets there that explains side effects, so I wasn’t struggling that much.”

— Current User, FSW

Suggestions for Improvements in IEC Materials
Respondents offered suggestions for improving the IEC materials, saying that they could be less text-heavy and yet provide more specific information about oral PrEP, such as more detailed messages about side effects, stopping oral PrEP, and whether oral PrEP is a good option for serodiscordant couples when the HIV-positive partner is virally suppressed. They also suggested translating the materials into local languages, making them available on social media, adding a toll-free helpline number, and possibly including testimonies from current oral PrEP users to encourage potential oral PrEP users.

Results of the Provider Survey

Knowledge of Oral PrEP Among Healthcare Providers Is High
All 30 providers who participated in the survey had received the standard NDOH national training on oral PrEP. The majority of providers (n=26, 86%) answered 11 or more of the 13 knowledge questions correctly. The question most commonly answered incorrectly was a true/false question: “A person can stop taking PrEP when their HIV infected partner who is on ART is virally suppressed.” Only 10 providers chose the correct answer (True), suggesting this should be a topic covered in future training.

The majority of providers felt they had sufficient skills and experience to provide oral PrEP. However, some providers stated that they would benefit from additional training on monitoring and evaluation (n=11), resistance risk (n=10), and clinical monitoring and management (n=9).

Providers Expressed Concerns about Oral PrEP Increasing Risky Behaviour
Providers were also asked about their concerns about providing oral PrEP. Most
providers thought clients should try using other HIV prevention options before using oral PrEP (n=24). Providers expressed concerns about its use leading to risky behaviour (n=13) and less frequent HIV testing (n=13). Fewer providers believed oral PrEP would lead to resistance to ARVs (n=4).

**Providers’ Perceptions about Challenges Clients face to access oral PrEP**
During IDIs providers highlighted certain challenges with client access to PrEP services. A few providers stated that clients preferred mobile facilities rather than fixed facilities. "Uptake has been extremely poor and here, it has been extremely poor... Hmm... I mean, I think any time that you bring services to people you are going to get a higher uptake." [Medical Officer]

Some providers suggested that barriers to access for services amongst sex workers may be economically driven as they had to choose between going to the mobile service and working. "Somebody can stay there with an STI more than 2 weeks. Waiting for the clinic to come, the mobile to come to the sites. And say ‘no I was waiting for you’. So they prioritise, even when you go there with the mobile sometimes, if that somebody is having a client when the mobile is there, she rather go with the client and leave the treatment." [Nurse]

One provider mentioned how they adopted strategies to mitigate against service access barriers, and highlighted a case where the brothel manager did not allow clients to go to the drop in centre, so PrEP had to be delivered to the brothel. "At the moment the problem with PrEP is more with adherence, we are finding that the clients are not adhering to treatment. […] most of them said they are not allowed to come into the drop in centres. So, we would rather drop the medication off at the sites." [Nurse]

**PrEP Perceptions among Service Providers (n=30)**

<table>
<thead>
<tr>
<th>Use of PrEP will lead to resistance to ARVs</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of PrEP will result in less frequent HIV testing among clients</td>
<td>4</td>
<td>1</td>
<td>9</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Use of PrEP will ause people to engage in riskier behaviour</td>
<td>3</td>
<td>10</td>
<td>2</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Clients should try using other HIV prevention options before using PrEP</td>
<td>5</td>
<td>8</td>
<td>5</td>
<td>9</td>
<td>3</td>
</tr>
</tbody>
</table>

Some providers mentioned substance abuse (taking alcohol or drugs) as a challenge to uptake and adherence. A few said that clients were worried about taking a pill daily and some providers said clients had poor adherence. "Someone tells you that they are not regularly taking the pills as they feel that they will only take the pill when they are going to have sex with someone. They don’t understand that it doesn’t work instantly when you take it." [Peer Educator]

Figure 6: PrEP Perceptions among Service Providers (n=30)

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A few providers said that some clients didn’t want to try oral PrEP because they prefer condom use.

**Implications for Oral PrEP Programs**

The ACCESS study has generated evidence that can be used to improve program implementation, identify best practices and areas for improvement, and guide scale-up of oral PrEP. Key findings and their implications include:

- **Missed opportunities to offer PrEP:** A lack of uptake of oral PrEP among never users could be attributed to not being offered oral PrEP, representing missed opportunities to provide counselling and offer PrEP to clients who perceived themselves to be at risk. Providers may need support and additional training to help them take advantage of opportunities to discuss oral PrEP with all clients.

- **Influence of perceived risk on PrEP initiation and continuation:** The study findings suggest that knowing and understanding the risk associated with sexual activity is the first step to oral PrEP initiation and a motivator for continuation. Finding ways to help more people, especially young women and girls, have a better understanding of their risk is critical for future HIV prevention efforts.

- **The effective use of IEC materials:** IEC materials played an integral role in clients’ decision to start and continue using oral PrEP, and the creative concepts used were empowering to clients. Simple, concise formats such as posters and fact sheets were favoured by clients.

- **Side effects’ influence on initiation and discontinuation:** Concerns about side effects were a barrier to oral PrEP initiation. Moreover, side effects were the main reason clients stopped using oral PrEP. Although ART patients using similar drugs report very limited side effects, users in this sample who discontinued oral PrEP seemed to find side effects challenging. Clients who continued using oral PrEP appeared to tolerate side effects differently from those who stopped using it. These findings highlight the critical importance of training and supporting health providers, as well as users and potential users, on side effects and their management.

- **Use of combination HIV prevention for HIV:** Condom use was high with SW and their clients and casual partners amongst clients using PrEP, but was lower with main partners. Clients who had stopped using PrEP displayed lower levels of condom use with main and casual partners, suggesting that they may be an important group to target for adherence support or less user-dependent prevention methods.

- **Understanding provider perceptions:** Provider perceptions play a critical role in how services are delivered, because providers are the gatekeepers for any new health intervention. Although providers did display adequate knowledge about oral PrEP, there was some uncertainty about PrEP use for serodiscordant couples where the HIV positive partner is virally suppressed, which highlights the need for additional training. Additionally the notion held by the majority of providers that other HIV prevention options should be tried before using oral PrEP needs further unpacking.

**Concluding Remarks**

As part of the phased rollout of PrEP, the NDoH has also been providing PrEP to adolescent girls and young women through implementing partner sites and public health facilities since late 2017. Although the ACCESS study generated evidence about oral PrEP provision to FSW and MSM, the findings could also provide useful insights for implementation at these additional sites.